1- 2011 Apr 8. [Epub ahead of print]

Prevention of atrial fibrillation with omega-3 fatty acids: a meta-analysis of randomised clinical trials.

Liu T, Korantzopoulos P, Shehata M, Li G, Wang X, Kaul S.

Abstract

Context Previous randomised controlled trials (RCT) regarding n-3 PUFA supplementation for atrial fibrillation (AF) prevention have yielded conflicting results. Objective A systematic review and meta-analysis of RCT was conducted to examine the role of n-3 PUFA in AF prevention. Data Sources MEDLINE, Web of Science and Cochrane clinical trials database were searched until November 2010. Study Selection Of 127 initially identified studies, 10 RCT with 1955 patients were finally analysed. Data Extraction Two blinded reviewers extracted data independently to a predefined form. Disagreements were resolved through discussion and consensus. Results n-3 PUFA had no significant effect on the prevention of AF (OR 0.81, 95% CI 0.57 to 1.15; p=0.24). There was significant heterogeneity among the studies (p=0.002, I(2)=65.0%). Subgroup analysis showed no significant beneficial effect of fish oils in any subset of population. Conclusions No significant effects of n-3 PUFA supplementation on AF prevention were observed in this meta-analysis. A large-scale trial with higher doses and longer follow-up might be required to rule out the possibility of any treatment benefit.

2- Br J Sports Med. 2011 Apr 6. [Epub ahead of print]

Prevention of sport injury II: a systematic review of clinical science research.

McBain K, Shrier I, Shultz R, Meeuwisse WH, Klügl M, Garza D, Matheson GO.

Abstract

Objective To characterise the nature of the sport injury prevention literature by reviewing published articles that evaluate specific clinical interventions designed to reduce sport injury risks. Data sources PubMed, Cinahl, Web of Science and Embase. Main results Only 139 of 2525 articles retrieved met the inclusion criteria. Almost 40% were randomised controlled trials and 30.2% were cohort studies. The focus of the study was protective equipment in 41%, training in 32.4%, education in 7.9%, rules and regulations in 4.3%, and 13.3% involved a combination of the above. Equipment research studied stability devices (42.1%), head and face protectors (33.3%), attenuating devices (17.5%) as well as other devices (7%). Training studies often used a combination of interventions (eg, balance and stretching); most included balance and coordination (63.3%), with strength and power (36.7%) and stretching (22.5%) being less common. Almost 70% of the studies examined lower extremity injuries, and a majority of these were joint (non-bone)-ligament injuries. Contact sports were most frequently studied (41.5%), followed by collision (39.8%) and non-contact (20.3%). Conclusion The authors found only 139 publications in the existing literature that examined interventions designed to prevent sports injury. Of these, the majority investigated equipment or training interventions whereas only 4% focused on changes to the rules and regulations that govern sport. The focus of intervention research is on acute injuries in collision and contact sports whereas only 20% of the studies focused on non-contact sports.

3- Eur Heart J. 2011 Apr 6. [Epub ahead of print]

Achievement of treatment goals for primary prevention of cardiovascular disease in clinical practice across Europe: the EURIKA study.

Banegas JR, López-García E, Dallongeville J, Guallar E, Halcox JP, Borghi C, Massó-González EL, Jiménez FJ, Perk J, Steg PG, De Backer G, Rodríguez-Artalejo F.

Abstract

Aims Most studies on the primary prevention of cardiovascular disease (CVD) have been limited to patients at high CVD risk. We assessed the achievement of treatment goals for CVD risk factors among patients with a substantial variation in CVD risk. Methods and results This study was conducted with 7641 outpatients aged ≥50 years, free of clinical CVD and with at least one major CVD risk factor, selected from 12 European countries in 2009. Risk factor definition and treatment goals were based on the 2007 European guidelines on CVD prevention. Cholesterol fractions and glycated haemoglobin (HbA1c) were measured in a central laboratory. Cardiovascular disease risk was estimated with the

SCORE equation. Patients' mean age was 63 years (48% men), and 40.1% had a high CVD risk. Among treated hypertensives (94.2%), only 38.8% achieved the blood pressure target of <140/90 mmHg [between-country range (BCR): 32.1-47.5%]. Among treated dyslipidaemic patients (74.4%), 41.2% attained both the total- and LDL-cholesterol target of <5 and <3 mmol/L, respectively (BCR: 24.3-68.4%). Among treated type 2 diabetic patients (87.2%), 36.7% achieved the <6.5% HbA1c target (BCR: 23.4-48.4%). Among obese patients on non-pharmacological treatment (92.2%), 24.7% reached the body mass index target of <30 kg/m(2) (BCR: 12.7-37.1%). About one-third of controlled patients on treatment were still at high remaining CVD risk. Although most patients were advised to reduce excess weight and to follow a low-calorie diet, less than half received written recommendations. Conclusions In Europe, a large proportion of patients in primary prevention have CVD risk factors that remain uncontrolled, and lifestyle counselling is not well implemented; moreover, there is substantial between-country variation, which indicates additional room for improvement. Raised residual CVD risk is relatively frequent among patients despite control of their primary risk factors and should be addressed.

4- Arch Pediatr Adolesc Med. 2011 Apr;165(4):306-12.

Couple-focused human immunodeficiency virus prevention for young latino parents: randomized clinical trial of efficacy and sustainability.

Koniak-Griffin D, Lesser J, Takayanagi S, Cumberland WG.

