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Record 1

Contribution of fibrinolysis to the physical component summary of the SF-36 after acute submassive pulmonary embolism

Stewart L.K., Peitz G.W., Nordenholz K.E., Courtney D.M., Kabrhel C., Jones A.E., Rondina M.T., Diercks D.B., Klinger J.R., Kline J.A.

Journal of Thrombosis and Thrombolysis 2015 **40:2** (161-166)

Acute pulmonary embolism (PE) can diminish patient quality of life (QoL). The objective was to test whether treatment with tenecteplase has an independent effect on a measurement that reflects QoL in patients with submassive PE. This was a secondary analysis of an 8-center, prospective randomized controlled trial, utilizing multivariate regression to control for predefined predictors of worsened QoL including: age, active malignancy, history of PE or deep venous thrombosis (DVT), recurrent PE or DVT, chronic obstructive pulmonary disease and heart failure. QoL was measured with the physical component summary (PCS) of the SF-36. Analysis included 76 patients (37 randomized to tenecteplase, 39 to placebo). Multivariate regression yielded an equation f(8, 67), P < 0.001, with R² = 0.303. Obesity had the largest effect on PCS (β = −8.6, P < 0.001), with tenecteplase second (β = 4.73, P = 0.056). After controlling for all interactions, tenecteplase increased the PCS by +5.37 points (P = 0.027). In patients without any of the defined comorbidities, the coefficient on the tenecteplase variable was not significant (−0.835, P = 0.777). In patients with submassive PE, obesity had the greatest influence on QoL, followed by use of fibrinolysis. Fibrinolysis had a marginal independent effect on patient QoL after controlling for comorbidities, but was not significant in patients without comorbid conditions.

Drug Terms

tenecteplase

Disease Terms

chronic obstructive lung disease, deep vein thrombosis, heart failure, **lung embolism**, obesity, recurrent disease

Other Terms

adolescent, age, article, body mass, comorbidity, controlled study, disease severity, **fibrinolysis**, human, major clinical study, medical history, multicenter study (topic), priority journal, **quality of life**, randomized controlled trial (topic), **Short Form 36**

Author Keywords

Fibrinolysis, Pulmonary embolism, Quality of life, Submassive

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CAS Registry Numbers	tenecteplase (191588-94-0)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00680628)

Record 2

Retinoid receptor signaling and autophagy in acute promyelocytic leukemia

Orfali N., McKenna S.L., Cahill M.R., Gudas L.J., Mongan N.P.

Experimental Cell Research 2014 **324:1** (1-12)

Retinoids are a family of signaling molecules derived from vitamin A with well established roles in cellular differentiation. Physiologically active retinoids mediate transcriptional effects on cells through interactions with retinoic acid (RARs) and retinoid-X (RXR) receptors. Chromosomal translocations involving the RARα gene, which lead to impaired retinoid signaling, are implicated in acute promyelocytic leukemia (APL). All-trans-retinoic acid (ATRA), alone and in combination with arsenic trioxide (ATO), restores differentiation in APL cells and promotes degradation of the abnormal oncogenic fusion protein through several proteolytic mechanisms. RAR. α fusion-protein elimination is emerging as critical to obtaining sustained remission and long-term cure in APL. Autophagy is a degradative cellular pathway involved in protein turnover. Both ATRA and ATO also induce autophagy in APL cells. Enhancing autophagy may therefore be of therapeutic benefit in resistant APL and could broaden the application of differentiation therapy to other cancers. Here we discuss retinoid signaling in hematopoiesis, leukemogenesis, and APL treatment. We highlight autophagy as a potential important regulator in anti-leukemic strategies. © 2014 Elsevier Inc.

Drug Terms

CCAAT enhancer binding protein, **retinoid**, retinol binding protein 4

Disease Terms

chromosome translocation, **promyelocytic leukemia**

Other Terms

acute myeloblastic leukemia, **autophagy**, catabolism, cell differentiation, cells, chromatin immunoprecipitation, clinical trial (topic), conformational transition, disease free survival, double stranded DNA break, embryo development, embryonic stem cell, erythropoiesis, fetus liver, gene expression, gene fusion, gene translocation, genetic transcription, genotype, granulocyte, hematopoiesis, hematopoietic stem cell, human, insulin sensitivity, intestine absorption, intron, leukemogenesis, membrane vesicle, metabolic regulation, metabolism, nonhuman, priority journal, protein degradation, protein metabolism, remission, review, **signal transduction**, transcription initiation

Author Keywords

AML, APL, Arsenic trioxide, ATRA, Autophagy, Differentiation, Hematopoiesis, PML-RARα, Retinoid

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Clinical Trial Numbers	ClinicalTrials.gov (NCT00002701, NCT00003405, NCT00003619, NCT00006239, NCT00049582, NCT00136461, NCT00143975, NCT00146120, NCT00151242, NCT00151255, NCT00175812, NCT00180128, NCT00196768, NCT00217412, NCT00326170, NCT00339196, NCT00413166, NCT00465933, NCT00482833, NCT00504764, NCT00520208, NCT00528450, NCT00615784, NCT00675870, NCT00867672, NCT00892190, NCT00893399, NCT00903422, NCT00985530, NCT00995332, NCT01020539, NCT01161550, NCT01237808, NCT01369368, NCT01404949, NCT01409161, NCT01575691, NCT01987297)

Record 3

Heme oxygenase-1 and acute kidney injury following cardiac surgery

Billings F.T., Yu C., Byrne J.G., Petracek M.R., Pretorius M.

CardioRenal Medicine 2014 **4:1** (12-21)

Background: Intraoperative hemolysis and inflammation are associated with acute kidney injury (AKI) following cardiac surgery. Plasma-free hemoglobin induces heme oxygenase-1 (HO-1) expression. HO-1 degrades heme but increases in experimental models of AKI. This study tested the hypothesis that plasma HO-1 concentrations are associated with intraoperative hemolysis and are increased in patients that develop AKI following cardiac surgery. Methods: We measured plasma HO-1, free hemoglobin, and inflammatory markers in 74 patients undergoing cardiopulmonary bypass (CPB). AKI was defined as an increase in serum creatinine concentration of 50% or 0.3 mg/dl within 72 h of surgery. Results: Twenty-eight percent of patients developed AKI. HO-1 concentrations increased from 4.2 ± 0.2 ng/ml at baseline to 6.6 ± 0.5 ng/ml on postoperative day (POD) 1 ($p < 0.001$). POD1 HO-1 concentrations were 3.1 ng/ml higher (95% CI 1.1-5.1) in AKI patients, as was the change in HO-1 from baseline to POD1 (4.4 ± 1.3 ng/ml in AKI patients vs. 1.5 ± 0.3 ng/ml in no-AKI patients, $p = 0.006$). HO-1 concentrations remained elevated in AKI patients even after controlling for AKI risk factors and preoperative drug therapy. Peak-free hemoglobin concentrations correlated with peak HO-1 concentrations on POD1 in patients that developed AKI ($p = 0.02$). Duration of CPB and post-CPB IL-6 and IL-10 concentrations were also associated with increased HO-1 on POD1. Conclusion: Plasma HO-1 is increased in patients that develop AKI, and CPB duration, hemolysis, and inflammation are associated with increased HO-1 concentrations following cardiac surgery. Strategies that alter hemolysis and HO-1 expression during cardiac surgery may affect risk for AKI. © 2014 S. Karger AG, Basel.

Drug Terms

heme oxygenase 1, hemoglobin, interleukin 10, interleukin 6, interleukin 8

Disease Terms

acute kidney failure, **hemolysis**, inflammation

Other Terms

aged, article, cardiopulmonary bypass, creatinine blood level, female, **heart surgery**, human, major clinical study, male, postoperative period, priority journal

Author Keywords

Acute kidney injury, Angiotensin-converting enzyme inhibitor, Cardiac surgery, Cardiopulmonary bypass, Heme oxygenase-1, Hemoglobin, Hemolysis, Interleukin

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Cited by in Scopus	
CAS Registry Numbers	hemoglobin (9008-02-0) interleukin 8 (114308-91-7)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00607672)

Record 4

Heme oxygenase-1 and acute kidney injury following cardiac surgery

Billings F.T., Yu C., Byrne J.G., Petracek M.R., Pretorius M.

CardioRenal Medicine 2014 **4:1** (12-21)

Background: Intraoperative hemolysis and inflammation are associated with acute kidney injury (AKI) following cardiac surgery. Plasma-free hemoglobin induces heme oxygenase-1 (HO-1) expression. HO-1 degrades heme but increases in experimental models of AKI. This study tested the hypothesis that plasma HO-1 concentrations are associated with intraoperative hemolysis and are increased in patients that develop AKI following cardiac surgery. Methods: We measured plasma HO-1, free hemoglobin, and inflammatory markers in 74 patients undergoing cardiopulmonary bypass (CPB). AKI was defined as an increase in serum creatinine concentration of 50% or 0.3 mg/dl within 72 h of surgery. Results: Twenty-eight percent of patients developed AKI. HO-1 concentrations increased from 4.2 ± 0.2 ng/ml at baseline to 6.6 ± 0.5 ng/ml on postoperative day (POD) 1 ($p < 0.001$). POD1 HO-1 concentrations were 3.1 ng/ml higher (95% CI 1.1-5.1) in AKI patients, as was the change in HO-1 from baseline to POD1 (4.4 ± 1.3 ng/ml in AKI patients vs. 1.5 ± 0.3 ng/ml in no-AKI patients, $p = 0.006$). HO-1 concentrations remained elevated in AKI patients even after controlling for AKI risk factors and preoperative drug therapy. Peak-free hemoglobin concentrations correlated with peak HO-1 concentrations on POD1 in patients that developed AKI ($p = 0.02$). Duration of CPB and post-CPB IL-6 and IL-10 concentrations were also associated with increased HO-1 on POD1. Conclusion: Plasma HO-1 is increased in patients that develop AKI, and CPB duration, hemolysis, and inflammation are associated with increased HO-1 concentrations following cardiac surgery. Strategies that alter hemolysis and HO-1 expression during cardiac surgery may affect risk for AKI.

Drug Terms

candesartan, creatinine, **heme oxygenase 1**, hemoglobin, interleukin 10, interleukin 6, interleukin 8, placebo, ramipril

Disease Terms

acute kidney failure, hemolysis, peroperative complication, **postoperative complication**

Other Terms

adult, aged, article, cardiopulmonary bypass, concentration process, controlled study, creatinine blood level, disease association, female, **heart surgery**, human, major clinical study, male, operation duration, patient risk, postoperative care, preoperative care, priority journal, protein blood level, protein expression, randomized controlled trial, risk assessment, risk factor, surgical risk

Author Keywords

Acute kidney injury, Angiotensin-converting enzyme inhibitor, Cardiac surgery, Cardiopulmonary bypass, Heme oxygenase-1, Hemoglobin, Hemolysis, Interleukin

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Clinical Trial Numbers	ClinicalTrials.gov (NCT00607672)

Record 5

Intraventricular Tissue Plasminogen Activator in Subarachnoid Hemorrhage Patients: A Prospective, Randomized, Placebo-Controlled Pilot Trial

Kramer A.H., Roberts D.J., Holodinsky J., Todd S., Hill M.D., Zygun D.A., Faris P., Wong J.H.

Neurocritical Care 2014 **21:2** (275-284)

Background: The quantity of subarachnoid (SAH) and intraventricular hemorrhage (IVH) occurring in the setting of a ruptured cerebral aneurysm is strongly associated with subsequent complications and poor outcomes.Methods: We randomly allocated aneurysmal SAH patients with a modified Fisher score of 4, who had been treated with endovascular coil embolization and ventricular drainage, to receive either 2 mg intraventricular tissue plasminogen activator (TPA) every 12 h (maximum 10 mg) or placebo. Computed tomography scans were performed 12, 48, and 72 h after administration. Primary outcomes included feasibility (enrollment and consent rates), safety (assessed by prospectively screening for complications), and rate of intracranial blood clearance (measured using sequential IVH, modified Graeb, and SAH sum scores). Secondary outcomes included angiographic vasospasm, delayed cerebral ischemia, need for ventriculoperitoneal shunting, and 6-month neurological outcomes.Results: Seventy-seven patients were screened, 17 were eligible, and 12 were randomized. The consent rate was 87 %. There were no cases of new intracranial hemorrhage complicating use of TPA. Models fit using generalized estimating equations demonstrated more rapid reduction in IVH volume ($p = 0.009$), modified Graeb score ($p < 0.001$), and SAH sum score ($p < 0.001$) among patients treated with TPA. SAH clearance at 48 h was enhanced by earlier drug administration ($p = 0.02$). There were no differences in secondary outcomes.Conclusions: Intraventricular TPA accelerates clearance of SAH and IVH, especially when administered early. A larger-scale clinical trial of intraventricular TPA is feasible, will need to be conducted at multiple centers, and is required to determine whether this practice reduces complications and improves outcomes.

Drug Terms

alteplase, placebo

Disease Terms

brain artery aneurysm rupture, brain ischemia, brain vasospasm,
subarachnoid hemorrhage

Other Terms

adult, aged, article, brain angiography, brain blood flow,
brain ventricle peritoneum shunt, clinical effectiveness, computer assisted tomography,
controlled study, double blind procedure, drug efficacy, female, human,
major clinical study, male, outcome assessment, pilot study, plasma clearance,
randomized controlled trial

Author Keywords

Delayed cerebral ischemia, External ventricular drain, Hydrocephalus, Intraventricular hemorrhage, Subarachnoid hemorrhage, Tissue plasminogen activator

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Cited by in Scopus	
Drug Tradenames	cathflo
CAS Registry Numbers	alteplase (105857-23-6)
Clinical Trial Numbers	ClinicalTrials.gov (NCT01098890)

Record 6

Effect of almond consumption on the serum fatty acid profile: A dose-response study

Nishi S., Kendall C.W.C., Gascoyne A.-M., Bazinet R.P., Bashyam B., Lapsley K.G., Augustin L.S.A., Sievenpiper J.L., Jenkins D.J.A.

British Journal of Nutrition 2014 **112:7** (1137-1146)

Consumption of almonds has been shown to be associated with a decreased risk of CHD, which may be related to their fatty acid (FA) composition. However, the effect of almond consumption on the serum FA composition is not known. Therefore, in the present study, we investigated whether almond consumption would alter the serum FA profile and risk of CHD, as calculated using Framingham's 10-year risk score, in a dose-dependent manner in hyperlipidaemic individuals when compared with a higher-carbohydrate control group using dietary interventions incorporating almonds. A total of twenty-seven hyperlipidaemic individuals consumed three isoenergetic (mean 1770 kJ/d) supplements during three 1-month dietary phases: (1) full-dose almonds (50-100 g/d); (2) half-dose almonds with half-dose muffins; (3) full-dose muffins. Fasting blood samples were obtained at weeks 0 and 4 for the determination of FA concentrations. Almond intake (g/d) was found to be inversely associated with the estimated Framingham 10-year CHD risk score (P= 0.026). In both the half-dose and full-dose almond groups, the proportions of oleic acid (OA) and MUFA in the TAG fraction (half-almond: OA P= 0.003; MUFA P= 0.004; full-almond: OA P< 0.001; MUFA P< 0.001) and in the NEFA fraction (half-almond: OA P= 0.01; MUFA P= 0.04; full-almond: OA P= 0.12; MUFA P= 0.06) increased. The estimated Framingham 10-year CHD risk score was inversely associated with the percentage change of OA (P= 0.011) and MUFA (P= 0.016) content in the TAG fraction. The proportions of MUFA in the TAG and NEFA fractions were positively associated with changes in HDL-cholesterol concentrations. Similarly, the estimated Framingham 10-year CHD risk score was inversely associated with the percentage change of OA (P = 0.069) and MUFA content in the NEFA fraction (P = 0.009). In conclusion, the results of the present study indicate that almond consumption increases OA and MUFA content in serum TAG and NEFA fractions, which are inversely associated with CHD lipid risk factors and overall estimated 10-year CHD risk.