Abstract

OBJECTIVE: To evaluate the efficacy and sustainability of a couple-focused human immunodeficiency virus (HIV) prevention intervention in reducing unprotected sex and increasing intent to use condoms and knowledge about AIDS.

DESIGN: Randomized controlled trial.

SETTING: Urban community settings in Southern California.

PARTICIPANTS: Primarily Latino couples (168 couples; 336 individuals) who were aged 14 to 25 years, English or Spanish speaking, and coparenting a child at least 3 months of age. Intervention A 12-hour theory-based, couple-focused HIV prevention program culturally tailored for young Latino parents, with emphasis on family protection, skill building, and issues related to gender and power. The 1½-hour control condition provided basic HIV-AIDS information.

MAIN OUTCOME MEASURES: Primary outcome measures included self-report of condom use during the past 3 months; secondary, intent to use condoms and knowledge about AIDS.

RESULTS: The HIV prevention intervention reduced the proportion of unprotected sex episodes (odds ratio, 0.87 per month from baseline to 6 months; 95% confidence interval [CI], 0.82-0.93) and increased intent to use condoms (slope increase, 0.20; 95% CI, 0.04-0.37) at the 6-month follow-up; however, these effects were not sustained at 12 months. Knowledge about AIDS was increased in both groups from baseline to 6 months (slope estimate, 0.57; 95% CI, 0.47-0.67) and was maintained in the intervention group only through 12 months. Female participants in both groups had higher intent to use condoms and knowledge about AIDS than male participants ($P \leq .01$).

CONCLUSIONS: The couple-focused HIV prevention intervention reduced risky sexual behaviors and improved intent to use condoms among young Latino parents at the 6-month evaluation. A maintenance program is needed to improve the sustainability of effects over time.

5- Cancer Prev Res (Phila). 2011 Apr;4(4):476-80.

Exercise for secondary prevention of breast cancer: moving from evidence to changing clinical practice.

Schmitz KH.

Abstract

Relating to the report of Irwin and colleagues in this issue of the journal (beginning on page 522), this perspective discusses exercise training interventions as secondary prevention in breast cancer survivors. Burgeoning observational evidence indicates that prescribing aerobic exercise of 3 hours or more per week could have meaningful mortality and morbidity benefits for breast cancer survivors. Adherence to this exercise prescription, however, will require an infrastructure to guide survivors and to address the common clinical treatment sequelae that might interfere with survivors' ability to regularly perform this level of activity (e.g., symptoms related to estrogen deprivation, arthralgias due

to aromatase inhibitors, fatigue, lymphedema, chemotherapy-induced peripheral neuropathy, osteoporosis, upper-extremity functional impairments, and overall functional decline). On the basis of cardiac rehabilitation, a model is proposed to integrate exercise prescription into breast cancer survivor clinical care, with referral to community-based programs for most women. Cancer Prev Res; 4(4); 476-80.

6- Cancer Causes Control. 2011 Apr 3. [Epub ahead of print]

Physical activity and cancer prevention: a systematic review of clinical trials.

Winzer BM, Whiteman DC, Reeves MM, Paratz JD.

Abstract

BACKGROUND: Physically active individuals have lower rates of many cancers and improved cancer outcomes. Controlled exercise trials measuring putative biomarkers of cancer risk are being conducted to further understand the role of exercise in cancer etiology and progression. We aimed to systematically review the effect of exercise on various biomarkers.

METHODS: A comprehensive search strategy identified 353 publications from January 1980 to August 2010. We included those clinical trials of exercise measuring biomarkers following minimum 4-week intervention among cancer survivors or people with one or more cancer risk factors. Two reviewers abstracted data and assessed quality independently. Effect sizes and 95% confidence intervals were estimated.

RESULTS: Four primary prevention and five tertiary prevention trials were included. Exercise had a small to moderate effect on improving concentrations of several blood biomarkers implicated in breast and colon cancer pathways including insulin, leptin, estrogens, and apoptosis regulation. In breast cancer survivors, exercise had a small to moderate effect on improving some biomarkers associated with prognosis including various insulin-like growth factor axis proteins, insulin, and inflammation; and a large effect on enhancing immune function.

CONCLUSION: Data are few, but there is some evidence to support the role of exercise in modulating various cancer pathways.

7- Endocr Pract. 2011 Feb 25:10-35. [Epub ahead of print]

Mechanistic and Clinical Aspects of Renin-Angiotensin-Aldosterone System (RAAS) Blockade in the Prevention of Diabetes and Cardiovascular Disease.

Hershon KS.

Abstract

Objectives: This review details the rationale for the use of renin-angiotensin-aldosterone system (RAAS) inhibition to prevent type 2 diabetes and cardiovascular events, and discusses clinical data evaluating the relationship between RAAS blockade and diabetes prevention.Methods: PubMed was searched to identify and present preclinical and clinical data addressing this aim.Results: Potential mechanisms of angiotensin II-mediated insulin resistance and type 2 diabetes may include impaired blood flow and sympathetic activity, increased oxidative stress, alterations in insulin signaling, and effects on adipose tissue. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers have demonstrated reduced incidences of new-onset diabetes in patients with prediabetes, hypertension, or other cardiovascular populations; however, insight into the corresponding impact on cardiovascular-related morbidity and mortality has been lacking. A recent trial (NAVIGATOR) was designed to evaluate incident diabetes and cardiovascular outcomes as part of its primary endpoint. In this trial, valsartan-based therapy reduced the incidence of new-onset diabetes by 14% relative to placebo over the 5-year followup period (P<.001). Cardiovascular outcomes, however, were not significantly affected by active treatment, which may be attributed to a number of potential confounding factors including the low rate of cardiovascular disease at baseline, concurrent implementation of lifestyle modification in all patients, and the substantial use of other risk-reducing agents.Conclusions: Angiotensin II has been implicated in a number of pathophysiologic processes with the potential to indirectly or directly influence the pathogenesis of insulin resistance and type 2 diabetes. Most clinical trials show a reduced risk of new-onset diabetes with RAAS blockade; however, recent results of the NAVIGATOR trial showed that the addition of valsartan to lifestyle modification reduced the risk of diabetes but did not improve cardiovascular outcomes.