Drug Terms

angiotensin 2 receptor antagonist, beta adrenergic receptor blocking agent, cholesterol ester, dipeptidyl carboxypeptidase inhibitor, **fatty acid**, high density lipoprotein cholesterol, hydroxymethylglutaryl coenzyme A reductase inhibitor, levothyroxine, low density lipoprotein cholesterol, palmitic acid, phospholipid, thiazide diuretic agent

Disease Terms

abdominal discomfort, hyperlipidemia, hypertension, ischemic heart disease

Other Terms

adult, aged, **almond**, article, blood pressure measurement, body mass, caloric intake, Canada, carbohydrate intake, clinical article, controlled study, crossover procedure, diet supplementation, dose response, **fatty acid blood level**, female, fetus weight, **food intake**, Framingham risk score, hormone substitution, human, intervention study, lipid composition, male, particle size, postmenopause, randomized controlled trial, risk factor, very elderly

Author Keywords

Almonds, Coronary/heart disease, Fatty acids, Nutrition

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Embase Accession Number	2015922518
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Cited by in Scopus	
CAS Registry Numbers	levothyroxine (51-48-9) palmitic acid (57-10-3)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00507520)

Record 7

Treatment of submassive pulmonary embolism with tenecteplase or placebo: Cardiopulmonary outcomes at 3 months: Multicenter double-blind, placebo-controlled randomized trial

Kline J.A., Nordenholz K.E., Courtney D.M., Kabrhel C., Jones A.E., Rondina M.T., Diercks D.B., Klinger J.R., Hernandez J.

Journal of Thrombosis and Haemostasis 2014 **12:4** (459-468)

Summary: Background: Acute pulmonary embolism (PE) can worsen quality of life due to persistent dyspnea or exercise intolerance. Objective: Test if tenecteplase increases the probability of a favorable composite patient-oriented outcome after submassive PE. Methods: Normotensive patients with PE and right ventricular (RV) strain (by echocardiography or biomarkers) were enrolled from eight hospitals. All patients received low-molecular-weight heparin followed by random assignment to either a single weight-based bolus of tenecteplase or placebo, administered in a double-blinded fashion. The primary composite outcome included: (i) death, circulatory shock, intubation or major bleeding within 5 days or (ii) recurrent PE, poor functional capacity (RV dysfunction with either dyspnea at rest or exercise intolerance) or an SF36® Physical Component Summary (PCS) score < 30 at 90-day follow-up. Results: Eighty-three patients were randomized; 40 to tenecteplase and 43 to placebo. The trial was terminated prematurely. Within 5 days, adverse outcomes occurred in three placebo-treated patients (death in one and intubation in two) and one tenecteplase-treated patient (fatal intracranial hemorrhage). At 90 days, adverse outcomes occurred in 13 unique placebo-treated patients and five unique tenecteplase-treated patients Thus, 16 (37%) placebo-treated and six (15%) tenecteplase-treated patients had at least one adverse outcome (exact two-sided P = 0.017). Conclusions: Treatment of patients with submassive pulmonary embolism with tenecteplase was associated with increased probability of a favorable composite outcome. © 2014 International Society on Thrombosis and Haemostasis.

Drug Terms

low molecular weight heparin, **placebo**, **tenecteplase**

Disease Terms

brain hemorrhage, deep vein thrombosis, drug fatality, dyspnea, exercise intolerance, exercise intolerance, fatal intracranial hemorrhage, fatal intracranial hemorrhage, hypotension, intraspinal hemorrhage, intraspinal hemorrhage, **lung embolism**, lung hemorrhage, right ventricle dysfunction, right ventricle dysfunction, shock, side effect, spinal cord disease

Other Terms

adolescent, article, computed tomographic angiography, controlled study, double blind procedure, echocardiography, female, functional status, hospital, human, major clinical study, male, multicenter study, outcome assessment, priority journal, randomized controlled trial, Short Form 36, single drug dose

Author Keywords

Pulmonary embolism, Quality of life, Randomized controlled trial, Thrombolytic therapy, Ventricular function, right

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Number of References	35
Cited by in Scopus	
Drug Tradenames	TNKase (Genentech, United States)
Drug Manufacturers	Genentech (United States)
CAS Registry Numbers	tenecteplase (191588-94-0)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00680628)

Record 8

Treatment of Malignant Brain Edema and Increased Intracranial Pressure After Stroke

Brogan M.E., Manno E.M.

Current Treatment Options in Neurology 2014 **17:1**

The management of patients with large territory ischemic strokes and the subsequent development of malignant brain edema and increased intracranial pressure is a significant challenge in modern neurology and neurocritical care. These patients are at high risk of subsequent neurologic decline and are best cared for in an intensive care unit or a comprehensive stroke center with access to neurosurgical support. Risks include hemorrhagic conversion, herniation, poor functional outcome, and death. This review discusses recent advances in understanding the pathophysiology of edema formation, identifying patients at risk, current management strategies, and emerging therapies.

Drug Terms

barbituric acid derivative, bumetanide, corticosteroid, enalapril, fibrinolytic agent, gelatinase inhibitor, glibenclamide, hydralazine, labetalol, mannitol, minocycline, nicardipine, norphenazone, progesterone, protein S 100, sodium chloride

Disease Terms

brain edema, brain infarction, brain ischemia, **cerebrovascular accident**, internal carotid artery occlusion, **intracranial hypertension**

Other Terms

anastomosis, article, bone graft, cerebrospinal fluid drainage, corticosteroid therapy, decompressive craniectomy, endotracheal intubation, human, induced hypothermia,

intracranial pressure monitoring, multicenter study (topic), neuroprotection, nonhuman, osmosis, pathophysiology, patient care, phase 2 clinical trial (topic), practice guideline, randomized controlled trial (topic), risk factor

Author Keywords

Brain edema, Decompressive craniectomy, Infarction, Intracranial pressure, Malignant cerebral edema, Patient care management, Stroke

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Additional Information

Abbreviated Journal Title	Curr. Treat. Options Neurol.
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CODEN	CTONB
Source Type	Journal
Source Publication Date	2014-11-05
Entry Date	2015-02-19 (Full record), 2015-02-13 (Article in Press/In process)
Publication Type	Article
Page Range	
Country of Author	United States
Country of Source	United Kingdom
Language of Article	English
Language of Summary	English
Embase Accession Number	2015726136
Number of References	84
Cited by in Scopus	
Drug Tradenames	glyburide
CAS Registry Numbers	bumetanide (28395-03-1) enalapril (75847-73-3) glibenclamide (10238-21-8) hydralazine (304-20-1 , 86-54-4) labetalol (32780-64-6 , 36894-69-6) mannitol (69-65-8 , 87-78-5) minocycline (10118-90-8 , 11006-27-2 , 13614-98-7) nicardipine (54527-84-3 , 55985-32-5) norphenazone (89-25-8) progesterone (57-83-0) sodium chloride (7647-14-5)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00630396, NCT01123161, NCT01794182)

Record 9

Minocycline repurposing in critical illness: Focus on stroke

Liao T.V., Forehand C.C., Hess D.C., Fagan S.C.

Current Topics in Medicinal Chemistry 2013 **13:18** (2283-2290)

Stroke is a devastating disease associated with high morbidity and mortality. Despite the approved indication of systemic thrombolytic therapy in the United States for the acute management of ischemic stroke, its use is limited given a strict eligibility criteria and a risk for hemorrhagic transformation as a feared adverse effect. Many agents have been studied without success for neuroprotection in patients with stroke to reduce vascular injury and improve long-term functional outcomes. Minocycline is a tetracycline antibiotic that shows promise for its neuroprotective effects in multiple animal models and three human trials. It affects multiple pathways to reduce apoptosis, neuroinflammation, infarct size, and vascular injury. The aim of this review is to discuss current evidence for minocycline from pre-clinical and early clinical trials and its potential role in neuroprotection in patients with acute ischemic stroke. © 2013 Bentham Science Publishers.

Drug Terms

collagen type 4, doxycycline, **minocycline**, placebo, protein bcl 2, tetracycline

Disease Terms

blood vessel injury, bradycardia, brain atrophy, brain hemorrhage, brain infarction size, **cerebrovascular accident**, heart palpitation, hypertension, hypotension, hypothermia, insomnia, nervous system inflammation, side effect, tachycardia

Other Terms

antioxidant activity, apoptosis, article, daily life activity, drug effect, drug megadose, drug safety, human, loading drug dose, mental health, neuroprotection, nonhuman, randomized controlled trial (topic), rating scale

Author Keywords

Critical illness, Ischemia, Minocycline, Neuroprotection, Stroke, Tetracycline

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Additional Information

Abbreviated Journal Title	Curr. Top. Med. Chem.
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CODEN	CTMCC
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Source Publication Date	2013-01-01
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Publication Type	Article
Page Range	2283-2290
Country of Author	United States
Country of Source	Netherlands
Language of Article	English
Language of Summary	English
MEDLINE PMID	24059465
Embase Accession Number	2013730601
Number of References	67
Cited by in Scopus	5
CAS Registry Numbers	doxycycline (10592-13-9 , 17086-28-1 , 564-25-0 , 94088-85-4) minocycline (10118-90-8 , 11006-27-2 , 13614-98-7) protein bcl 2 (219306-68-0) tetracycline (23843-90-5 , 60-54-8 , 64-75-5 , 8021-86-1)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00630396)

Record 10

Role of inflammation and its mediators in acute ischemic stroke

Jin R., Liu L., Zhang S., Nanda A., Li G.

Journal of Cardiovascular Translational Research 2013 **6:5** (834-851)

Inflammation plays an important role in the pathogenesis of ischemic stroke and other forms of ischemic brain injury. Increasing evidence suggests that inflammatory response is a double-edged sword, as it not only exacerbates secondary brain injury in the acute stage of stroke but also beneficially contributes to brain recovery after stroke. In this article, we provide an overview on the role of inflammation and its mediators in acute ischemic stroke. We discuss various pro-inflammatory and anti-inflammatory responses in different phases after ischemic stroke and the possible reasons for their failures in clinical trials. Undoubtedly, there is still much to be done in order to translate promising pre-clinical findings into clinical practice. A better understanding of the dynamic balance between pro- and anti-inflammatory responses and identifying the discrepancies between pre-clinical studies and clinical trials may serve as a basis for designing effective therapies. © 2013 Springer Science+Business Media New York.

Drug Terms

arundic acid, CD11b antigen, CD31 antigen, enlimomab, fractalkine, gelatinase B, immunoglobulin enhancer binding protein, intercellular adhesion molecule 1, intercellular adhesion molecule 1 antibody, interleukin 10, interleukin 1alpha, interleukin 1beta, interleukin 6, L selectin, minocycline, mitogen activated protein kinase, mucosal addressin cell adhesion molecule 1, neuroprotective agent, PADGEM protein, recombinant interleukin 6, selectin, somatomedin C, stress activated protein kinase inhibitor, toll like receptor 2, toll like receptor 4, transforming growth factor beta, tumor necrosis factor alpha, unclassified drug, unindexed drug, vascular cell adhesion molecule 1, vascular cell adhesion molecule 1 antibody

Disease Terms

atherosclerosis, **brain ischemia**, cerebrovascular accident, **inflammation**

Other Terms

antiinflammatory activity, article, astrocyte, brain cell, cell damage, cell death, cell infiltration, cell proliferation, cytokine production, drug efficacy, drug response,

human, immunocompetent cell, inflammatory cell, leukocyte, microglia, neuroprotection, neutrophil chemotaxis, nonhuman, pathogenesis, pharmacological blocking, priority journal, protein expression, protein function, protein phosphorylation, protein secretion, protein targeting, T lymphocyte, upregulation

Author Keywords

Brain ischemia, Inflammation, Inflammatory mediators, Leukocytes

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Additional Information

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Publication Type	Article
Page Range	834-851
Country of Author	United States
Country of Source	United States
Language of Article	English
Language of Summary	English
MEDLINE PMID	24006091
Embase Accession Number	2013652118
Number of References	197
Cited by in Scopus	
Drug Tradenames	ono 2506
CAS Registry Numbers	L selectin (126880-86-2) arundic acid (185517-21-9) enlimomab (142864-19-5) fractalkine (199619-66-4) gelatinase B (146480-36-6) intercellular adhesion molecule 1 (126547-89-5) minocycline (10118-90-8 , 11006-27-2 , 13614-98-7) mitogen activated protein kinase (142243-02-5) mucosal addressin cell adhesion molecule 1 (181789-23-1) somatomedin C (67763-96-6) toll like receptor 2 (203811-81-8) toll like receptor 4 (203811-83-0)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00229177, NCT00630396)

Record 11

D-penicillamine and other low molecular weight thiols: Review of anticancer effects and related mechanisms

Wadhwa S., Mumper R.J.

Cancer Letters 2013 **337:1** (8-21)

Low molecular weight thiols (LMWTs) like N-acetyl cysteine, D-penicillamine, captopril, Disulfiram and Amifostine, etc. have been used as chemo-preventive agents. Recent studies have reported cell growth inhibition and cytotoxicity in several different types of cancer cells following treatment with several LMWTs. Cytotoxic and cytostatic effects of LMWTs may involve interaction of the thiol group with cellular lipids, proteins, intermediates or enzymes. Some of the mechanisms that have been proposed include a p53 mediated apoptosis, thiyl radical induced DNA damage, membrane damage through lipid peroxidation, anti-angiogenic effects induced by inhibition of matrix metalloproteinase enzymes and angiostatin generation. LMWTs are strong chelators of transition metals like copper, nickel, zinc, iron and cobalt and may cause metal co-factor depletion resulting in cytotoxicity. Oxidation of thiol group can also generate cytotoxic reactive oxygen species (ROS). © 2013 Elsevier Ireland Ltd.