8- Br J Sports Med. 2011 Apr;45(4):357-8.

The fate of clinical sports injury prevention abstracts presented at the 1st world conference on sports injury prevention in oslo 2005.

Knobloch K, Yoon U.

Abstract

Background The World Congress of Sports Injury Prevention initiates in Oslo in 2005 as a unique and comprehensive sports medicine prevention conference. Objective The number and quality of presented abstracts published in BJSM followed by a full paper in the subsequent years is unknown. Hypothesis Randomised controlled trials (RCT) are more likely to be published as full paper versus observational studies following the conference presentation. Design All 154 oral abstracts of the World Congress of Sports Injury Prevention 2005 Oslo and the potential subsequent full text were analysed. Main outcome measures Frequency of publication, time to publication, impact factor, score of CONSORT criteria for RCTs and STROBE for observational studies, as well as minor and major inconsistencies. Results Overall, 76 of the 154 (49%) presented abstracts were published in a peer-reviewed journal with an impact factor of 1.946±0.812. There was no significant difference between the impact factor for RCTs (2.122±1.015) versus observational studies (1.913±0.765, p=0.469). The full paper of RCTs abstracts was published after 17±13 months and after 12±14 months in observational studies (p=0.323) There was a trend towards more observational abstracts being published as a full paper rather than RCTs (71% vs 47%, p=0.078). All of the published abstracts had at least one minor inconsistency while 65% had at least major inconsistencies. Results changed in 90% versus 68% (p=0.158), data were added in 60% versus 30% (p=0.065), and deleted in 40% versus 30%, (p=0.534). An opposite result was published in 0% versus 5% (p=0.481). Conclusion There was no significant difference in the likelihood between RCTs and observational studies being published as full papers after the World Congress of Sports Injury Prevention 2005, neither for impact factor and time to publication. Only about half of the presented abstracts get published in a peer-reviewed journal within 4 years after the conference presentation.

9- Curr Diabetes Rev. 2011 Mar 24. [Epub ahead of print]

Prevention and Treatment of Diabetic Retinopathy: Evidence from Clinical Trials and Perspectives.

Abbate M, Cravedi P, Iliev I, Remuzzi G, Ruggenenti P.

Abstract

Diabetic retinopathy is the most common microvascular complication of diabetes mellitus and is the leading cause of blindness amongst working-age adults in Western countries. Large observational and randomized studies have consistently shown that optimal blood glucose and blood pressure control is the key component of intervention strategies aimed to halt or regress the disease, and limit the risk of progression to the proliferative stage, with consequent visual loss up to blindness in most severe cases. Amelioration of dyslipidemia by statins, especially if combined with fenofibrate, may also ameliorate retinopathy in line with a potential pathogenic role of hyperlipidemia. Recently, evidence has also emerged that renin-angiotensin system (RAS) inhibitors may electively prevent or delay progression of retinopathy, possibly because of specific protective effect against the structural and functional retinal changes sustained by local RAS activation. Thus, metabolic and blood pressure control by RAS inhibition is to prevent or limit the onset of retinopathy and its progression towards visual-threatening stages. Topic treatment with anti-vascular endothelial growth factor (VEGF) agents is emerging as a treatment option for retinopathy in advanced stages to limit the need for laser photocoagulation. This option however should be considered with caution due to the risk of systemic adverse events.

10- Ann Oncol. 2011 Mar 22. [Epub ahead of print]

Impact of dental care in the prevention of bisphosphonate-associated osteonecrosis of the jaw: a single-center clinical experience.

Vandone AM, Donadio M, Mozzati M, Ardine M, Polimeni MA, Beatrice S, Ciuffreda L, Scoletta M.

Abstract

BACKGROUND: Osteonecrosis of the jaw (ONJ) is associated with bisphosphonate (BP) therapy and invasive dental care. An Interdisciplinary Care Group (ICG) was created to evaluate dental risk factors and the efficacy of a preventive restorative dental care in the reduction of ONJ risk.

PATIENTS AND METHODS: This prospective single-center study included patients with bone metastases from solid tumors. Patients who received at least one BP infusion between October 2005 and 31 August 2009 underwent one or more ICG evaluation and regular dental examinations. We also retrospectively evaluated patients with bone metastases from solid tumors who did not undergo dental preventive measures.

RESULTS: Of 269 patients, 211 had received at least one infusion of BP therapy: 62% were BP naive and 38% had previous BP exposure. Of these 211 patients followed for 47 months, 6 patients developed ONJ (2.8%). Of 200 patients included in the retrospective analysis, 11 patients developed ONJ (5.5%).