Drug Terms

acetylcysteine, amifostine, angiostatin, bucillamine, captopril, cell enzyme, cell protein, cobalt, collagen, copper, disulfiram, dithiocarbamic acid derivative, interstitial collagenase, iron, lipid, **low molecular weight thiol**, matrix metalloproteinase, matrix metalloproteinase inhibitor, mesna, nickel, nov 002, **penicillamine**, protein lysine 6 oxidase, protein p53, reactive oxygen metabolite,

tetrathiomolybdic acid, **thiol derivative**, thiol group, unclassified drug, unindexed drug, zinc

Disease Terms

drug cytotoxicity, membrane damage

Other Terms

antiangiogenic activity, **antineoplastic activity**, apoptosis, cancer cell, cancer inhibition, chemoprophylaxis, cytostasis, DNA damage, **drug mechanism**, human, lipid peroxidation, molecular weight, nonhuman, oxidation, priority journal, short survey

Author Keywords
Angiogenesis, Apoptosis, Free radical, Lipid peroxidation, P53

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Additional Information

Abbreviated Journal Title	Cancer Lett.
ISSN	03043835, 18727980 (electronic)
CODEN	CALED
Source Type	Journal
Source Publication Date	2013-08-28
Entry Date	2013-11-22 (Full record), 2013-06-18 (Article in Press/In process)
Publication Type	Short Survey
Page Range	8-21
Country of Author	United States
Country of Source	Ireland
Language of Article	English
Language of Summary	English
Publisher Item Identifier	S0304383513004096
MEDLINE PMID	23727371
Embase Accession Number	2013435730
Number of References	213
Cited by in Scopus	
Drug Tradenames	nov 002
CAS Registry Numbers	acetylcysteine (616-91-1) amifostine (20537-88-6) angiostatin (172642-30-7 , 86090-08-6) bucillamine (65002-17-7) captopril (62571-86-2) cobalt (7440-48-4) collagen (9007-34-5) copper (15158-11-9 , 7440-50-8) disulfiram (97-77-8) interstitial collagenase (9001-12-1) iron (14093-02-8 , 53858-86-9 , 7439-89-6) lipid (66455-18-3) mesna (19767-45-4 , 3375-50-6) nickel (7440-02-0) penicillamine (2219-30-9 , 52-67-5) protein lysine 6 oxidase (99676-44-5) tetrathiomolybdic acid (13718-35-9 , 16330-92-0) thiol derivative (13940-21-1) zinc (14378-32-6 , 7440-66-6)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00086723)

Record 12

RNA in blood is altered prior to hemorrhagic transformation in ischemic stroke

Jickling G.C., Ander B.P., Stamova B., Zhan X., Liu D., Rothstein L., Verro P., Khoury J., Jauch E.C., Pancioli A.M., Broderick J.P., Sharp F.R.
Annals of Neurology 2013 **74:2** (232-240)
Objective Hemorrhagic transformation (HT) is a major complication of ischemic stroke

that worsens outcomes and increases mortality. Disruption of the blood-brain barrier is a central feature of HT pathogenesis, and leukocytes may contribute to this process. We sought to determine whether ischemic strokes that develop HT have differences in RNA expression in blood within 3 hours of stroke onset prior to treatment with thrombolytic therapy. Methods Stroke patient blood samples were obtained prior to treatment with thrombolysis, and leukocyte RNA was assessed by microarray analysis. Strokes that developed HT (n = 11) were compared to strokes without HT (n = 33) and controls (n = 14). Genes were identified (corrected p < 0.05, fold change ≥|1.2|), and functional analysis was performed. RNA prediction of HT in stroke was evaluated using cross-validation, and in a second stroke cohort (n = 52). Results Ischemic strokes that developed HT had differential expression of 29 genes in circulating leukocytes prior to treatment with thrombolytic therapy. A panel of 6 genes could predict strokes that later developed HT with 80% sensitivity and 70.2% specificity. Key pathways involved in HT of human stroke are described, including amphiregulin, a growth factor that regulates matrix metalloproteinase-9; a shift in transforming growth factor-β signaling involving SMAD4, INPP5D, and IRAK3; and a disruption of coagulation factors V and VIII. Interpretation Identified genes correspond to differences in inflammation and coagulation that may predispose to HT in ischemic stroke. Given the adverse impact of HT on stroke outcomes, further evaluation of the identified genes and pathways is warranted to determine their potential as therapeutic targets to reduce HT and as markers of HT risk. © 2013 American Neurological Association.

Drug Terms

alteplase, amphiregulin, blood clotting factor 5, blood clotting factor 7, eptifibatide, gelatinase B, growth factor, interleukin 1 receptor associated kinase 3, **RNA**, Smad4 protein, synaptojanin, transforming growth factor beta

Disease Terms

bleeding, **brain ischemia**, **hemorrhagic transformation**

Other Terms

adult, aged, article, blood clot lysis, blood sampling, clinical article, controlled study, disease course, double blind procedure, female, fibrinolytic therapy, functional assessment, gene expression, gene identification, human, leukocyte, male, microarray analysis, multicenter study, prediction, priority journal, randomized controlled trial, RNA analysis, stroke patient

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Additional Information

Abbreviated Journal Title	Ann. Neurol.
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CODEN	ANNED
Source Type	Journal
Source Publication Date	August 2013
Entry Date	2013-10-10 (Full record), 2013-09-16 (Article in Press/In process)
Publication Type	Article
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Language of Article	English
Language of Summary	English
MEDLINE PMID	23468366
Embase Accession Number	2013616209
Number of References	64
Cited by in Scopus	
CAS Registry Numbers	RNA (63231-63-0) Smad4 protein (282562-18-9) alteplase (105857-23-6) amphiregulin (117147-70-3) blood clotting factor 5 (9001-24-5 , 9013-23-4) blood clotting factor 7 (9001-25-6) eptifibatide (148031-34-9) gelatinase B (146480-36-6) synaptojanin (119699-77-3)

Clinical Trial Numbers	ClinicalTrials.gov (NCT00250991)

Record 13

Diagnosis and management of pulmonary embolism

Lapner S.T., Kearon C.

BMJ (Online) 2013 **346:7896** Article Number f757

Drug Terms

anticoagulant agent, antithrombocytic agent, apixaban, D dimer, dabigatran, fondaparinux, heparin, low molecular weight heparin, rivaroxaban

Disease Terms

lung embolism, venous thromboembolism

Device Terms

vena cava filter

Other Terms

clinical assessment, clinical effectiveness, clinical feature, computed tomographic angiography, diagnostic test, differential diagnosis, embolectomy, human, lung scintiscanning, mechanical thrombectomy, note, population risk, priority journal, probability, risk factor, sensitivity and specificity, treatment indication

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Additional Information

Abbreviated Journal Title	BMJ (Online)
ISSN	17561833 (electronic)
CODEN	BMJOA
Source Type	Journal
Source Publication Date	2013-02-23
Entry Date	2013-03-11 (Full record), 2013-03-05 (Article in Press/In process)
Publication Type	Note
Page Range	
Country of Author	Canada
Country of Source	United Kingdom
Language of Article	English
MEDLINE PMID	23427133
Embase Accession Number	2013127554
Article Number	f757
Number of References	39
Cited by in Scopus	19
CAS Registry Numbers	apixaban (503612-47-3) fondaparinux (104993-28-4 , 114870-03-0) heparin (37187-54-5 , 8057-48-5 , 8065-01-8 , 9005-48-5) rivaroxaban (366789-02-8)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00639743, NCT00680628)

Record 14

Imaging and treatment response after ischaemic stroke

Muir K.W.

The Lancet Neurology 2012 **11:10** (838-839)

Drug Terms

alteplase, placebo

Disease Terms

brain ischemia

Device Terms

revascularization

Other Terms

brain blood flow, brain metabolism, brain oxygen consumption, brain perfusion, human,

letter, **neuroimaging**, nuclear magnetic resonance imaging, perfusion weighted imaging, positron, positron emission tomography, priority journal, risk benefit analysis, thrombectomy, **treatment response**

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Additional Information

Abbreviated Journal Title	Lancet Neurol.
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CODEN	LNAEA
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Entry Date	2012-10-01 (Full record), 2012-09-07 (Article in Press/In process)
Publication Type	Letter
Page Range	838-839
Country of Author	United Kingdom
Country of Source	United Kingdom
Language of Article	English
Publisher Item Identifier	S1474442212702077
MEDLINE PMID	22954706
Embase Accession Number	2012556798
Number of References	12
Cited by in Scopus	0
CAS Registry Numbers	alteplase (105857-23-6)
Clinical Trial Numbers	ISRCTN (ISRCTN10888758) ClinicalTrials.gov (NCT00389467, NCT00640367, NCT01062698)

Record 15

Thrombolytic therapy for submassive pulmonary embolism

Lankeit M., Konstantinides S.

Best Practice and Research: Clinical Haematology 2012 **25:3** (379-389)

Approximately 10% of all patients with acute pulmonary embolism (PE) die within the first three months after diagnosis. However, PE is not universally life-threatening, but covers a wide spectrum of clinical severity and death risk. Thrombolytic treatment is indicated patients with acute massive PE who are at high risk for early death, i.e. those patients who present with arterial hypotension and shock. On the other hand, low molecular-weight heparin or fondaparinux is adequate treatment for most normotensive patients with PE. Recombinant tissue plasminogen activator, given as 100 mg infusion over 2 h, is the treatment of choice for patients with PE, although older regimens using urokinase or streptokinase are also efficacious. Beyond the relatively small numbers of patients with massive, high-risk PE as a target population for thrombolysis, there is increasing awareness of the need for risk stratification of normotensive patients and the search for an intermediate-risk group (also called submassive PE). Recent meta-analyses of cohort studies suggest that imaging of the right ventricle or biomarkers of myocardial injury alone may be insufficient for guiding therapeutic decisions. Instead, accumulating evidence appears to support strategies which combine the information provided by an imaging procedure with a biomarker test. These data provide the rationale for a large multinational randomized trial which has set out to determine whether normotensive patients with right ventricular dysfunction, detected by echocardiography or computed tomography, plus evidence of myocardial injury as indicated by a positive troponin test, may benefit from early thrombolytic treatment. This study, which is underway in 13 European countries, will enroll a total of 1000 patients and will be completed in 2012. Together with a parallel trial currently being conducted in the United States, it will hopefully answer the question whether thrombolysis is indicated in submassive PE, thus terminating a 40-year-old debate and filling an important gap in our management concept for acute pulmonary embolism. © 2012 Published by Elsevier Ltd.

Drug Terms

alteplase, biological marker, fondaparinux, low molecular weight heparin, reteplase, streptokinase, tenecteplase, troponin I, troponin T, urokinase

Disease Terms

heart muscle injury, hypotension, **lung embolism**, shock

Other Terms

article, awareness, blood pressure, clinical assessment, continuous infusion, diagnostic imaging, disease severity, drug efficacy, drug indication,

fibrinolytic therapy, heart right ventricle, heart right ventricle function, high risk patient, human, priority journal, risk, risk assessment, risk benefit analysis, risk factor

Author Keywords
pulmonary embolism, risk stratification, therapy, thrombolysis

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Source Publication Date	September 2012
Entry Date	2012-09-20 (Full record), 2012-09-18 (Article in Press/In process)
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Page Range	379-389
Country of Author	Greece
Country of Source	United Kingdom
Language of Article	English
Language of Summary	English
Publisher Item Identifier	S1521692612000552
MEDLINE PMID	22959553
Embase Accession Number	2012531559
Number of References	83
Cited by in Scopus	8
CAS Registry Numbers	alteplase (105857-23-6) fondaparinux (104993-28-4 , 114870-03-0) reteplase (133652-38-7) streptokinase (9002-01-1) tenecteplase (191588-94-0) troponin I (77108-40-8) troponin T (60304-72-5) urokinase (139639-24-0)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00680628)

Record 16

Prediction of cardioembolic, arterial, and lacunar causes of cryptogenic stroke by gene expression and infarct location

Jickling G.C., Stamova B., Ander B.P., Zhan X., Liu D., Sison S.-M., Verro P., Sharp F.R.

Stroke 2012 **43:8** (2036-2041)

BACKGROUND AND PURPOSE-: The cause of ischemic stroke remains unclear, or cryptogenic, in as many as 35% of patients with stroke. Not knowing the cause of stroke restricts optimal implementation of prevention therapy and limits stroke research. We demonstrate how gene expression profiles in blood can be used in conjunction with a measure of infarct location on neuroimaging to predict a probable cause in cryptogenic stroke. METHODS-: The cause of cryptogenic stroke was predicted using previously described profiles of differentially expressed genes characteristic of patients with cardioembolic, arterial, and lacunar stroke. RNA was isolated from peripheral blood of 131 cryptogenic strokes and compared with profiles derived from 149 strokes of known cause. Each sample was run on Affymetrix U133 Plus 2.0 microarrays. Cause of cryptogenic stroke was predicted using gene expression in blood and infarct location. RESULTS-: Cryptogenic strokes were predicted to be 58% cardioembolic, 18% arterial, 12% lacunar, and 12% unclear etiology. Cryptogenic stroke of predicted cardioembolic etiology had more prior myocardial infarction and higher CHA2DS2-VASc scores compared with stroke of predicted arterial etiology. Predicted lacunar strokes had higher systolic and diastolic blood pressures and lower National Institutes of Health Stroke Scale compared with predicted arterial and cardioembolic strokes. Cryptogenic strokes of unclear predicted etiology were less likely to have a prior transient ischemic attack or ischemic stroke. CONCLUSIONS-: Gene expression in conjunction with a measure of infarct location can predict a probable cause in cryptogenic strokes. Predicted groups require further evaluation to determine whether relevant clinical, imaging, or therapeutic differences exist for each group. © 2012 American Heart Association, Inc.

Drug Terms

RNA

Disease Terms

brain ischemia, cardioembolic stroke, heart infarction, lacunar stroke, **cerebrovascular accident**, transient ischemic attack

Other Terms

adult, arterial stroke, article, blood sampling, brain ventricle, diastolic blood pressure, female, gene expression profiling, human, human tissue, major clinical study, male, microarray analysis, National Institutes of Health Stroke Scale, neuropathology, priority journal, RNA isolation, stroke patient, systolic blood pressure

Author Keywords
cryptogenic stroke, diagnosis, gene expression, ischemic stroke

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Additional Information

Abbreviated Journal Title	Stroke
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Publication Type	Article
Page Range	2036-2041
Country of Author	United States
Country of Source	United States
Language of Article	English
Language of Summary	English
MEDLINE PMID	22627989
Embase Accession Number	2012438217
Number of References	26
Cited by in Scopus	18
CAS Registry Numbers	RNA (63231-63-0)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00250991)

Record 17

A double blind randomized cross over trial comparing rate of decortication and efficacy of intrapleural instillation of alteplase vs placebo in patients with empyemas and complicated parapneumonic effusions

Thommi G., Shehan J.C., Robison K.L., Christensen M., Backemeyer L.A., McLeay M.T.

Respiratory Medicine 2012 **106:5** (716-723)

Aim: A double blind randomized cross over trial to compare the rate of decortication, safety and efficacy of intrapleural instillation of Alteplase vs. Placebo in empyema and complicated parapneumonic effusions (CPE). Methods: Patients diagnosed with empyema or CPE and considered for surgery were given the option to enter into this trial. Intrapleural instillation of the 'Drug' was given daily for three days. Patient that failed the first arm of the trial were offered surgery or to cross over to the second arm. Failure was documented if pleural effusions did not improve by 50% on CT scans after three doses of the 'Drug' or if these effusions recurred within six weeks. Results: One hundred and eight patients were evaluated and one hundred enrolled in the trial. 32 patients were excluded, 29 for noninfectious loculated effusions, two for protocol violation and one for bleeding at chest tube site. There were 17 patients with empyema and 51 patients with CPE. 58 of the 61 patients (26 crossed over) with empyema/CPE resolved with Alteplase therapy compared to 4 of the 32 patients (one crossed over) treated with Placebo (p value <0.001). None of the patients went to surgery. Adverse events with Alteplase therapy compared to Placebo were not statistically significant, with chest pain and bleeding complications being the most common. Conclusion: Intrapleural instillation of Alteplase is significantly more effective than Placebo in patients with empyema and PPE (95% vs.12%). This study demonstrates it is safe and efficacious with minimal adverse reactions.

Drug Terms

alteplase, placebo

Disease Terms

anemia, bleeding, hypotension, **pleura effusion**, **pleura empyema**, thorax pain

Device Terms

tube

Other Terms

adult, aged, article, clinical evaluation, computer assisted tomography, controlled study, crossover procedure, decortication, double blind procedure, drug efficacy, drug instillation, drug safety, drug treatment failure, female, human, major clinical study, male, priority journal, randomized controlled trial, statistical significance

Author Keywords

Alteplase, CPE (complicated parapneumonic effusion), Empyema, Tissue plaminogen activator (tPA)

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Additional Information

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Country of Source	United Kingdom
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Publisher Item Identifier	S095461111200073X
MEDLINE PMID	22398159
Embase Accession Number	2012181569
Number of References	35
Cited by in Scopus	15
CAS Registry Numbers	alteplase (105857-23-6)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00468104)

Record 18

Thrombolysis and Deferoxamine in Middle Cerebral Artery Occlusion (TANDEM-1). A randomized controlled trial

Millán M., Pérez De La Ossa N., Reverté S., Silva Y., Nombela F., Rodríguez-Yáñez M., Costa J., Giner P., Castillo J., Serena J., Vivancos J., Dávalos A.

Cerebrovascular Diseases 2012 **33** SUPPL. 2 (714)

Background and Purpose:Iron overload is associated with greater brain injury whereas deferoxamine (DFO), an iron chelator, offers neuroprotection in animal models of cerebral ischemia and reperfusion. We aimed to evaluate safety and prove of concept of efficacy of IV DFO in patients with acute ischemic stroke (AIS) of middle cerebral artery territory treated with IV tissue plasminogen activator (tPA) within 3 hours from symptoms onset. Methods:TANDEM-1 was a placebo-controlled, double-blind, randomized, dose-finding phase II clinical trial (NCT00777140). A single 10mg/Kg bolus of DFO followed by a 72-hour continuous infusion escalating through 20, 40 and 60 mg/Kg/24h (n=15 per group) or placebo (n=5 per group) was initiated within the 1-hour of tPA infusion. A non blinded independent investigator evaluated serious adverse events (SAE) after each dose tier. Primary efficacy endpoint was good clinical outcome (modified Rankinscale ≤ 2) at 90 days. Results:The three parts terminated without crossing the safety stopping rules. Two patients with violation of inclusion criteria were substituted, but considered for safety analyses. Forty-seven patients received DFO and 15 placebo. Mean age and NIHSS score were 66.7 versus 64.6 years and 13.4 versus 17.2. SAE were reported in 13/47 (27.7%) and 4/15 (26.6%) patients. No SAE was related to DFO infusion except a non-fatal anaphylactic reaction. DFO was also discontinued in three patients because of asymptomatic bradicardia (n=2) and early neurological worsening (n=1). Symptomatic ICH (4.3% versus 0%) and mortality (14.9% versus 13.3%) were not different between groups. Good outcome was found in 55.6% of DFOtreated patients (53.3%, 53.3%, 60% for each tier) and in 40% of placebo group. Conclusions:Intravenous DFO initiated during the tPA infusion time is safe and well-tolerated up to doses of 60 mg/Kg/ day for three days. These findings provide the basis for a second trial aimed to demonstrate safety and efficacy of DFO.

Drug Terms

deferoxamine, placebo, chelating agent, iron, tissue plasminogen activator,

nitrogen 15

Disease Terms

middle cerebral artery occlusion, **cerebrovascular accident**, brain ischemia, brain injury, iron overload, anaphylaxis

Other Terms

blood clot lysis, **human**, **randomized controlled trial**, patient, safety, infusion, neuroprotection, dose calculation, continuous infusion, mortality, animal model, middle cerebral artery, reperfusion, phase 2 clinical trial, National Institutes of Health Stroke Scale

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Additional Information

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Entry Date	2014-10-30 (Full record)
Publication Type	Conference Abstract
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Language of Article	English
Language of Summary	English
Cited by in Scopus	

Record 19

Y chromosome gene expression in the blood of male patients with ischemic stroke compared with male controls

Tian Y., Stamova B., Jickling G.C., Xu H., Liu D., Ander B.P., Bushnell C., Zhan X., Turner R.J., Davis R.R., Verro P., Pevec W.C., Hedayati N., Dawson D.L., Khoury J., Jauch E.C., Pancioli A., Broderick J.P., Sharp F.R.

Gender Medicine 2012 **9:2** (68-75.e3)

Background: Sex is suggested to be an important determinant of ischemic stroke risk factors, etiology, and outcome. However, the basis for this remains unclear. The Y chromosome is unique in males. Genes expressed in males on the Y chromosome that are associated with stroke may be important genetic contributors to the unique features of males with ischemic stroke, which would be helpful for explaining sex differences observed between men and women. Objective: We compared Y chromosome gene expression in males with ischemic stroke and male controls. Methods: Blood samples were obtained from 40 male patients ≤3, 5, and 24 hours after ischemic stroke and from 41 male controls (July 2003-April 2007). RNA was isolated from blood and was processed using Affymetrix Human U133 Plus 2.0 expression arrays (Affymetrix Inc., Santa Clara, California). Y chromosome genes differentially expressed between male patients with stroke and male control subjects were identified using an ANCOVA adjusted for age and batch. A $P < 0.05$ and a fold change >1.2 were considered significant. Results: Seven genes on the Y chromosome were differentially expressed in males with ischemic stroke compared with controls. Five of these genes (VAMP7, CSF2RA, SPRY3, DHRSX, and PLCXD1) are located on pseudoautosomal regions of the human Y chromosome. The other 2 genes (EIF1AY and DDX3Y) are located on the nonrecombining region of the human Y chromosome. The identified genes were associated with immunology, RNA metabolism, vesicle fusion, and angiogenesis. Conclusions: Specific genes on the Y chromosome are differentially expressed in blood after ischemic stroke. These genes provide insight into potential molecular contributors to sex differences in ischemic stroke. © 2012 Elsevier HS Journals, Inc. All rights reserved.

Drug Terms

DEAD box protein, DEAD box protein 3, eukaryotic translation initiation factor 1A, initiation factor, membrane protein, sprouty protein, unclassified drug, vesicle associated membrane protein 7

Disease Terms

brain ischemia, hypertension

Other Terms

aged, angiogenesis, article, clinical article, controlled study, CSF2RA gene, DDX3Y gene, DHRSX gene, EIF1AY gene, gene, gene expression, gene location, human, human tissue, immunology, male, PLCXD1 gene, priority journal, RNA metabolism, SPRY3 gene, upregulation, VAMP7 gene, X chromosome, **Y chromosome**

Author Keywords

blood, gene expression, ischemic stroke, sex, Y chromosome

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Country of Source	United States
Language of Article	English
Language of Summary	English
Publisher Item Identifier	S1550857912000241
MEDLINE PMID	22365286
Embase Accession Number	2012205252
Number of References	31
Cited by in Scopus	5
Clinical Trial Numbers	ClinicalTrials.gov (NCT00250991)

Record 20

NF-κB and the link between inflammation and cancer

Didonato J.A., Mercurio F., Karin M.

Immunological Reviews 2012 **246:1** (379-400)

The nuclear factor-κB (NF-κB) transcription factor family has been considered the central mediator of the inflammatory process and a key participant in innate and adaptive immune responses. Coincident with the molecular cloning of NF-κB/RelA and identification of its kinship to the v-Rel oncogene, it was anticipated that NF-κB itself would be involved in cancer development. Oncogenic activating mutations in NF-κB genes are rare and have been identified only in some lymphoid malignancies, while most NF-κB activating mutations in lymphoid malignancies occur in upstream signaling components that feed into NF-κB. NF-κB activation is also prevalent in carcinomas, in which NF-κB activation is mainly driven by inflammatory cytokines within the tumor microenvironment. Importantly, however, in all malignancies, NF-κB acts in a cell type-specific manner: activating survival genes within cancer cells and inflammation-promoting genes in components of the tumor microenvironment. Yet, the complex biological functions of NF-κB have made its therapeutic targeting a challenge. © 2012 John Wiley & Sons A/S.

Drug Terms

2 amino 3 phosphonopropionic acid, azoxymethane, beta catenin, bortezomib, butylated hydroxyanisole, complementary DNA, dextran sulfate, glucocorticoid receptor, I kappa B alpha, I kappa B beta, I kappa B kinase gamma, I kappa B kinase inhibitor, **immunoglobulin enhancer binding protein**, interleukin 11, interleukin 12, interleukin 2, interleukin 22, interleukin 23, interleukin 6, Janus kinase, mitogen activated protein kinase, osteoclast differentiation factor, protein bcl 3, protein c jun, protein p100, protein p105, protein p52, STAT3 protein, transcription factor Rel, unindexed drug

Disease Terms

carcinogenesis, carcinoma, castration resistant prostate cancer, fatty liver, hepatitis B, hepatitis C, **inflammation**, liver carcinogenesis, liver cell carcinoma, lymphoma, ulcerative colitis

Other Terms

antineoplastic activity, apoptosis, article, bone marrow cell, cancer cell, cancer inhibition, cell differentiation, cell proliferation, cell stimulation, cell survival, chemical analysis, cytoplasm, dendritic cell, disease association, DNA binding, DNA sequence, fibroblast, gene activation, gene expression, gene locus, gene mutation, gene targeting, human, intestine epithelium cell, keratinocyte, liver, liver cell, macrophage, molecularly targeted therapy, morphology, neutrophil, nonhuman, phenotype, polymerase chain reaction, prevalence, priority journal, protein degradation, protein expression, protein function, protein purification, protein transport, signal transduction, tumor microenvironment, ubiquitination

Author Keywords

Cancer, Inflammation, NF-κB

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Publication Type	Article
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Country of Source	United Kingdom
Language of Article	English
Language of Summary	English
MEDLINE PMID	22435567
Embase Accession Number	2012171293
Number of References	215
Cited by in Scopus	262
CAS Registry Numbers	2 amino 3 phosphonopropionic acid (5652-28-8) I kappa B alpha (151217-48-0) Janus kinase (161384-16-3) azoxymethane (25843-45-2) bortezomib (179324-69-7 , 197730-97-5) butylated hydroxyanisole (25013-16-5) dextran sulfate (9011-18-1 , 9042-14-2) interleukin 12 (138415-13-1) interleukin 2 (85898-30-2) interleukin 22 (457106-70-6 , 478219-35-1 , 554460-75-2) mitogen activated protein kinase (142243-02-5) osteoclast differentiation factor (200145-93-3) protein p52 (220245-41-0)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00883584, NCT01113333)

Record 21

Cardiac hypertrophy and fibrosis in the metabolic syndrome: A role for aldosterone and the mineralocorticoid receptor

Essick E.E., Sam F.

International Journal of Hypertension 2011 **2011** Article Number 346985

Obesity and hypertension, major risk factors for the metabolic syndrome, render individuals susceptible to an increased risk of cardiovascular complications, such as adverse cardiac remodeling and heart failure. There has been much investigation into the role that an increase in the renin-angiotensin-aldosterone system (RAAS) plays in the pathogenesis of metabolic syndrome and in particular, how aldosterone mediates left

ventricular hypertrophy and increased cardiac fibrosis via its interaction with the mineralocorticoid receptor (MR). Here, we review the pertinent findings that link obesity with elevated aldosterone and the development of cardiac hypertrophy and fibrosis associated with the metabolic syndrome. These studies illustrate a complex cross-talk between adipose tissue, the heart, and the adrenal cortex. Furthermore, we discuss findings from our laboratory that suggest that cardiac hypertrophy and fibrosis in the metabolic syndrome may involve cross-talk between aldosterone and adipokines (such as adiponectin). © 2011 Eric E. Essick and Flora Sam.

Drug Terms

adipocytokine, adiponectin, **aldosterone**, angiotensin receptor antagonist, candesartan, captopril, dipeptidyl carboxypeptidase inhibitor, enalapril, eplerenone, fenofibrate, losartan, mineralocorticoid antagonist, **mineralocorticoid receptor**, pioglitazone, spironolactone

Disease Terms

cardiovascular disease, heart failure, **heart muscle fibrosis**, **heart ventricle hypertrophy**, hypertension, **metabolic syndrome X**, obesity

Other Terms

add on therapy, adipose tissue, adrenal cortex, disease association, heart, human, nonhuman, pathogenesis, priority journal, renin angiotensin aldosterone system, review, risk factor

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Country of Source	United States
Language of Article	English
Language of Summary	English
Embase Accession Number	2012644387
Article Number	346985
Number of References	153
Cited by in Scopus	8
CAS Registry Numbers	adiponectin (283182-39-8) aldosterone (52-39-1 , 6251-69-0) candesartan (139481-59-7) captopril (62571-86-2) enalapril (75847-73-3) eplerenone (107724-20-9) fenofibrate (49562-28-9) losartan (114798-26-4) pioglitazone (105355-27-9 , 111025-46-8) spironolactone (52-01-7)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00498433, NCT00608465)

Record 22

Intravitreal tissue plasminogen activator to treat refractory diabetic macular edema by induction of posterior vitreous detachment

Abrishami M., Moosavi M.N., Shoeibi N., Hosseinpoor S.S.
Retina 2011 **31:10** (2065-2070)

PURPOSE:: To evaluate the effects of intravitreal injection of recombinant tissue plasminogen activator (TPA) for the treatment of refractory diabetic macular edema. METHODS:: A total of 27 patients with refractory diabetic macular edema with no evidence of posterior vitreous detachment were randomly assigned into follow-up (F/U) or TPA treatment groups. To control for the effects of intravitreal injection, an additional 14 patients with diabetic macular edema who were candidates for first-time intravitreal bevacizumab injection were enrolled as the IVB group. For the TPA and IVB groups, 25

μg of TPA or 1.25 mg of bevacizumab, respectively, were intravitreally injected. Fundoscopy, optical coherence tomography, and B-scan ultrasonography were performed at 1 week, 1 month, and 3 months after initiation of the study. RESULTS:: The incidence of posterior vitreous detachment in fundoscopy over the follow-up period was 69.2% in the TPA group, which was significantly higher than that of the F/U and IVB groups (P = 0.001). Best-corrected visual acuity and changes in macular thickness did not significantly differ between the TPA and F/U groups over the 3-month period. CONCLUSION:: Intravitreal TPA injection induces posterior vitreous detachment in patients with diabetic macular edema refractory to standard treatment but has no effect on macular thickness or best-corrected visual acuity within 3 months. © The Ophthalmic Communications Society, Inc.

Drug Terms

alteplase, bevacizumab

Disease Terms

refractory diabetic macular edema, refractory diabetic macular edema, **macular edema**, vitreous body detachment

Other Terms

article, clinical article, controlled study, echography, follow up, human, incidence, ophthalmoscopy, optical coherence tomography, randomized controlled trial, visual acuity

Author Keywords

Posterior vitreous detachment, Refractory diabetic macular edema, Tissue plasminogen activator

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Abbreviated Journal Title	Retina
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Country of Author	Iran
Country of Source	United States
Language of Article	English
Language of Summary	English
MEDLINE PMID	21983248
Embase Accession Number	2011598883
Number of References	23
Cited by in Scopus	2
Drug Tradenames	actilyse (Boehringer, Germany), avastin (Genentech, United States)
Drug Manufacturers	Boehringer (Germany), Genentech (United States)
CAS Registry Numbers	alteplase (105857-23-6) bevacizumab (216974-75-3)
Clinical Trial Numbers	ClinicalTrials.gov (NCT01141881)

Record 23

Protective conditioning of the brain: Expressway or roadblock?

Mergenthaler P., Dirnagl U.

Journal of Physiology 2011 **589:17** (4147-4155)

The brain responds to noxious stimulation with protective signalling. Over the last decades, a number of experimental strategies have been established to study endogenous brain protection. Pre-, per-, post- and remote 'conditioning' are now widely used to unravel the underlying mechanisms of endogenous neuroprotection. Some of these strategies are currently being tested in clinical trials to protect the human brain against anticipated damage or to boost protective responses during or after injury. Here we summarize the principles of 'conditioning' research and current efforts to translate this knowledge into effective treatment of patients. Conditioning to induce protected brain states provides an experimental window into endogenous brain protection and can lead to the discovery of drugs mimicking the effects of conditioning. Mechanisms of endogenous brain tolerance can be activated through a wide variety of stimuli that

signal 'danger' to the brain. These danger signals lead to the induction of regulator and effector mechanisms, which suppress death and induce survival pathways, decrease metabolism, as well as increase substrate delivery. We conclude that preclinical research on endogenous brain protection has greatly benefited from conditioning strategies, but that clinical applications are challenging, and that we should not prematurely rush into ill-designed and underpowered clinical trials. © 2011 The Authors. Journal compilation © 2011 The Physiological Society.