CONCLUSIONS: In comparison with published ONJ rates and those extrapolated from the retrospective analysis, the observed ONJ rate in the prospective group was lower, suggesting that implementation of a preventive dental program may reduce the risk of ONJ in metastatic patients treated with i.v. BP therapy.

11- Vaccine. 2011 Mar 15. [Epub ahead of print]

A clinical trial to evaluate the safety and immunogenicity of the LEISH-F1+MPL-SE vaccine for use in the prevention of visceral leishmaniasis.

Chakravarty J, Kumar S, Trivedi S, Rai VK, Singh A, Ashman JA, Laughlin EM, Coler RN, Kahn SJ, Beckmann AM, Cowgill KD, Reed SG, Sundar S, Piazza FM.

Abstract

Healthy Indian adult volunteers, with or without a history of leishmaniasis, were evaluated for evidence of previous infection with Leishmania donovani based on the direct agglutination test (DAT). Three cohorts of 6 DAT-negative and 6 DAT-positive subjects were enrolled in an open-label, dose-escalating, uncontrolled clinical trial and received three injections of the LEISH-F1+MPL-SE vaccine (consisting of 5μg, 10μg, or 20μg recombinant Leishmania polyprotein LEISH-F1 antigen+25μg MPL(®)-SE adjuvant). The study injections were given subcutaneously on days 0, 28, and 56, and the subjects were followed through day 168 for safety and immunological endpoints. The vaccine was safe and well-tolerated in DAT-negative and DAT-positive subjects and induced T-cell production of IFN-γ and other cytokines in response to stimulation with the LEISH-F1 antigen. This clinical trial shows that the LEISH-F1+MPL-SE vaccine is safe and immunogenic in healthy subjects with and without history of previous infection with Leishmania donovani.

12- Infect Disord Drug Targets. 2011 Mar 15. [Epub ahead of print]

The Global Status of HIV Drug Resistance: Clinical and Public-Health Approaches for Detection, Treatment and Prevention.

Hong SY, Nachega JB, Kelley K, Bertagnolio S, Marconi VC, Jordan MR.

Abstract

Antiretroviral therapy (ART) scale-up in resource limited settings (RLS) has been successful, utilizing a standardized population-based approach to ART delivery. An unintended consequence of treatment scale-up is the inevitable emergence of HIV drug resistance (HIVDR) in populations even when patient adherence to ART is optimally supported. HIVDR has the potential to undermine the dramatic gains that ART has had in reducing the morbidity and mortality of HIV-infected patients in RLS. Sustaining and expanding ART coverage in RLS will depend upon the ability of ART programs to deliver ART in a way that minimizes the emergence of HIVDR. Fortunately, current evidence demonstrates that HIVDR in RLS has neither emerged nor been transmitted to the degree that had initially been feared. However, due to a lack of standardized methodologies, HIVDR data from RLS can be difficult to interpret and may not provide the programmatic evidence necessary for public health action. The World Health Organization has developed simple, standardized surveys that generate comparable results to assess acquired and transmitted HIVDR for routine public health implementation in RLS. These HIVDR surveys are designed to be implemented in conjunction with annual monitoring of program and site factors known to be associated with the emergence of HIVDR.

13- Clin Microbiol Infect. 2011 Apr;17 Suppl 2:1-24. doi: 10.1111/j.1469-0691.2011.03477.x.

Guidelines for the prevention of invasive mould diseases caused by filamentous fungi by the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC).

Ruiz-Camps I, Aguado JM, Almirante B, Bouza E, Ferrer-Barbera CF, Len O, Lopez-Cerero L, Rodríguez-Tudela JL, Ruiz M, Solé A, Vallejo C, Vazquez L, Zaragoza R, Cuenca-Estrella M; GEMICOMED (Medical Mycology Study Group of SEIMC).

Abstract

Invasive fungal infections (IFIs) caused by filamentous fungi still have high rates of mortality, associated with difficulties in early detection of the infection and therapeutic limitations. Consequently, a useful approach is to prevent patients at risk of fungal infection from coming into contact with conidia of Aspergillus and other mould species. This document describes the recommendations for preventing IFI caused by filamentous fungi worked out by Spanish experts from different medical and professional fields. The article reviews the incidence of IFI in different risk populations, and questions related to environmental measures for prevention, control of hospital infections, additional procedures for prevention, prevention of IFI outside of hospital facilities and antifungal prophylaxis are also analysed.

14-- PLoS One. 2011 Mar 2;6(3):e16986.

Viral Linkage in HIV-1 Seroconverters and Their Partners in an HIV-1 Prevention Clinical Trial.

Campbell MS, Mullins JI, Hughes JP, Celum C, Wong KG, Raugi DN, Sorensen S, Stoddard JN, Zhao H, Deng W, Kahle E, Panteleeff D, Baeten JM, McCutchan FE, Albert J, Leitner T, Wald A, Corey L, Lingappa JR; for the Partners in Prevention HSV/HIV Transmission Study Team.

Abstract

BACKGROUND: Characterization of viruses in HIV-1 transmission pairs will help identify biological determinants of infectiousness and evaluate candidate interventions to reduce transmission. Although HIV-1 sequencing is frequently used to substantiate linkage between newly HIV-1 infected individuals and their sexual partners in epidemiologic and forensic studies, viral sequencing is seldom applied in HIV-1 prevention trials. The Partners in Prevention HSV/HIV Transmission Study (ClinicalTrials.gov #NCT00194519) was a prospective randomized placebo-controlled trial that enrolled serodiscordant heterosexual couples to determine the efficacy of genital herpes suppression in reducing HIV-1 transmission; as part of the study analysis, HIV-1 sequences were examined for genetic linkage between seroconverters and their enrolled partners.