Drug Terms

antioxidant, ax 200, deferoxamine, glyceraldehyde 3 phosphate dehydrogenase, hypoxia inducible factor 1, hypoxia inducible factor 1alpha, immunoglobulin enhancer binding protein, mitogen activated protein kinase, mitogen activated protein kinase p38, phosphoinositide dependent protein kinase 1, protein bcl 2, protein kinase C, recombinant granulocyte colony stimulating factor, sevoflurane, toll like receptor, tumor necrosis factor alpha, unclassified drug

Disease Terms

brain artery aneurysm, brain hypoxia, brain infection, brain injury, brain ischemia, brain vasospasm, ischemic heart disease, cerebrovascular accident, subarachnoid hemorrhage

Other Terms

blood clot lysis, **brain conditioning**, **brain protection**, cell cycle regulation, cell proliferation, **conditioning**, continuous infusion, deacetylation, DNA methylation, electroacupuncture, gene expression, heart surgery, homeostasis, human, ischemic preconditioning, oxidative phosphorylation, priority journal, review, signal transduction, vasomotor reflex

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Additional Information

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Country of Author	Germany
Country of Source	United Kingdom
Language of Article	English
Language of Summary	English
Embase Accession Number	2011484501
Number of References	83
Cited by in Scopus	18
Drug Tradenames	ax 200
CAS Registry Numbers	deferoxamine (70-51-9) glyceraldehyde 3 phosphate dehydrogenase (9001-50-7) mitogen activated protein kinase (142243-02-5) protein bcl 2 (219306-68-0) protein kinase C (141436-78-4) recombinant granulocyte colony stimulating factor (121181-53-1) sevoflurane (28523-86-6) toll like receptor (409141-78-2)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00756249, NCT00777140, NCT00877305, NCT00927836, NCT00975962, NCT01020266, NCT01110239, NCT01158508, NCT01204268, NCT01247545)

Record 24

Profiles of lacunar and nonlacunar stroke

Jickling G.C., Stamova B., Ander B.P., Zhan X., Tian Y., Liu D., Xu H., Johnston S.C., Verro P., Sharp F.R.

Annals of Neurology 2011 **70:3** (477-485)

Objective: Determining which small deep infarcts (SDIs) are of lacunar, arterial, or cardioembolic etiology is challenging, but important in delivering optimal stroke

prevention therapy. We sought to distinguish lacunar from nonlacunar causes of SDIs using a gene expression profile. Methods: A total of 184 ischemic strokes were analyzed. Lacunar stroke was defined as a lacunar syndrome with infarction <15mm in a region supplied by penetrating arteries. RNA from blood was processed on whole genome microarrays. Genes differentially expressed between lacunar (n = 30) and nonlacunar strokes (n = 86) were identified (false discovery rate ≤0.05, fold changegt|1.5|) and used to develop a prediction model. The model was evaluated by cross-validation and in a second test cohort (n = 36). The etiology of SDIs of unclear cause (SDIs a;circyen 15mm or SDIs with potential embolic source) (n = 32) was predicted using the derived model. Results: A 41-gene profile discriminated lacunar from nonlacunar stroke with>90% sensitivity and specificity. Of the 32 SDIs of unclear cause, 15 were predicted to be lacunar, and 17 were predicted to be nonlacunar. The identified profile represents differences in immune response between lacunar and nonlacunar stroke. Interpretation: Profiles of differentially expressed genes can distinguish lacunar from nonlacunar stroke. SDIs of unclear cause were frequently predicted to be of nonlacunar etiology, suggesting that comprehensive workup of SDIs is important to identify potential cardioembolic and arterial causes. Further study is required to evaluate the gene profile in an independent cohort and determine the clinical and treatment implications of SDIs of predicted nonlacunar etiology. © 2011 American Neurological Association.

Disease Terms

brain hemorrhage, brain infarction, brain infarction size, **brain ischemia**, hyperlipidemia, hypertension, **lacunar stroke**, **cerebrovascular accident**, transient ischemic attack

Other Terms

adult, African American, aged, article, Asian, blood sampling, Caucasian, clinical evaluation, controlled study, diastolic blood pressure, female, gene expression profiling, atrial fibrillation, Hispanic, human, immune response, major clinical study, male, microarray analysis, neuroimaging, nuclear magnetic resonance imaging, prediction, priority journal, sensitivity and specificity, small deep infarction, systolic blood pressure

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Additional Information

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Country of Source	United States
Language of Article	English
Language of Summary	English
MEDLINE PMID	21796664
Embase Accession Number	2011502832
Number of References	56
Cited by in Scopus	14
Clinical Trial Numbers	ClinicalTrials.gov (NCT00250991)

Record 25

A phase III, open-label, single-arm study of tenecteplase for restoration of function in dysfunctional central venous catheters

Tebbi C., Costanzi J., Shulman R., Dreisbach L., Jacobs B.R., Blaney M., Ashby M., Gillespie B.S., Begelman S.M.

Journal of Vascular and Interventional Radiology 2011 **22:8** (1117-1123)

Purpose: To evaluate, in a phase III, single-arm study, the safety and efficacy of the thrombolytic agent tenecteplase in restoring function to dysfunctional central venous catheters (CVCs). Materials and Methods: Pediatric and adult patients with dysfunctional CVCs were eligible to receive as much as 2 mL (2 mg) of intraluminal tenecteplase, which was left to dwell in the CVC lumen for a maximum of 120 minutes. If CVC function was not restored at 120 minutes, a second dose was instilled for an additional 120 minutes. Results: Tenecteplase was administered to 246 patients. Mean patient age was 44 years (range, 092 y); 72 patients (29%) were younger than 17 years of age.

Chemotherapy was the most common reason for catheter insertion. Restoration of CVC function was achieved in 177 patients (72%) within 120 minutes after the first dose. After instillation of a maximum of two doses of tenecteplase, CVC function was restored in 200 patients (81%), with similar frequencies in pediatric (83%) and adult (80%) patients. Adverse events (AEs) were reported in 31 patients (13%); fever (2%), neutropenia (1%), and nausea (0.8%) were most common. One serious AE, an allergic hypersensitivity reaction, was judged to be related to tenecteplase and/or a chemotherapeutic agent that the patient was receiving concurrently. Conclusions: Consecutive administration of one or two doses of tenecteplase into CVCs showed efficacy in the restoration of catheter function in patients with dysfunctional CVCs. © 2011 SIR.

Drug Terms

tenecteplase

Disease Terms

allergic reaction, **catheter complication**, dehydration, fever, nausea, neutropenia

Device Terms

central venous catheter

Other Terms

adolescent, adult, aged, article, child, drug efficacy, drug instillation, drug safety, female, human, infant, major clinical study, male, multicenter study, newborn, phase 3 clinical trial, preschool child, priority journal, school child

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Language of Article	English
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Publisher Item Identifier	S1051044311007421
MEDLINE PMID	21570873
Embase Accession Number	2011417254
Number of References	21
Cited by in Scopus	1
CAS Registry Numbers	tenecteplase (191588-94-0)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00396318)

Record 26

Risk stratification for acute pulmonary embolism

Kline J.A., Miller D.W.

JNCCN Journal of the National Comprehensive Cancer Network 2011 **9:7** (800-810)

This article discusses state-of-the-art techniques for predicting risk of death after acute pulmonary embolism (PE), with special attention to how underlying malignancy adversely affects survival after an episode. Current methods of risk stratification generally categorize patients with PE as low-, moderate-, and high-risk for inhospital adverse outcomes of respiratory failure, circulatory shock, and death. Published risk stratification studies find that patients with PE and an underlying malignancy have a worse prognosis, but no validated risk stratification criteria have been published

specifically for these patients. Standard treatment is full-dose heparin followed by oral anticoagulation. The term escalated treatment refers to the use of systemic or intrapulmonary fibrinolytic agents, catheter-based treatment, or surgical embolectomy. Most patients with low-risk PE (normal vital signs and normal serum troponin, brain natriuretic peptide, and normal echocardiography) are treated successfully with standard anticoagulation, and many can be treated as outpatients. In contrast, patients with high-risk PE (systolic blood pressure < 90 mm Hg and no contraindications) often benefit from escalated treatment. Treatment decisions for patients with moderate-risk PE (normotension with evidence of right ventricular damage or dysfunction) are most controversial. Most patients in this category of risk recover with standard therapy, but some benefit from escalated treatment. Patients with cancer with an incidentally discovered PE should be risk stratified the same as those who have clinically suspected PE. © JNCCN-Journal of the National Comprehensive Cancer Network.

Drug Terms

alteplase, amino terminal pro brain natriuretic peptide, brain natriuretic peptide, heparin, low molecular weight heparin, protamine, tenecteplase, troponin

Disease Terms

lung embolism, respiratory failure, shock

Other Terms

anticoagulation, article, clinical decision making, death, embolectomy, fibrinolysis, human, mortality, prognosis, risk assessment, survival

Author Keywords

Acute pulmonary embolism, Anticoagulation, Heparin, Respiratory failure, Risk stratification

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Country of Source	United States
Language of Article	English
Language of Summary	English
MEDLINE PMID	21715726
Embase Accession Number	2011379419
Number of References	93
Cited by in Scopus	5
CAS Registry Numbers	alteplase (105857-23-6) brain natriuretic peptide (114471-18-0) heparin (37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5) protamine (11061-43-1, 9007-31-2, 9012-00-4) tenecteplase (191588-94-0)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00639743, NCT00680628)

Record 27

Stroke and the immune system: From pathophysiology to new therapeutic strategies

Macrez R., Ali C., Toutirais O., Le Mauff B., Defer G., Dirnagl U., Vivien Denis D.

The Lancet Neurology 2011 **10:5** (471-480)

Stroke is the second most common cause of death worldwide and a major cause of acquired disability in adults. Despite tremendous progress in understanding the pathophysiology of stroke, translation of this knowledge into effective therapies has largely failed, with the exception of thrombolysis, which only benefits a small proportion of patients. Systemic and local immune responses have important roles in causing stroke and are implicated in the primary and secondary progression of ischaemic lesions, as well as in repair, recovery, and overall outcome after a stroke. However, potential therapeutic targets in the immune system and inflammatory responses have not been

well characterised. Development of novel and effective therapeutic strategies for stroke will require further investigation of these pathways in terms of their temporal profile (before, during, and after stroke) and risk-to-benefit therapeutic ratio of modulating them. © 2011 Elsevier Ltd.

Drug Terms

acetylsalicylic acid, alteplase, antihypertensive agent, clopidogrel, cyt 006 angqb 90, dipyridamole, endothelial leukocyte adhesion molecule 1, eprosartan, fibrinogen receptor antagonist, fibrinolytic agent, hydroxymethylglutaryl coenzyme A reductase inhibitor, influenza vaccine, intercellular adhesion molecule 1 antibody, interleukin 1 receptor blocking agent, lotrafiban, low molecular weight heparin, minocycline, nitrendipine, peptide vaccine, perindopril, placebo, pmd 3117 89, Pneumococcus vaccine, ticlopidine, tissue plasminogen activator, triflusal, unclassified drug, warfarin

Disease Terms

brain damage, brain hemorrhage, brain ischemia, infection, inflammation, influenza, physical disability, pneumococcal infection, **cerebrovascular accident**, unspecified side effect

Other Terms

adaptive immunity, anticoagulant therapy, antigen specificity, antiinflammatory activity, autoimmunity, blood pressure regulation, cause of death, central nervous system, chemoprophylaxis, clinical research, disease course, drug efficacy, fibrinolytic therapy, gamma delta T lymphocyte, human, immunological tolerance, immunomodulation, immunopathogenesis, influenza vaccination, **innate immunity**, low drug dose, molecular interaction, neuromodulation, neuropathology, nonhuman, pathophysiology, priority journal, regulatory mechanism, regulatory T lymphocyte, renin angiotensin aldosterone system, review, risk benefit analysis, risk reduction, T lymphocyte activation, vaccination

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Country of Source	United Kingdom
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Publisher Item Identifier	S1474442211700667
MEDLINE PMID	21511199
Embase Accession Number	2011215203
Number of References	135
Cited by in Scopus	81
Drug Tradenames	aspirin
CAS Registry Numbers	acetylsalicylic acid (493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1) alteplase (105857-23-6) clopidogrel (113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8) dipyridamole (58-32-2) endothelial leukocyte adhesion molecule 1 (128875-25-2) eprosartan (133040-01-4) lotrafiban (171049-14-2)

	minocycline (10118-90-8 , 11006-27-2 , 13614-98-7) nitrendipine (39562-70-4) perindopril (82834-16-0 , 99149-83-4) ticlopidine (53885-35-1 , 55142-85-3) tissue plasminogen activator (105913-11-9) triflusal (322-79-2) warfarin (129-06-6 , 2610-86-8 , 3324-63-8 , 5543-58-8 , 81-81-2)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00012454, NCT00069069, NCT00630396)

Record 28

Proteolytic networks in cancer

Mason S.D., Joyce J.A.

Trends in Cell Biology 2011 **21:4** (228-237)

Proteases are important for multiple processes during malignant progression, including tumor angiogenesis, invasion and metastasis. Recent evidence reveals that tumor-promoting proteases function as part of an extensive multidirectional network of proteolytic interactions, in contrast to the unidirectional caspase cascade. These networks involve different constituents of the tumor microenvironment and key proteases, such as cathepsin B, urokinase-type plasminogen activator and several matrix metalloproteinases, occupy central nodes for amplifying proteolytic signals passing through the network. The proteolytic network interacts with other important signaling pathways in tumor biology, involving chemokines, cytokines, and kinases. Viewing these proteolytic interactions as a system of activating and inhibiting reactions provides insight into tumor biology and reveals relevant pharmaceutical targets. This review examines recent advances in understanding proteases in cancer and summarizes how the network of activity is co-opted to promote tumor progression. © 2010 Elsevier Ltd.

Drug Terms

alteplase, antineoplastic agent, bortezomib, caspase, cathepsin B, cathepsin K inhibitor, cathepsin L, enzyme precursor, gelatinase A, gelatinase B, gemcitabine, indinavir, matrilysin, matrix metalloproteinase, matrix metalloproteinase 14, matrix metalloproteinase inhibitor, nelfinavir, plasminogen, proteasome inhibitor, proteinase, proteinase inhibitor, saquinavir, scleroprotein, tissue inhibitor of metalloproteinase, urokinase

Disease Terms

bone metastasis, Kaposi sarcoma, multiple myeloma, **neoplasm**, pancreas cancer, prostate cancer, solid tumor

Other Terms

apoptosis, cancer cell, cancer research, cancer therapy, carcinogenesis, catalysis, cell death, cell migration, clinical trial (topic), drug efficacy, drug inhibition, drug targeting, enzyme activity, extracellular matrix, gene regulatory network, gene targeting, human, in vivo study, nonhuman, plasminogen activation, priority journal, protein cleavage, **protein degradation**, protein function, **protein processing**, protein synthesis, proteomics, review, signal transduction, tumor growth, tumor microenvironment

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Publisher Item Identifier	S0962892410002709
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Number of References	99

Cited by in Scopus	124
CAS Registry Numbers	alteplase (105857-23-6) bortezomib (179324-69-7 , 197730-97-5) caspase (186322-81-6) cathepsin B (9047-22-7) cathepsin L (60616-82-2) gelatinase A (146480-35-5) gelatinase B (146480-36-6) gemcitabine (103882-84-4) indinavir (150378-17-9 , 157810-81-6 , 180683-37-8) matrilysin (141256-52-2) nelfinavir (159989-64-7 , 159989-65-8) plasminogen (9001-91-6) proteinase (9001-92-7) proteinase inhibitor (37205-61-1) saquinavir (127779-20-8 , 149845-06-7) tissue inhibitor of metalloproteinase (97837-28-0) urokinase (139639-24-0)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00086723, NCT00499265)

Record 29

Venous thromboembolism in the patient with cancer

Lyman G.H.

Cancer 2011 **117:7** (1334-1349)

Venous thromboembolism (VTE) is a significant cause of morbidity and mortality in patients with cancer. The risk of VTE varies over the natural history of cancer, with the highest risk occurring during hospitalization and after disease recurrence. Patient and disease characteristics are associated with further increased risk of VTE in this setting. Specific factors include cancer type (eg, pancreatic cancer, brain cancer, lymphoma) and the presence of metastatic disease at the time of diagnosis. VTE is a significant predictor of increased mortality during the first year among all types and stages of cancer, with metastatic disease reported to be the strongest predictor of mortality. VTE is also associated with early death in ambulatory patients with cancer. These data highlight the need for close monitoring, prompt treatment, and appropriate preventive strategies for VTE in patients with cancer. The American Society of Clinical Oncology and the National Comprehensive Cancer Network have issued guidelines regarding the prophylaxis and treatment of patients with cancer. This review summarizes the impact of VTE on patients with cancer, the effects of VTE on clinical outcomes, the importance of thromboprophylaxis in this population, relevant ongoing clinical trials examining the prevention of VTE, and new pharmacologic treatment options. Cancer 2011. © 2010 American Cancer Society.

Drug Terms

acenocoumarol, acetylsalicylic acid, antianemic agent, anticoagulant agent, antithrombin, antivitamin K, apixaban, bemiparin, bevacizumab, certoparin, dalteparin, dexamethasone, enoxaparin, fondaparinux, heparin, lenalidomide, low molecular weight heparin, nadroparin, placebo, rivaroxaban, semuloparin, thalidomide, tinzaparin, warfarin

Disease Terms

bleeding, brain cancer, colorectal cancer, deep vein thrombosis, lung cancer, lung embolism, lymphoma, metastasis, multiple myeloma, myelodysplastic syndrome, pancreas cancer, recurrent disease, thromboembolism, thrombosis, **venous thromboembolism**

Other Terms

cancer patient, cancer staging, disease course, hospitalization, human, medical society, morbidity, mortality, outcome assessment, practice guideline, prediction, priority journal, review, risk assessment, thrombosis prevention

Author Keywords

anticoagulant, cancer, chemotherapy, low molecular weight heparin (LMWH), thromboprophylaxis, venous thromboembolism (VTE)

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MEDLINE PMID	21425133
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Number of References	88
Cited by in Scopus	41
CAS Registry Numbers	acenocoumarol (152-72-7) acetylsalicylic acid (493-53-8 , 50-78-2 , 53663-74-4 , 53664-49-6 , 63781-77-1) antithrombin (9000-94-6) apixaban (503612-47-3) bevacizumab (216974-75-3) dexamethasone (50-02-2) enoxaparin (679809-58-6) fondaparinux (104993-28-4 , 114870-03-0) heparin (37187-54-5 , 8057-48-5 , 8065-01-8 , 9005-48-5) lenalidomide (191732-72-6) nadroparin (104521-37-1) rivaroxaban (366789-02-8) thalidomide (50-35-1) warfarin (129-06-6 , 2610-86-8 , 3324-63-8 , 5543-58-8 , 81-81-2)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00014352, NCT00031837, NCT00135876, NCT00216866, NCT00219973, NCT00239980, NCT00293501, NCT00320255, NCT00381888, NCT00394382, NCT00423683, NCT00462852, NCT00475098, NCT00519805, NCT00633061, NCT00662688, NCT00679588, NCT00694382, NCT00718354, NCT00723216, NCT00785421, NCT00876915, NCT00908960, NCT00952380, NCT00981903, NCT01130025)

Record 30

Improved glycemic control induced by both metformin and repaglinide is associated with a reduction in blood levels of 3-deoxyglucosone in nonobese patients with type 2 diabetes

Engelen L., Lund S.S., Ferreira I., Tarnow L., Parving H.-H., Gram J., Winther K., Pedersen O., Teerlink T., Barto R., Stehouwer C.D.A., Vaag A.A., Schalkwijk C.G.

European Journal of Endocrinology, Supplement 2011 **164:3** (371-379)

Objective: Metformin has been reported to reduce α-dicarbonyls, which are known to contribute to diabetic complications. It is unclear whether this is due to direct quenching of α-dicarbonyls or to an improvement in glycemic control. We therefore compared the effects of metformin versus repaglinide, an antihyperglycemic agent with an insulin-secreting mechanism, on the levels of the α-dicarbonyl 3-deoxyglucosone (3DG). Methods: We conducted a single-center, double-masked, double-dummy, crossover study involving 96 nonobese patients with type 2 diabetes. After a 1-month run-in on diet-only treatment, patients were randomized to either repaglinide (6 mg daily) followed by metformin (2 g daily) or vice versa each during 4 months with a 1-month washout between interventions. Results: 3DG levels decreased after both metformin (-19.3% (95% confidence interval (CI): -23.5, -14.8)) and repaglinide (-20.8% (95% CI:-24.9,-16.3)) treatments, but no difference was found between treatments (1.8% (95% CI: -3.8, 7.8)). Regardless of the treatment, changes in glycemic variables were associated with changes in 3DG. Specifically, 3DG decreased by 22.7% (95% CI: 19.0, 26.5) per S.D. decrease in fasting plasma glucose (PG), by 20.0% (95% CI: 16.2, 23.9) per S.D. decrease in seven-point mean plasma glucose, by 22.5% (95% CI: 18.6, 26.6) per S.D. decrease in area under the curve for PG, by 17.2% (95% CI: 13.8, 20.6) per S.D. decrease in HbAlc, and by 10.9% (95% CI: 6.4, 15.5) per S.D. decrease in Amadori albumin. In addition, decreases in 3DG were associated with decreases in advanced glycation endproducts and endothelial markers. Conclusion: Improved glycemic control induced by both metformin and repaglinide is associated with a reduction in 3DG levels in nonobese individuals with type 2 diabetes. This may constitute a shared metabolic pathway through which both treatments have a beneficial impact on the cardiovascular risk. © 2011 European Society of Endocrinology.

Drug Terms

3 deoxyglucosone, advanced glycation end product, alpha dicarbonyl 3 deoxyglucosone, hemoglobin A1c, **metformin**, **repaglinide**, unclassified drug

Disease Terms

endothelial dysfunction, inflammation, **non insulin dependent diabetes mellitus**

Other Terms

adult, article, controlled study, crossover procedure, drug efficacy, drug safety, female, glucose blood level, **glycemic control**, hemoglobin blood level, human, major clinical study, male, protein blood level, randomized controlled trial

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Number of References	32
Cited by in Scopus	6
CAS Registry Numbers	3 deoxyglucosone (4084-27-9) hemoglobin A1c (62572-11-6) metformin (1115-70-4 , 657-24-9) repaglinide (135062-02-1)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00118950)

Record 31

Novel IκB kinase inhibitors for treatment of nuclear factor-κB-related diseases

Suzuki J.-I., Ogawa M., Muto S., Itai A., Isobe M., Hirata Y., Nagai R.
Expert Opinion on Investigational Drugs 2011 **20:3** (395-405)

NF-κB is a key regulator of inflammation and immunity in cancer development. The IκB kinase (IKK) is a multisubunit complex containing catalytic subunits termed IKK-α, -β and -γ. It is well known that many pro-inflammatory stimuli require the IKK-β subunit for NF-κB activation. Areas covered: NF-κB affects the progression of inflammation-related diseases, such as myocardial ischemia, bronchial asthma, arthritis, cancer and other diseases. We review the characteristics and effects of these inhibitors on inflammatory and other diseases. Expert opinion: Various synthesized IKK inhibitors have been developed and they will be used clinically in the near future. © 2011 Informa UK, Ltd.

Drug Terms

1 [5 hydroxy 2 (2 thienyl) 4 quinazolinylamino] 3 methyl 2,5 pyrroledione,
2 amino 6 [2 (cyclopropylmethoxy) 6 hydroxyhydroxyphenyl] 4 piperidin 4 yl nicotinonitrile
4 (2 aminoethylamino) 1,8 dimethylimidazo[1,2 a]quinoxaline,
5 (thien 3 yl) 3 aminothiophene 2 carboxamide, 6 chloro 8 nicotinamido beta carboline,
7 [2 (cyclopropylmethoxy) 6 hydroxyphenyl] 5 (3 piperidinyl) 1,4 dihydro 2h pyrido[2,3 d]
bay 65 1942, brain natriuretic peptide, catechin, epigallocatechin gallate,
I kappa B kinase inhibitor, imd 0354, imd 0560, imd 1041,
immunoglobulin enhancer binding protein, intercellular adhesion molecule 1,
interleukin 1, interleukin 13, mitogen activated protein kinase 1,
n [2,5 bis(trifluoromethylphenyl)] 5 chloro 2 hydroxybenzamide,
n [3,5 bis(trifluoromethylphenyl)] 5 chloro 2 hydroxybenzamide,
nonsteroid antiinflammatory agent, placebo, sar 113945, sc 514, STAT3 protein,
stress activated protein kinase, theaflavin 3,3' digallate, tumor necrosis factor alpha,
unclassified drug

Disease Terms

acute lung injury, arthritis, asthma, atherosclerosis, cardiovascular disease,
chronic myeloid leukemia, chronic obstructive lung disease, dermatitis, fatty liver,
graft rejection, heart infarction, heart injury, heart muscle ischemia,
immune deficiency, knee osteoarthritis, liver disease, lung fibrosis, myocarditis,
neoplasm, neurologic disease, rheumatoid arthritis, skin disease

Other Terms

clinical trial (topic), cytokine production, down regulation, drug activity, drug effect,
drug half life, drug screening, gene deletion, graft survival, human, IC50, macrophage,
nonhuman, phase 2 clinical trial (topic), protein blood level, protein expression,
protein phosphorylation, randomized controlled trial (topic), review, signal transduction,
treatment outcome

Author Keywords

chemical compounds, IκB kinase, inflammation, NF-κB

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Language of Article	English
Language of Summary	English
MEDLINE PMID	21314234
Embase Accession Number	2011096161
Number of References	83
Cited by in Scopus	22
Drug Tradenames	as 602868, bay 65 1942, bms 345541, imd 0354, imd 0560, ps 1145, sc 514
CAS Registry Numbers	brain natriuretic peptide (114471-18-0) catechin (13392-26-2 , 154-23-4) epigallocatechin gallate (989-51-5) intercellular adhesion molecule 1 (126547-89-5) interleukin 13 (148157-34-0) mitogen activated protein kinase 1 (137632-08-7) stress activated protein kinase (155215-87-5) theaflavin 3,3' digallate (31629-80-8 , 33377-72-9)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00883584, NCT01113333)

Record 32

Improvement of hemodialysis catheter function with tenecteplase: A phase III, Open-label study: TROPICS 4

Fishbane S., Milligan S.L., Lempert K.D., Hertel J.E.W., Wetmore J.B., Oliver M.J., Blaney M., Gillespie B.S., Jacobs J.R., Begelman S.M.

Journal of Thrombosis and Thrombolysis 2011 **31:1** (99-106)

Hemodialysis (HD) catheters are prone to thrombotic occlusion. We evaluated tenecteplase, a thrombolytic, for the treatment of dysfunctional HD catheters. Patients with tunneled HD catheters and blood flow rate (BFR) <300 mL/min received open-label tenecteplase (2 mg/lumen) for a 1 h intracatheter dwell. Treatment success was defined as BFR ≥300 mL/min and a ≥25 mL/min increase from baseline BFR, 30 min before and at the end of HD. Patients without treatment success at the end of the initial visit received another 2 mg dose of tenecteplase for an up to 72 h extended dwell. Of 223 enrolled patients, 34% (95% confidence interval [CI], 28-40%) had treatment success after a 1 h dwell. Mean (standard deviation [SD]) BFR change from baseline was 82 (124) mL/min. Treatment success in those who received extended-dwell tenecteplase (n = 116) was 49% (95% CI, 40-58%), with mean (SD) BFR change from baseline of 117 (140) mL/min. Reported targeted adverse events included five catheter-related bloodstream infections and one thrombosis. No intracranial hemorrhage, major bleeding, embolic events, or catheter-related complications were reported. Tenecteplase administered as a 1 h or 1 h plus extended dwell was associated with improved HD catheter function in the TROPICS 4 trial. © 2010 Springer Science+Business Media, LLC.

Drug Terms

tenecteplase

Disease Terms

bacteremia, catheter infection, catheter occlusion, **catheter thrombosis**, gangrene, headache, hypertension, hypotension, muscle spasm, nausea, pruritus, side effect, thrombosis

Device Terms

dialysis catheter

Other Terms

adolescent, adult, aged, antibody titer, article, blood flow velocity, controlled clinical trial, drug efficacy, drug response, drug safety, female, **hemodialysis**, hemodynamics, human, male, patient assessment, phase 3 clinical trial, priority journal

Author Keywords

Chronic renal failure, Dialysis catheter, End-stage renal disease, Hemodialysis, Tenecteplase, Thrombolytic

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Country of Source	Netherlands
Language of Article	English
Language of Summary	English
MEDLINE PMID	20623319
Embase Accession Number	2011036925

Number of References	40
Cited by in Scopus	1
CAS Registry Numbers	tenecteplase (191588-94-0)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00396253)

Record 33

Neuroprotective drugs in traumatic CNS injury

Samantaray S., Thakore N.P., Matzelle D.D., Varma A., Ray S.K., Banik N.L.

Open Drug Discovery Journal 2010 **2:SPEC. ISS.3** (174-180)

Despite extensive experimental research, the numbers of neuroprotective drugs that have proven efficacy following treatment of patients with traumatic CNS injuries still remain meager. It would be worthwhile to emphasize that majority of the victims are mostly in the second or third decades of their lives. A survey on the neuroprotective molecules that has been tested experimentally and subsequently tried clinically has been found somewhat beneficial. In the present review, we consolidated the updates on a number of such drugs, which hold promise for therapy of traumatic CNS injuries. Two such agents, endogenous molecules estrogen and melatonin have been under investigation in our laboratory for their efficacy in experimental spinal cord injury in rats.

Drug Terms

armodafinil, citicoline, deferoxamine, dexanabinol, erythropoietin, **estrogen**, estrogen receptor alpha, estrogen receptor beta, **melatonin**, methylprednisolone, modafinil, phenytoin, recombinant erythropoietin, riluzole, rivastigmine, tirilazad, topiramate

Disease Terms

acute disease, brain edema, brain ischemia, cognitive defect, daytime somnolence, encephalomalacia, epilepsy, fatigue, seizure, spinal cord injury, **traumatic brain injury**

Other Terms

disease activity, disease association, drug effect, drug efficacy, drug mechanism, human, molecular pathology, neuroprotection, nonhuman, priority journal, review

Author Keywords

Estrogen, Melatonin, Neuroprotective agents, Spinal cord injury

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Source Publication Date	2010-01-01
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Publication Type	Review
Page Range	174-180
Country of Author	United States
Country of Source	Netherlands
Language of Article	English
Language of Summary	English
Embase Accession Number	2012422022
Number of References	35
Cited by in Scopus	2
CAS Registry Numbers	armodafinil (112111-43-0) citicoline (56257-85-3 , 987-78-0) deferoxamine (70-51-9) dexanabinol (112924-45-5) erythropoietin (11096-26-7) melatonin (73-31-4) methylprednisolone (6923-42-8 , 83-43-2) modafinil (68693-11-8) phenytoin (57-41-0 , 630-93-3) recombinant erythropoietin (113427-24-0 , 122312-54-3 , 130455-76-4 , 148363-16-0 , 154725-65-2 ,

	879555-13-2) riluzole (1744-22-5) rivastigmine (129101-54-8) tirilazad (110101-66-1 , 110101-67-2 , 111793-42-1) topiramate (97240-79-4)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00004759, NCT00129857, NCT00171795, NCT00219245, NCT00233090, NCT00413946, NCT00449961, NCT00489892, NCT00545662, NCT00561067, NCT00598923, NCT00702637, NCT00777140, NCT00808704, NCT00876889, NCT00879892, NCT00893789, NCT00910234, NCT00934700)

Record 34

Signatures of cardioembolic and large-vessel ischemic stroke

Jickling G.C., Xu H., Stamova B., Ander B.P., Zhan X., Tian Y., Liu D., Turner R.J., Mesias M., Verro P., Khoury J., Jauch E.C., Pancioli A., Broderick J.P., Sharp F.R.