METHODOLOGY/PRINCIPAL FINDINGS: We obtained partial consensus HIV-1 env and gag sequences from blood plasma for 151 transmission pairs and performed deep sequencing of env in some cases. We analyzed sequences with phylogenetic techniques and developed a Bayesian algorithm to evaluate the probability of linkage. For linkage, we required monophyletic clustering between enrolled partners' sequences and a Bayesian posterior probability of ≥50%. Adjudicators classified each seroconversion, finding 108 (71.5%) linked, 40 (26.5%) unlinked, and 3 (2.0%) indeterminate transmissions, with linkage determined by consensus env sequencing in 91 (84%). Male seroconverters had a higher frequency of unlinked transmissions than female seroconverters. The likelihood of transmission from the enrolled partner was related to time on study, with increasing numbers of unlinked transmissions occurring after longer observation periods. Finally, baseline viral load was found to be significantly higher among linked transmitters.

CONCLUSIONS/SIGNIFICANCE: In this first use of HIV-1 sequencing to establish endpoints in a large clinical trial, more than one-fourth of transmissions were unlinked to the enrolled partner, illustrating the relevance of these methods in the design of future HIV-1 prevention trials in serodiscordant couples. A hierarchy of sequencing techniques, analysis methods, and expert adjudication contributed to the linkage determination process.

15- Int J Clin Pharm. 2011 Mar 12. [Epub ahead of print]

Role of clinical pharmacists' interventions in detection and prevention of medication errors in a medical ward.

Khalili H, Farsaei S, Rezaee H, Dashti-Khavidaki S.

Abstract

Objective Frequency and type of medication errors and role of clinical pharmacists in detection and prevention of these errors were evaluated in this study. Method During this interventional study,

clinical pharmacists monitored 861 patients' medical records and detected, reported, and prevented medication errors in the infectious disease ward of a major referral teaching hospital in Tehran, Iran. Error was defined as any preventable events that lead to inappropriate medication use related to the health care professionals or patients regardless of outcomes. Classification of the errors was done based on Pharmaceutical Care Network Europe Foundation drug-related problem coding. Results During the study period, 112 medication errors (0.13 errors per patient) were detected by clinical pharmacists. Physicians, nurses, and patients were responsible for 55 (49.1%), 54 (48.2%), and 3 (2.7%) of medication errors, respectively. Drug dosing, choice, use and interactions were the most causes of error in medication processes, respectively. All of these errors were detected, reported, and prevented by infectious diseases ward clinical pharmacists. Conclusion Medication errors occur frequently in medical wards. Clinical pharmacists' interventions can effectively prevent these errors. The types of errors indicate the need for continuous education and implementation of clinical pharmacist's interventions.

16- Cancer Prev Res (Phila). 2011 Mar;4(3):354-64.

Phase IIa Clinical Trial of Curcumin for the Prevention of Colorectal Neoplasia.

Carroll RE, Benya RV, Turgeon DK, Vareed S, Neuman M, Rodriguez L, Kakarala M, Carpenter PM, McLaren C, Meyskens FL Jr, Brenner DE.

Abstract

Curcumin is derived from the spice tumeric and has antiinflammatory and antineoplastic effects in vitro and in animal models, including preventing aberrant crypt foci (ACF) and adenomas in murine models of colorectal carcinogenesis. Inhibiting the production of the procarcinogenic eicosanoids prostaglandin E(2) (PGE(2)) and 5-hydroxyeicosatetraenoic acid (5-HETE) can suppress carcinogenesis in rodents. Curcumin reduces mucosal concentrations of PGE(2) (via inhibition of cyclooxygenases 1 and 2) and 5-HETE (via inhibition of 5-lipoxygenase) in rats. Although preclinical data support curcumin activity in many sites, the poor bioavailability reported for this agent supports its use in the colorectum. We assessed the effects of oral curcumin (2 g or 4 g per day for 30 days) on PGE(2) within ACF (primary endpoint), 5-HETE, ACF number, and proliferation in a nonrandomized, open-label clinical trial in 44 eligible smokers with eight or more ACF on screening colonoscopy. We assessed pre- and posttreatment concentrations of PGE(2) and 5-HETE by liquid chromatography tandem mass spectroscopy in ACF and normal-tissue biopsies; ACF number via rectal endoscopy; proliferation by Ki-67 immunohistochemistry; and curcumin concentrations by high-performance liquid chromatography in serum and rectal mucosal samples. Forty-one subjects completed the study. Neither dose of curcumin reduced PGE(2) or 5-HETE within ACF or normal mucosa or reduced Ki-67 in normal mucosa. A significant 40% reduction in ACF number occurred with the 4-g dose ($P < 0.005$), whereas ACF were not reduced in the 2-g group. The ACF reduction in the 4-g group was associated with a significant, five-fold increase in posttreatment plasma curcumin/conjugate levels (versus pretreatment; $P = 0.009$). Curcumin was well tolerated at both 2 g and 4 g. Our data suggest that curcumin can decrease ACF number, and this is potentially mediated by curcumin conjugates delivered systemically. Cancer Prev Res; 4(3); 354-64. ©2011 AACR.