Annals of Neurology 2010 **68:5** (681-692)

Objective: The cause of stroke remains unknown or cryptogenic in many patients. We sought to determine whether gene expression signatures in blood can distinguish between cardioembolic and large-vessel causes of stroke, and whether these profiles can predict stroke etiology in the cryptogenic group. Methods: A total of 194 samples from 76 acute ischemic stroke patients were analyzed. RNA was isolated from blood and run on Affymetrix U133 Plus2.0 microarrays. Genes that distinguish large-vessel from cardioembolic stroke were determined at 3, 5, and 24 hours following stroke onset. Predictors were evaluated using cross-validation and a separate set of patients with known stroke subtype. The cause of cryptogenic stroke was predicted based on a model developed from strokes of known cause and identified predictors. Results: A 40-gene profile differentiated cardioembolic stroke from large-vessel stroke with >95% sensitivity and specificity. A separate 37-gene profile differentiated cardioembolic stroke due to atrial fibrillation from nonatrial fibrillation causes with >90% sensitivity and specificity. The identified genes elucidate differences in inflammation between stroke subtypes. When applied to patients with cryptogenic stroke, 17% are predicted to be large-vessel and 41% to be cardioembolic stroke. Of the cryptogenic strokes predicted to be cardioembolic, 27% were predicted to have atrial fibrillation. Interpretation: Gene expression signatures distinguish cardioembolic from large-vessel causes of ischemic stroke. These gene profiles may add valuable diagnostic information in the management of patients with stroke of unknown etiology though they need to be validated in future independent, large studies. Ann Neurol 2010;68:681-692 © 2010 American Neurological Association.

Drug Terms

alteplase, B lymphocyte receptor, eptifibatide,
immunoglobulin enhancer binding protein, interleukin 10, interleukin 6,
mitogen activated protein kinase p38, phosphatidylinositol 4 phosphate,
thrombopoietin, toll like receptor, transcription factor NFAT

Disease Terms

brain ischemia, **cardioembolic stroke**, inflammation, **cerebrovascular accident**

Other Terms

adult, aged, article, cell proliferation, clinical trial, female, **gene expression profiling**, gene identification, atrial fibrillation, human, leukocyte, major clinical study, male, oxidative stress, prediction, predictor variable, priority journal,
renin angiotensin aldosterone system, RNA isolation, sensitivity and specificity, statistical model, T lymphocyte, validation process

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Additional Information

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	2010-11-30 (Full record), 2010-11-23 (Article

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Publication Type	Article
Page Range	681-692
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Country of Source	United States
Language of Article	English
Language of Summary	English
MEDLINE PMID	21031583
Embase Accession Number	2010621468
Number of References	25
Cited by in Scopus	40
Device Tradenames	Affymetrix U133
CAS Registry Numbers	alteplase (105857-23-6) eptifibatide (148031-34-9) thrombopoietin (9014-42-0) toll like receptor (409141-78-2) transcription factor NFAT (292890-46-1)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00250991)

Record 35

New devices for treating acute ischemic stroke

Rosenberg N., Chen M., Prabhakaran S.

Recent Patents on CNS Drug Discovery 2010 **5:2** (118-132)

The past decade has witnessed an explosion of devices available for treating acute ischemic stroke. Here, we review a range of recently patented devices and the data supporting their use. These include devices to enhance thrombolysis, thrombectomy devices, stents, devices for augmenting global brain tissue perfusion, and devices that provide neuroprotection after stroke. We discuss specific design elements of these devices and directions for future research. Ultimately, individually tailored combinations of these devices will likely prove most useful in treating patients with acute ischemic stroke. © 2010 Bentham Science Publishers Ltd.

Drug Terms

alteplase, heparin, perflutren, placebo, prourokinase, shu 508, sonovue

Disease Terms

brain ischemia, middle cerebral artery occlusion

Device Terms

stent, surgical equipment

Other Terms

article, blood clot lysis, brain tissue, clinical trial, cooling, human, induced hypothermia, low drug dose, low level laser therapy, neuroprotection, nonhuman, priority journal, recanalization, thrombectomy, tissue perfusion

Author Keywords

Angioplasty, Aortic occlusion, External counterpulsation [ecp], Hypothermia, Laser, Microbubble, Stent, Thrombectomy, Ultrasound

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Additional Information

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Page Range	118-132
Country of Author	United States
Country of Source	United Kingdom
Language of Article	English
Language of Summary	English
MEDLINE PMID	20408809
Embase Accession Number	2010352772
Number of References	164
Cited by in Scopus	2

Drug Manufacturers	Bayer (Germany), Bracco (United States)
CAS Registry Numbers	alteplase (105857-23-6) heparin (37187-54-5 , 8057-48-5 , 8065-01-8 , 9005-48-5) perflutren (184181-95-1 , 76-19-7) prourokinase (82657-92-9) shu 508 (127279-08-7)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00283088, NCT00336596, NCT00359424, NCT00389467, NCT00640367, NCT00653536, NCT00785161, NCT00963989, NCT01006993)

Record 36

Repurposing an old drug to improve the use and safety of tissue plasminogen activator for acute ischemic stroke: Minocycline

Hess D.C., Fagan S.C.

Pharmacotherapy 2010 **30:7 PART 2** (55S-61S)

Tissue plasminogen activator (tPA) is the only drug approved by the United States Food and Drug Administration for treatment of acute ischemic stroke. Because the drug must be used soon after symptom onset and is associated with intracerebral hemorrhage, tPA remains underutilized. Research has therefore focused on identifying other drugs that can be used concomitantly with tPA to improve the odds of a favorable recovery and to reduce the risk of intracerebral hemorrhage. Minocycline is a broad-spectrum antibiotic that has been found to be a neuroprotective agent in preclinical ischemic stroke models. Minocycline inhibits matrix metalloproteinase-9, a biomarker for intracerebral hemorrhage associated with tPA use. Minocycline is also an antiinflammatory agent and inhibits poly(ADP-ribose) polymerase-1. Minocycline has been safe and well tolerated in clinical trials. Additional safety and efficacy data are needed, and a phase III trial of minocycline with tPA in patients experiencing acute ischemic stroke is planned.

Drug Terms

biological marker, doxycycline, fibrinolytic agent, gelatinase B, **minocycline**, n (5,6 dihydro 6 oxo 2 phenanthridinyl) 2 dimethylaminoacetamide, nicotinamide adenine dinucleotide adenosine diphosphate ribosyltransferase 1, nicotinamide adenine dinucleotide adenosine diphosphate ribosyltransferase inhibitor, nonsteroid antiinflammatory agent, tetracycline, tigecycline, **tissue plasminogen activator**

Disease Terms

absence of side effects, acne, **acute disease**, adjuvant arthritis, brain hemorrhage, brain infarction size, **brain ischemia**, middle cerebral artery occlusion, periodontal disease, rheumatoid arthritis

Other Terms

clinical trial, convalescence, drug dose escalation, drug half life, drug mechanism, **drug safety**, drug tolerability, **drug use**, drug utilization, enzyme inhibition, food and drug administration, human, neuroprotection, nonhuman, recanalization, reperfusion, review, risk reduction, sex difference, symptom

Author Keywords

Acute ischemic stroke, Minocycline, MMP-9, PARP-1, Tissue plasminogen activator

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Country of Source	United States
Language of Article	English
Language of Summary	English
MEDLINE PMID	20575623
Embase Accession Number	2010395588
Number of References	66

Cited by in Scopus	8
Drug Tradenames	pj 34
CAS Registry Numbers	doxycycline (10592-13-9 , 17086-28-1 , 564-25-0) gelatinase B (146480-36-6) minocycline (10118-90-8 , 11006-27-2 , 13614-98-7) n (5,6 dihydro 6 oxo 2 phenanthridinyl) 2 dimethylaminoacetamide (344458-15-7 , 344458-19-1) tetracycline (23843-90-5 , 60-54-8 , 64-75-5 , 8021-86-1) tigecycline (220620-09-7) tissue plasminogen activator (105913-11-9)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00630396)

Record 37

Gene expression profiling of blood for the prediction of ischemic stroke

Stamova B., Xu H., Jickling G., Bushnell C., Tian Y., Ander B.P., Zhan X., Liu D., Turner R., Adamczyk P., Khoury J.C., Pancioli A., Jauch E., Broderick J.P., Sharp F.R.

Stroke 2010 **41:10** (2171-2177)

Background And Purpose-: A blood-based biomarker of acute ischemic stroke would be of significant value in clinical practice. This study aimed to (1) replicate in a larger cohort our previous study using gene expression profiling to predict ischemic stroke; and (2) refine prediction of ischemic stroke by including control groups relevant to ischemic stroke. Methods-: Patients with ischemic stroke (n=70, 199 samples) were compared with control subjects who were healthy (n=38), had vascular risk factors (n=52), and who had myocardial infarction (n=17). Whole blood was drawn ≤3 hours, 5 hours, and 24 hours after stroke onset and from control subjects. RNA was processed on whole genome microarrays. Genes differentially expressed in ischemic stroke were identified and analyzed for predictive ability to discriminate stroke from control subjects. Results-: The 29 probe sets previously reported predicted a new set of ischemic strokes with 93.5% sensitivity and 89.5% specificity. Sixty- and 46-probe sets differentiated control groups from 3-hour and 24-hour ischemic stroke samples, respectively. A 97-probe set correctly classified 86% of ischemic strokes (3 hour+24 hour), 84% of healthy subjects, 96% of vascular risk factor subjects, and 75% with myocardial infarction. Conclusions-: This study replicated our previously reported gene expression profile in a larger cohort and identified additional genes that discriminate ischemic stroke from relevant control groups. This multigene approach shows potential for a point-of-care test in acute ischemic stroke. © 2010 American Heart Association, Inc.

Drug Terms

alteplase, biological marker, blood clotting factor 5, eptifibatide, RNA, thrombomodulin

Disease Terms

cerebrovascular accident, heart infarction

Other Terms

aged, article, blood, cardiovascular risk, clinical trial, cohort analysis, controlled study, diagnostic accuracy, female, **gene expression profiling**, genome, human, major clinical study, male, microarray analysis, **prediction**, priority journal, sensitivity and specificity

Author Keywords

biomarkers, blood, gene expression profiling, ischemia, stroke

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Embase Accession Number	2010574726
Number of References	13
Cited by in Scopus	41
CAS Registry Numbers	alteplase (105857-23-6) blood clotting factor 5 (9001-24-5 , 9013-23-4) eptifibatide (148031-34-9) RNA (63231-63-0) thrombomodulin (112049-68-0)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00250991)

Record 38

The complexity of neurobiological processes in acute ischemic stroke

Brouns R., De Deyn P.P.

Clinical Neurology and Neurosurgery 2009 **111:6** (483-495)

There is an urgent need for improved diagnostics and therapeutics for acute ischemic stroke. This is the focus of numerous research projects involving in vitro studies, animal models and clinical trials, all of which are based on current knowledge of disease mechanisms underlying acute focal cerebral ischemia. Insight in the chain of events occurring during acute ischemic injury is essential for understanding current and future diagnostic and therapeutic approaches. In this review, we summarize the actual knowledge on the pathophysiology of acute ischemic stroke. We focus on the ischemic cascade, which is a complex series of neurochemical processes that are unleashed by transient or permanent focal cerebral ischemia and involves cellular bioenergetic failure, excitotoxicity, oxidative stress, blood-brain barrier dysfunction, microvascular injury, hemostatic activation, post-ischemic inflammation and finally cell death of neurons, glial and endothelial cells.

Drug Terms

cutamesine, acetylsalicylic acid, activated protein C, albumin, alteplase, argatroban, arundic acid, candesartan, chorionic gonadotropin, citicoline, desmoteplase, eptifibatide, fibrinolytic agent, herbaceous agent, insulin, magnesium, minocycline, mk 0724, plasminogen, recombinant erythropoietin, tenecteplase, tinzaparin, unclassified drug, v 10153

Disease Terms

brain damage, brain ischemia, **cerebrovascular accident**, excitotoxicity, hypercoagulability, inflammation, microangiopathy, nerve cell necrosis, reperfusion injury

Other Terms

bioenergy, blood brain barrier, brain perfusion, cell death, clinical trial, continuous infusion, embolectomy, endothelium cell, Ginkgo biloba, glia cell, hematopoietic stem cell transplantation, hemostasis, human, neurochemistry, **neuropathology**, neuroprotection, oxidative stress, oxygen therapy, pathophysiology, positive end expiratory pressure, review, thrombocyte activation, transcranial magnetic stimulation

Author Keywords

Acute ischemic stroke, Bioenergetic failure, Blood-brain barrier dysfunction, Excitoxicity, Hemostatic activation, Microvascular injury, Oxidative stress, Pathophysiology, Post-ischemic inflammation

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Additional Information

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Language of Article	English
Language of Summary	English
Publisher Item Identifier	S0303846709000821
MEDLINE PMID	19446389
Embase Accession Number	2009245214
Number of References	243
Cited by in Scopus	135
Drug Tradenames	mk 0724, sa 4503, v 10153
CAS Registry Numbers	acetylsalicylic acid (493-53-8 , 50-78-2 , 53663-74-4 , 53664-49-6 , 63781-77-1) alteplase (105857-23-6) argatroban (74863-84-6) arundic acid (185517-21-9) candesartan (139481-59-7) chorionic gonadotropin (9002-61-3) citicoline (56257-85-3 , 987-78-0) desmoteplase (145137-38-8) eptifibatide (148031-34-9) insulin (9004-10-8) magnesium (7439-95-4) minocycline (10118-90-8 , 11006-27-2 , 13614-98-7) plasminogen (9001-91-6) recombinant erythropoietin (113427-24-0 , 122312-54-3 , 130455-76-4 , 879555-13-2) tenecteplase (191588-94-0)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00059332, NCT00061373, NCT00119717, NCT00120003, NCT00144014, NCT00235495, NCT00252239, NCT00268762, NCT00276380, NCT00299416, NCT00331890, NCT00359424, NCT00368628, NCT00389467, NCT00401310, NCT00414726, NCT00472381, NCT00533546, NCT00535197, NCT00630396, NCT00639249, NCT00640367, NCT00663416, NCT00697645, NCT00715364, NCT00790920)

Record 39

Transcranial ultrasound in clinical sonothrombolysis (TUCSON) trial

Molina C.A., Barreto A.D., Tsivgoulis G., Sierzenski P., Malkoff M.D., Rubiera M., Gonzales N., Mikulik R., Pate G., Ostrem J., Singleton W., Manvelian G., Unger E.C., Grotta J.C., Schellinger P.D., Alexandrov A.V.

Annals of Neurology 2009 **66:1** (28-38)

Objective: Microspheres (μS) reach intracranial occlusions and transmit energy momentum from an ultrasound wave to residual flow to promote recanalization. We report a randomized multicenter phase II trial of μS dose escalation with systemic thrombolysis. Methods: Stroke patients receiving 0.9mg/kg tissue plasminogen activator (tPA) with pretreatment proximal intracranial occlusions on transcranial Doppler (TCD) were randomized (2:1 ratio) to μS (MRX-801) infusion over 90 minutes (Cohort 1, 1.4ml; Cohort 2, 2.8ml) with continuous TCD insonation, whereas controls received tPA and brief TCD assessments. The primary endpoint was symptomatic intracerebral hemorrhage (sICH) within 36 hours after tPA. Results: Among 35 patients (Cohort 1 = 12, Cohort 2 = 11, controls = 12) no sICH occurred in Cohort 1 and controls, whereas 3 (27%, 2 fatal) sICHs occurred in Cohort 2 (p = 0.028). Sustained complete recanalization/clinical recovery rates (end of TCD monitoring/3 month) were 67%/75% for Cohort 1, 46%/50% for Cohort 2, and 33%/36% for controls (p = 0.255/0.167). The median time to any recanalization tended to be shorter in Cohort 1 (30 min; interquartile range [IQR], 6) and Cohort 2 (30 min; IQR, 69) compared to controls (60 min; IQR, 5; p = 0.054). Although patients with sICH had similar screening and pretreatment systolic blood pressure (SBP) levels in comparison to the rest, higher SBP levels were documented in sICH+ patients at 30 minutes, 60 minutes, 90 minutes, and 24-36 hours following tPA bolus. Interpretation: Perflutren lipid μS can be safely combined with systemic tPA and ultrasound at a dose of 1.4ml. Safety concerns in the second dose tier may necessitate extended enrollment and further experiments to determine the mechanisms by which microspheres interact with tissues. In both dose tiers, sonothrombolysis with μS and tPA shows a trend toward higher early recanalization and clinical recovery rates compared to standard intravenous tPA therapy.

Drug Terms

hemoglobin, **perflutren**, **perflutren**, **tissue plasminogen activator**, unclassified drug

Disease Terms

acute kidney failure, angioneurotic edema, atelectasis, brain hemorrhage, dyspnea, hematuria, hepatobiliary disease, hypoxia, lung edema, lung embolism, **cerebrovascular accident**, urinary tract infection

Other Terms

adult, aged, article, blood pressure, clinical article, clinical trial, computer assisted tomography, controlled clinical trial, controlled study, demography, Doppler echography, drug efficacy, drug safety, **fibrinolytic therapy**, hematocrit, human, international normalized ratio, liver function test, mortality, multicenter study, phase 2 clinical trial, priority journal, randomized controlled trial, recanalization, single blind procedure, **sonothrombolysis**, statistical analysis, ultrasound, urine volume

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Language of Article	English
Language of Summary	English
MEDLINE PMID	19670432
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Number of References	40
Cited by in Scopus	99
Drug Tradenames	mrx 801
CAS Registry Numbers	hemoglobin (9008-02-0) perflutren (184181-95-1 , 76-19-7) tissue plasminogen activator (105913-11-9)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00504842)

Record 40

Ultrasound enhancement of fibrinolysis

Alexandrov A.V.

Stroke 2009 **40:3 SUPPL. 1** (S107-S110)

Systemic administration of tissue plasminogen activator (tPA) remains the fastest way to initiate treatment for acute ischemic stroke. The presence of a proximal arterial occlusion should not be viewed as an insurmountable predictor of tPA failure. Because tPA works by induction of partial recanalization of large thrombi, early augmentation of fibrinolysis to improve recanalization is desirable. This augmentation is feasible and can be safely achieved at the bedside with diagnostic Doppler ultrasound. In the CLOTBUST trial, 83% of patients achieved any recanalization (46% complete, 27% partial) with

tPA+transcranial Doppler vs 50% (17% complete, 33% partial) with tPA alone within 2 hours of treatment (P<0.001). Sustained, complete recanalization at 2 hours was 38% vs 13%, respectively (f=0.03). A recent meta-analysis of 6 randomized and 3 nonrandomized clinical studies of sonothrombolysis showed that any diagnostic ultrasound monitoring can at least double the chance of early complete arterial recanalization at no increase in the risk of symptomatic intracerebral hemorrhage. Because application in humans of frequencies below the diagnostic range resulted in increased symptomatic bleeding rates, mechanisms by which megahertz and kilohertz frequencies interact with the clot-residual flow interface and endothelium are currently under renewed investigations. Catheter-based ultrasound delivery to arterial thrombi and intraventricular clots is the subject of ongoing clinical trials. Addition of gaseous perflutren-lipid microspheres to tPA and transcranial Doppler can further facilitate early flow improvement, with a 50% rate of early, complete recanalization in a recent feasibility study. Transcranial ultrasound delivery in an operator-independent and dose-controlled manner is being tested in a clinical trial. © 2009 American Heart Association, Inc.

Drug Terms

contrast medium, **fibrinolytic agent**, **microsphere**, **perflutren**, shu 508, sonovue, **tissue plasminogen activator**

Disease Terms

acute disease, bleeding, brain hemorrhage, brain ischemia, occlusive cerebrovascular disease, **cerebrovascular accident**

Device Terms

catheter

Other Terms

brain angiography, clinical trial, computed tomographic angiography, conference paper, digital subtraction angiography, **Doppler echography**, **drug delivery system**, drug dose escalation, drug efficacy, drug safety, **fibrinolytic therapy**, human, image quality, magnetic resonance angiography, neuroimaging, priority journal, treatment outcome, **ultrasound**

Author Keywords

Outcomes, Stroke, Thrombolysis, tPA, Ultrasound

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Page Range	S107-S110
Country of Author	United States
Country of Source	United States
Language of Article	English
Language of Summary	English
MEDLINE PMID	19064806
Embase Accession Number	2009143859
Number of References	38
Cited by in Scopus	28
Drug Tradenames	levovist, sonovue (Bracco)
Drug Manufacturers	Bracco
CAS Registry Numbers	perflutren (184181-95-1 , 76-19-7) shu 508 (127279-08-7) tissue plasminogen activator (105913-11-9)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00504842)

Record 41

Effect of almonds on insulin secretion and insulin resistance in nondiabetic hyperlipidemic subjects: a randomized controlled crossover trial

Jenkins D.J.A., Kendall C.W.C., Marchie A., Josse A.R., Nguyen T.H., Faulkner D.A., Lapsley K.G., Singer W.

Metabolism: Clinical and Experimental 2008 **57:7** (882-887)

Nuts appear to have a marked effect in cohort studies in reducing the risk of coronary heart disease (CHD), but their demonstrated ability to lower cholesterol can only explain a proportion of the reduction in risk. Our aim was to assess whether improvement in carbohydrate metabolism provides a further explanation for the effect of nuts in reducing CHD. The effects of whole almonds, taken as snacks, were compared with the effects of low saturated fat (<5% energy) whole-wheat muffins (control) in the therapeutic diets of hyperlipidemic subjects. In a randomized crossover study, 27 hyperlipidemic men and women consumed 3 isoenergetic (mean, 423 kcal/d) supplements each for 1 month. Supplements provided 22.2% of energy and consisted of full-dose almonds (73 ± 3 g/d), half-dose almonds plus half-dose muffins, and full-dose muffins. Subjects were assessed at weeks 0, 2, and 4 and fasting blood samples were obtained. Twenty-four-hour urinary output was collected at the end of week 4 on each treatment. Mean body weights differed by less than 300 g between treatments. No differences were seen in baseline or treatment values for fasting glucose, insulin, C-peptide, or insulin resistance as measured by homeostasis model assessment of insulin resistance. However, 24-hour urinary C-peptide output as a marker of 24-hour insulin secretion was significantly reduced on the half-and full-dose almonds by comparison to the control after adjustment for urinary creatinine output (P = .002 and P = .004, respectively). We conclude that reductions in 24-hour insulin secretion appear to be a further metabolic advantage of nuts that in the longer term may help to explain the association of nut consumption with reduced CHD risk.

Drug Terms

biological marker, C peptide, carbohydrate, creatinine, insulin, saturated fatty acid

Disease Terms

diabetes mellitus, **hyperlipidemia**, **insulin resistance**, ischemic heart disease

Other Terms

adult, aged, **almond**, article, blood sampling, body weight, carbohydrate metabolism, clinical trial, controlled clinical trial, controlled study, crossover procedure, diet restriction, diet therapy, energy consumption, female, human, insulin release, male, priority journal, randomized controlled trial, urine volume, wheat

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Country of Source	United States
Language of Article	English
Language of Summary	English
Publisher Item Identifier	S0026049508000656
MEDLINE PMID	18555827
Embase Accession Number	2008283422
Number of References	46
Cited by in Scopus	19
CAS Registry Numbers	C peptide (59112-80-0) creatinine (19230-81-0 , 60-27-5) insulin (9004-10-8)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00507520)

Record 42

Ultrasound-enhanced thrombolysis: From bedside to bench

Tsivgoulis G., Alexandrov A.

Stroke 2008 **39:5** (1404-1405)

Drug Terms

microsphere, **tissue plasminogen activator**

Disease Terms

brain hemorrhage, brain ischemia, **cerebrovascular accident**, occlusive cerebrovascular disease, cerebrovascular accident, subarachnoid hemorrhage

Other Terms

blood clot lysis, clinical trial, echography, editorial, fibrinolysis, human, nonhuman, priority journal, recanalization, **ultrasound**

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Page Range	1404-1405
Country of Source	United States
Language of Article	English
Publisher Item Identifier	000076702008050000002
MEDLINE PMID	18340099
Embase Accession Number	2009251862
Number of References	16
Cited by in Scopus	13
CAS Registry Numbers	tissue plasminogen activator (105913-11-9)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00504842)

Record 43

Almonds reduce biomarkers of lipid peroxidation in older hyperlipidemic subjects

Jenkins D.J.A., Kendall C.W.C., Marchie A., Josse A.R., Nguyen T.H., Faulkner D.A., Lapsley K.G., Blumberg J.

Journal of Nutrition 2008 **138:5** (908-913)

Nut consumption has been associated with reduced coronary heart disease (CHD) risk. In addition to cholesterol-lowering properties, almonds have been shown to lower oxidized LDL concentrations. However, little is known regarding their effects on other markers of oxidative stress. The dose-response effects of whole almonds, taken as snacks, were compared with low-saturated fat (<5% energy) whole-wheat muffins (control) in the therapeutic diets of hyperlipidemic subjects. In a randomized crossover study, 27 hyperlipidemic men and women consumed 3 isoenergetic (mean 423 kcal/d or 1770 kJ/d) supplements each for 1 mo. Supplements consisted of full-dose almonds (73 ± 3 g/d), half-dose almonds plus half-dose muffins (half-dose almonds), and full-dose muffins (control). Subjects were assessed at wk 0, 2 and 4. Mean body weights differed ≤300 g between treatments, although the weight loss on the half-dose almond treatment was greater than on the control ($P < 0.01$). At 4 wk, the full-dose almonds reduced serum concentrations of malondialdehyde (MDA) ($P = 0.040$) and creatinine-adjusted urinary isoprostane output ($P = 0.026$) compared with the control. Serum concentrations of α- or γ-tocopherol, adjusted or unadjusted for total cholesterol, were not affected by the treatments. Almond antioxidant activity was demonstrated by their effect on 2 biomarkers of lipid peroxidation, serum MDA and urinary isoprostanes, and supports the previous finding that almonds reduced oxidation of LDL-C. Antioxidant activity provides an additional possible mechanism, in addition to lowering cholesterol, that may account for the reduction in CHD risk with nut consumption. © 2008 American Society for Nutrition.

Drug Terms

angiotensin 2 receptor antagonist, **biological marker**, hydroxymethylglutaryl coenzyme A reductase inhibitor, isoprostane derivative, levothyroxine, malonaldehyde, thiazide diuretic agent

Disease Terms

hyperlipidemia

Other Terms

almond, antioxidant activity, article, cardiovascular risk, cholesterol blood level,

clinical article, clinical trial, controlled clinical trial, controlled study, crossover procedure, diet supplementation, diet therapy, female, human, **lipid oxidation**, low fat diet, male, oxidative stress, randomized controlled trial, risk reduction, weight reduction

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Source Publication Date	May 2008
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Country of Author	Canada
Country of Source	United States
Language of Article	English
Language of Summary	English
MEDLINE PMID	18424600
Embase Accession Number	2008195737
Number of References	58
Cited by in Scopus	57
CAS Registry Numbers	levothyroxine (51-48-9) malonaldehyde (542-78-9)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00507520)

Record 44

Antiplatelet therapy and the risk of intracranial hemorrhage after intravenous tissue plasminogen activator therapy for acute ischemic stroke

Hallevi H., Grotta J.C.
Archives of Neurology 2008 **65:5** (575-576)

Drug Terms

acetylsalicylic acid, argatroban, dipyridamole, eptifibatide, fibrin, thrombin, **tissue plasminogen activator**

Disease Terms

acute disease, artery occlusion, brain hemorrhage, **cerebrovascular accident**

Other Terms

clinical trial, combination chemotherapy, disease association, drug mechanism, editorial, human, monotherapy, nuclear magnetic resonance imaging, priority journal, risk assessment, thrombocyte activation, thrombocyte function, treatment outcome

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Abbreviated Journal Title	Arch. Neurol.
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CODEN	ARNEA
Source Type	Journal
Source Publication Date	May 2008

Entry Date	2008-06-20 (Full record)
Publication Type	Editorial
Page Range	575-576
Country of Author	United States
Country of Source	United States
Language of Article	English
MEDLINE PMID	18474730
Embase Accession Number	2008237154
Number of References	9
Cited by in Scopus	3
Drug Tradenames	aspirin
CAS Registry Numbers	acetylsalicylic acid (493-53-8 , 50-78-2 , 53663-74-4 , 53664-49-6 , 63781-77-1) argatroban (74863-84-6) dipyridamole (58-32-2) eptifibatide (148031-34-9) fibrin (9001-31-4) thrombin (9002-04-4) tissue plasminogen activator (105913-11-9)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00250991)

Record 45

A pilot study of central venous catheter survival in cancer patients using low-molecular-weight heparin (dalteparin) and warfarin without catheter removal for the treatment of upper extremity deep vein thrombosis (The Catheter Study)

Kovacs M.J., Kahn S.R., Rodger M., Anderson D.R., Andreou R., Mangel J.E., Morrow B., Clement A.M., Wells P.S.

Journal of Thrombosis and Haemostasis 2007 **5:8** (1650-1653)

Background: Central venous catheters in patients with cancer are associated with development of deep vein thrombosis (DVT); however, there is no accepted standard treatment. Objectives: To assess the safety and effectiveness of a management strategy for central venous catheter-related DVT in cancer patients consisting of dalteparin and warfarin without the need for line removal. Patients/methods: Patients older than 18 years of age with an active malignancy and who had symptomatic, acute, objectively documented UEDVT were eligible. Patients were treated with dalteparin 200 IU kg -1 per day for 5-7 days and warfarin with a target International Normalized Ratio of 2.0-3.0. Patients were followed for 3 months for recurrent venous thromboembolism, major hemorrhage and survival of the central venous catheter. Results: There were 74 patients (48 males). The average age was 58 years. There were no episodes of recurrent venous thromboembolism and three (4%) major bleeds. No lines were removed because of infusion failure or recurrence/extension of DVT. Conclusion: Treatment of UEDVTs secondary to central catheters in cancer patients with standard dalteparin/warfarin can allow the central line to remain in situ with little risk of line failure or recurrence/extension of the DVT. © 2007 International Society on Thrombosis and Haemostasis.

Drug Terms

dalteparin, low molecular weight heparin, **warfarin**

Disease Terms

catheter thrombosis, **deep vein thrombosis**, epistaxis, lung embolism, menorrhagia, recurrent disease, side effect, upper gastrointestinal bleeding, venous thromboembolism

Device Terms

central venous catheter

Other Terms

adult, arm, article, cancer patient, catheter removal, clinical effectiveness, clinical trial, cohort analysis, disease association, drug efficacy, drug response, drug safety, drug substitution, drug withdrawal, female, follow up, human, international normalized ratio, major clinical study, male, multicenter study, pilot study, priority journal, risk assessment

Author Keywords

Cancer, Central venous catheter, Low-molecular weight heparin, Treatment, Upper extremity deep vein thrombosis

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Country of Source	United Kingdom
Language of Article	English
Language of Summary	English
MEDLINE PMID	17488349
Embase Accession Number	2007356425
Number of References	17
Cited by in Scopus	66
CAS Registry Numbers	warfarin (129-06-6 , 2610-86-8 , 3324-63-8 , 5543-58-8 , 81-81-2)
Clinical Trial Numbers	ClinicalTrials.gov (NCT00216866)

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