17- Pharmacotherapy. 2011 Mar;31(3):280-97.

Clinical perspectives on the role of the human papillomavirus vaccine in the prevention of cancer.

Julius JM, Ramondeta L, Tipton KA, Lal LS, Schneider K, Smith JA.

Division of Pharmacy, The University of Texas M.D. Anderson Cancer Center, Houston, Texas, USA.

Abstract

The role of human papillomavirus (HPV) in the genesis of cervical cancer has been well documented, and an increasing body of literature exists with regard to the role of HPV in other cancers, including cancers of the head and neck. With the recent expansion of the United States Food and Drug Administration's approval of the quadrivalent HPV virus-like particle vaccine to include men and boys and approval of the bivalent vaccine this year, the controversies regarding who should be vaccinated, at what age is vaccination most appropriate, and the limitations of the available HPV vaccines are increasing. Health care providers are challenged with evaluating the current, but continually changing, clinical evidence when making critical decisions for their patients. A literature search of MEDLINE and SciVerse Scopus was conducted for articles published from 1998-April 2010 regarding HPV, HPV-

related cancers, and HPV vaccines. Although both HPV vaccines were greater than 90% effective in the prevention of cervical cancer precursors in an according-to-protocol cohort, both vaccines were significantly less effective in the intent-to-treat population. In patients who achieved seroconversion, the geometric mean titers decrease dramatically within the first 2 years after vaccination, and then continue to decline at a slower rate. No effective antibody titer has been defined for either vaccine, and no studies have been conducted with documented HPV exposure after vaccination. With low efficacy rates in an intent-to-treat population and the potential for waning immunity, it is imperative for women to continue to receive regular Pap tests and gynecologic examinations. Although vaccine administration was shown to be cost-effective when administered to adolescent girls, many of these simulations overestimated the durability of protection, efficacy rates in sexually active women, impact of incomplete vaccination, or necessity of boosters in the future. Whereas the introduction of the HPV vaccine was an enormous advancement in the cancer prevention research arena, optimization of its clinical use is still needed.

18- Europace. 2011 Mar;13(3):308-28.

Upstream therapies for management of atrial fibrillation: review of clinical evidence and implications for European Society of Cardiology guidelines. Part I: primary prevention.

Savelieva I, Kakouros N, Kourliouros A, Camm AJ.

Abstract

Atrial fibrillation (AF) is associated with significant morbidity and mortality. It is also a progressive disease secondary to continuous structural remodelling of the atria due to AF itself, to changes associated with ageing, and to deterioration of underlying heart disease. Current management aims at preventing the recurrence of AF and its consequences (secondary prevention) and includes risk assessment and prevention of stroke, ventricular rate control, and rhythm control therapies including antiarrhythmic drugs and catheter or surgical ablation. The concept of primary prevention of AF with interventions targeting the development of substrate and modifying risk factors for AF has emerged as a result of recent experiments that suggested novel targets for mechanism-based therapies. Upstream therapy refers to the use of non-antiarrhythmic drugs that modify the atrial substrate- or target-specific mechanisms of AF to prevent the occurrence or recurrence of the arrhythmia. Such agents include angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), statins, n-3 (ω-3) polyunsaturated fatty acids, and possibly corticosteroids. Animal experiments have compellingly demonstrated the protective effect of these agents against electrical and structural atrial remodelling in association with AF. The key targets of upstream therapy are structural changes in the atria, such as fibrosis, hypertrophy, inflammation, and oxidative stress, but direct and indirect effects on atrial ion channels, gap junctions, and calcium handling are also applied. Although there have been no formal randomized controlled studies (RCTs) in the primary prevention setting, retrospective analyses and reports from the studies in which AF was a pre-specified secondary endpoint have shown a sustained reduction in new-onset AF with ACEIs and ARBs in patients with significant underlying heart disease (e.g. left ventricular dysfunction and hypertrophy), and in the incidence of AF after cardiac surgery in patients treated with statins. In the secondary prevention setting, the results with upstream therapies are significantly less encouraging. Although the results of hypothesis-generating small clinical studies or retrospective analyses in selected patient categories have been positive, larger prospective RCTs have yielded controversial, mostly negative, results. Notably, the controversy exists on whether upstream therapy may impact mortality and major non-fatal cardiovascular events in patients with AF. This has been addressed in retrospective analyses and large prospective RCTs, but the results remain inconclusive pending further reports. This review provides a contemporary evidence-based insight into the role of upstream therapies in primary (Part I) and secondary (Part II) prevention of AF.

19- Anesth Analg. 2011 Mar;112(3):582-6. Epub 2011 Jan 13.

Clinical testing of the apnea prevention device: proof of concept data.

Zornow MH.

Abstract

INTRODUCTION: Narcotic-induced respiratory depression is a major cause of perioperative morbidity and mortality. Current monitoring modalities are inadequate to detect and treat respiratory

depression in postoperative patients. Intermittent nursing assessments, even if conducted frequently, may not capture the rapid onset of airway obstruction, apnea, and hypoxia that can occur in many of these patients. Continuous nursing observation, as in an intensive care unit setting, is cost-prohibitive and impractical, given the large number of patients at risk. In an effort to address this problem, the author has created and tested the Apnea Prevention Device (APD), which is designed to detect the onset of hypoxia and instantly intervene to restore respiration and oxygen saturation in narcotized patients.

METHODS: The prototype APD used in this study consisted of a laptop computer running custom software, a pulse oximeter, and a nerve stimulator. Oxygen saturation data were acquired by the computer from the pulse oximeter, and stimuli to the patient were delivered either by headphones (verbal prompts) or a nerve stimulator (cutaneous). The APD program was written to analyze oximetry data and when indicated, deliver a series of stimuli of increasing intensity to arouse patients from narcosis. The device was tested on surgical patients in the postanesthesia care unit. An intervention delivered by the APD was scored as a success if the patient took a large tidal volume breath (as evidenced by chest rise) and there was a subsequent increase in oxygen saturation. The APD maintained a data log of oxygen saturations and interventions. In a subset of patients, it was possible to compare the functioning of the APD with routine nursing care.

RESULTS: A total of 125 interventions were delivered by the APD to 10 patients with a 97% success rate. The depth of desaturations was less when the APD was in use than when patients received routine 1:1 nursing care. When the APD was functioning, the frequency with which nurses prompted the subjects to breathe was dramatically reduced.

DISCUSSION: This study demonstrates that the prototype APD can successfully treat narcotic-induced respiratory depression in postoperative patients and does so in a manner that is superior to that provided by routine 1:1 nursing care. Such a device has the potential to decrease the morbidity associated with narcotic-induced respiratory depression in postoperative patients.

20- Brain Dev. 2011 Apr;33(4):289-93. Epub 2010 Jul 13.

Levetiracetam in brain ischemia: Clinical implications in neuroprotection and prevention of post-stroke epilepsy.

Belcastro V, Pierguidi L, Tambasco N.

Abstract

Several new antiepileptic drugs (AEDs) have been introduced for clinical use recently. These new AEDs, like the classic AEDs, target multiple cellular sites both pre- and postsynaptically. The use of AEDs as a possible neuroprotective strategy in brain ischemia is receiving increasing attention and the antiepileptic drug levetiracetam, a 2S-(2-oxo-1-pyrrolidiny1) butanamide, belonging to the pyrrolidone family, could have a crucial role in regulation of epileptogenesis and neuroprotection. Recent observations suggest that levetiracetam is both safe and effective against post-stroke seizures. In this review, the potential neuroprotective role in brain ischemia and the therapeutic implications of levetiracetam in post-stroke epilepsy are discussed.

21- J Acquir Immune Defic Syndr. 2011 Mar 1;56(3):e87-94.

The cost-effectiveness of HIV prevention interventions for HIV-infected patients seen in clinical settings.

Marseille E, Shade SB, Myers J, Morin S.

Abstract

BACKGROUND: The US Health Resources and Services Administration sponsored a 5-year initiative to test three types of counseling-based interventions to reduce HIV transmission among HIV-infected patients delivered in clinical settings. We assessed the cost and cost-effectiveness of the three types of interventions at 13 sites: primary care provider-based (clinical provider); social worker or peer educator-based (specialist); and a mix of primary care and specialist-based (mixed).

METHODS: We developed a cost-effectiveness model to calculate average and incremental cost-effectiveness ratios and the cost-effectiveness of the 13 sites combined.

RESULTS: Spending over all 3 years of the demonstration averaged $1004, $3173, and $3430 per client served for clinical provider, specialist, and mixed services, respectively. Unit costs declined with the volume of services provided for all three intervention types. The cost-effectiveness of the clinical

provider sites was $107,656 per HIV case averted compared with no intervention. Clinical provider sites were less costly and more effective than the specialist or mixed sites.

CONCLUSIONS: Compared with the lifetime cost of HIV/AIDS care and with other effective HIV prevention interventions, the clinical provider-led interventions in this study are cost-effective. In an incremental comparison with clinical provider sites, specialist and mixed intervention sites were not cost-effective.

22- J Ocul Pharmacol Ther. 2011 Feb 12. [Epub ahead of print]

Clinical Pharmacology of Alcaftadine, a Novel Antihistamine for the Prevention of Allergic Conjunctivitis.

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Abstract

Abstract Purpose: In this report, we characterize the in vitro pharmacokinetic properties of a new antihistamine, alcaftadine. In addition, we report results from phase 1 studies of several ophthalmic formulations of alcaftadine and examine the pharmacokinetic properties of one formulation in detail. Methods: In vitro pharmacology employed a human liver microsome assay combined with index substrates or inhibitors for specific cytochromes. Metabolic fate of (14)C-alcaftadine was determined by high-performance liquid chromatography-based separation of parent compound from metabolites. Plasma protein binding was determined by equilibrium dialysis using (3)H-labeled alcaftadine and (3)H-labeled alcaftadine carboxylic acid metabolite. Relative tolerability (comfort) of 4 concentrations and 3 formulations of alcaftadine ophthalmic solution was assessed in 2 double-masked, randomized, placebo-controlled, contralateral studies in which formulations were compared to Tears Naturale II (placebo) in normal adult subjects. Data analysis focused on the mean differences in subject-reported drop comfort scores (within each dose level, at each time point) and compared the study-treatment eye with the placebo eye. Pharmacokinetics of alcaftadine 0.25% ophthalmic solution were determined in an open-label, single-center study after a single bilateral dose and after 7 days of once-a-day bilateral doses in healthy subjects 18-55 years old. Results: Alcaftadine is not significantly metabolized by microsomal cytochromes, but it is rapidly converted to the carboxylic acid metabolite by one or more cytosolic enzymes. Neither the parent compound nor its carboxylic acid metabolite displayed significant plasma protein binding. Over a range of formulations and concentrations (0.05%-0.5%), alcaftadine was well tolerated and subjects reported little or no discomfort or taste perversion in any treatment group. Pharmacokinetic studies showed that both the parent compound and the carboxylic acid metabolite reach peak serum levels within minutes of administration and fall below detectable levels within 3h of dosing. Conclusions: Based upon pharmacokinetic and phase 1 studies, the novel antihistamine alcaftadine is an appropriate drug for use as an ophthalmic formulation for prevention and treatment of ocular allergic conditions such as allergic conjunctivitis (alcaftadine ophthalmic solution 0.25% was recently approved for use by the FDA). Topical administration of alcaftadine 0.25% ophthalmic solution was well tolerated and had an acceptable safety profile

23- Lancet. 2011 Apr 5. [Epub ahead of print]

Priority actions for the non-communicable disease crisis.

Beaglehole R, Bonita R, Horton R, Adams C, Alleyne G, Asaria P, Baugh V, Bekedam H, Billo N, Casswell S, Cecchini M, Colagiuri R, Colagiuri S, Collins T, Ebrahim S, Engelgau M, Galea G, Gaziano T, Geneau R, Haines A, Hospedales J, Jha P, Keeling A, Leeder S, Lincoln P, McKee M, Mackay J, Magnusson R, Moodie R, Mwatsama M, Nishtar S, Norrving B, Patterson D, Piot P, Ralston J, Rani M, Reddy KS, Sassi F, Sheron N, Stuckler D, Suh I, Torode J, Varghese C, Watt J; for The Lancet NCD Action Group and the NCD Alliance.

Abstract

The UN High-Level Meeting on Non-Communicable Diseases (NCDs) in September, 2011, is an unprecedented opportunity to create a sustained global movement against premature death and preventable morbidity and disability from NCDs, mainly heart disease, stroke, cancer, diabetes, and chronic respiratory disease. The increasing global crisis in NCDs is a barrier to development goals including poverty reduction, health equity, economic stability, and human security. The Lancet NCD

Action Group and the NCD Alliance propose five overarching priority actions for the response to the crisis-leadership, prevention, treatment, international cooperation, and monitoring and accountability-and the delivery of five priority interventions-tobacco control, salt reduction, improved diets and physical activity, reduction in hazardous alcohol intake, and essential drugs and technologies. The priority interventions were chosen for their health effects, cost-effectiveness, low costs of implementation, and political and financial feasibility. The most urgent and immediate priority is tobacco control. We propose as a goal for 2040, a world essentially free from tobacco where less than 5% of people use tobacco. Implementation of the priority interventions, at an estimated global commitment of about US$9 billion per year, will bring enormous benefits to social and economic development and to the health sector. If widely adopted, these interventions will achieve the global goal of reducing NCD death rates by 2% per year, averting tens of millions of premature deaths in this decade.

24- N Engl J Med. 2011 Mar 24;364(12):1093-1103.

Tiotropium versus salmeterol for the prevention of exacerbations of COPD.

Vogelmeier C, Hederer B, Glaab T, Schmidt H, Rutten-van Mölken MP, Beeh KM, Rabe KF, Fabbri LM; POET-COPD Investigators.

Abstract

BACKGROUND: Treatment guidelines recommend the use of inhaled long-acting bronchodilators to alleviate symptoms and reduce the risk of exacerbations in patients with moderate-to-very-severe chronic obstructive pulmonary disease (COPD) but do not specify whether a long-acting anticholinergic drug or a β(2)-agonist is the preferred agent. We investigated whether the anticholinergic drug tiotropium is superior to the β(2)-agonist salmeterol in preventing exacerbations of COPD.

METHODS: In a 1-year, randomized, double-blind, double-dummy, parallel-group trial, we compared the effect of treatment with 18 μg of tiotropium once daily with that of 50 μg of salmeterol twice daily on the incidence of moderate or severe exacerbations in patients with moderate-to-very-severe COPD and a history of exacerbations in the preceding year.

RESULTS: A total of 7376 patients were randomly assigned to and treated with tiotropium (3707 patients) or salmeterol (3669 patients). Tiotropium, as compared with salmeterol, increased the time to the first exacerbation (187 days vs. 145 days), with a 17% reduction in risk (hazard ratio, 0.83; 95% confidence interval [CI], 0.77 to 0.90; P<0.001). Tiotropium also increased the time to the first severe exacerbation (hazard ratio, 0.72; 95% CI, 0.61 to 0.85; P<0.001), reduced the annual number of moderate or severe exacerbations (0.64 vs. 0.72; rate ratio, 0.89; 95% CI, 0.83 to 0.96; P=0.002), and reduced the annual number of severe exacerbations (0.09 vs. 0.13; rate ratio, 0.73; 95% CI, 0.66 to 0.82; P<0.001). Overall, the incidence of serious adverse events and of adverse events leading to the discontinuation of treatment was similar in the two study groups. There were 64 deaths (1.7%) in the tiotropium group and 78 (2.1%) in the salmeterol group.

CONCLUSIONS: These results show that, in patients with moderate-to-very-severe COPD, tiotropium is more effective than salmeterol in preventing exacerbations. (Funded by Boehringer Ingelheim and Pfizer; ClinicalTrials.gov number, NCT00563381.).