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Title: Omadacycline for Community-Acquired Bacterial Pneumonia.

Publication Type: Comparative Study

Journal-Name:The New England journal of medicine

Journal ID: 0255562

Publication date: 2019/02/26 06:00 [medline]

BACKGROUND: Omadacycline, a new once-daily aminomethylcycline antibiotic agent that can be administered intravenously or orally, reaches high concentrations in pulmonary tissues and is active against common pathogens that cause community-acquired bacterial pneumonia. METHODS: In a double-blind trial, we randomly assigned (in a 1:1 ratio) adults with community-acquired bacterial pneumonia (Pneumonia Severity Index risk class II, III, or IV) to receive omadacycline (100 mg intravenously every 12 hours for two doses, then 100 mg intravenously every 24 hours), or moxifloxacin (400 mg intravenously every 24 hours). A transition to oral omadacycline (300 mg every 24 hours) or moxifloxacin (400 mg every 24 hours), respectively, was allowed after 3 days; the total treatment duration was 7 to 14 days. The primary end point was early <P 0> clinical response </>, defined as <P 1> survival </> with improvement in at least two of four <P 0> symptoms </> ( <P 0> cough </>, <P 0> sputum production </>, <P 0> pleuritic chest pain </>, and <P 0> dyspnea </>) and no worsening of <P 0> symptoms </> at 72 to 120 hours, without receipt of <P 36> rescue antibacterial therapy </>. A secondary end point was investigator-assessed <P 0> clinical response </> at a post-treatment evaluation 5 to 10 days after the last dose, with clinical response defined as resolution or improvement in <P 0> signs </> or <P 0> symptoms </> to the extent that further antibacterial therapy was unnecessary. A noninferiority margin of 10 percentage points was used. RESULTS: The intention-to-treat population included 386 patients in the omadacycline group and 388 patients in the moxifloxacin group. Omadacycline was noninferior to moxifloxacin for early <P 0> clinical response </> (81.1% and 82.7%, respectively; difference, -1.6 percentage points; 95% confidence interval [CI], -7.1 to 3.8), and the rates of investigator-assessed <P 0> clinical response </> at the post-treatment evaluation were 87.6% and 85.1%, respectively (difference, 2.5 percentage points; 95% CI, -2.4 to 7.4). <P 38> Adverse events </> that emerged after treatment initiation were reported in 41.1% of the patients in the omadacycline group and 48.5% of the patients in the moxifloxacin group; the most frequent events were <P 0> gastrointestinal </> (10.2% and 18.0%, respectively), and the largest difference was for <P 0> diarrhea </> (1.0% and 8.0%). Twelve <P 1> deaths </> (8 in the omadacycline group and 4 in the moxifloxacin group) occurred during the trial. CONCLUSIONS: Omadacycline was noninferior to moxifloxacin for the treatment of community-acquired bacterial pneumonia in adults. (Funded by Paratek Pharmaceuticals; OPTIC ClinicalTrials.gov number, NCT02531438 .).

30726693\_PD.txt

Title: Phase 1 Trial of an RNA Interference Therapy for Acute Intermittent Porphyria.

Publication Type: Journal Article

Journal-Name:The New England journal of medicine

Journal ID: 0255562

Publication date: 2019/02/26 06:00 [medline]

BACKGROUND: Induction of delta aminolevulinic acid synthase 1 ( ALAS1) gene expression and accumulation of neurotoxic intermediates result in neurovisceral attacks and disease manifestations in patients with acute intermittent porphyria, a rare inherited disease of heme biosynthesis. Givosiran is an investigational RNA interference therapeutic agent that inhibits hepatic ALAS1 synthesis. METHODS: We conducted a phase 1 trial of givosiran in patients with acute intermittent porphyria. In part A of the trial, patients without recent porphyria attacks (i.e., no attacks in the 6 months before baseline) were randomly assigned to receive a single subcutaneous injection of one of five ascending doses of givosiran (0.035, 0.10, 0.35, 1.0, or 2.5 mg per kilogram of body weight) or placebo. In part B, patients without recent attacks were randomly assigned to receive once-monthly injections of one of two doses of givosiran (0.35 or 1.0 mg per kilogram) or placebo (total of two injections 28 days apart). In part C, patients who had recurrent attacks were randomly assigned to receive injections of one of two doses of givosiran (2.5 or 5.0 mg per kilogram) or placebo once monthly (total of four injections) or once quarterly (total of two injections) during a 12-week period, starting on day 0. Safety, pharmacokinetic, pharmacodynamic, and exploratory efficacy outcomes were evaluated. RESULTS: A total of 23 patients in parts A and B and 17 patients in part C underwent randomization. Common <P 38> adverse events </> included <P 0> nasopharyngitis </>, <P 0> abdominal pain </>, and <P 0> diarrhea </>. <P 38> Serious adverse events </> occurred in 6 patients who received givosiran in parts A through C combined. In part C, all 6 patients who were assigned to receive once-monthly injections of givosiran had sustained reductions in <P 0> ALAS1 messenger RNA (mRNA) </>, <P 0> delta aminolevulinic acid </>, and <P 0> porphobilinogen </> levels to near normal. These reductions were associated with a 79% lower mean annualized <P 0> attack </> rate than that observed with placebo (exploratory efficacy end point). CONCLUSIONS: Once-monthly injections of givosiran in patients who had recurrent <P 0> porphyria </> attacks resulted in mainly low-grade <P 38> adverse events </>, reductions in induced <P 0> ALAS1 mRNA </> levels, nearly normalized levels of the neurotoxic intermediates <P 0> delta aminolevulinic acid </> and <P 0> porphobilinogen </>, and a lower <P 0> attack </> rate than that observed with placebo. (Funded by Alnylam Pharmaceuticals; ClinicalTrials.gov number, NCT02452372 .).

30727982\_PD.txt

Title: Combined phacoemulsification and viscocanalostomy with Ologen implant versus combined phacoemulsification and viscocanalostomy.

Publication Type: Randomized Controlled Trial

Journal-Name:BMC ophthalmology

Journal ID: 100967802

Publication date: 2019/02/08 06:00 [entrez]

BACKGROUND: To study the efficacy of the biodegradable collagen implant Ologen(R) as an adjuvant in phaco-viscocanalostomy in patients with coexisting cataract and primary open angle glaucoma. METHODS: This prospective, interventional, randomized clinical study was done at Alpha Vision Center, Zagazig, Egypt. Patients with coexisting cataract and glaucoma were randomized to receive either phaco-viscocanalostomy (Phacovisco group) (39 eyes) or phaco-viscocanalostomy with Ologen(R) implant (OloPhacovisco group) (40 eyes). Follow-up period was 2 years. Nd:YAG laser goniopuncture was done in cases where the intraocular pressure (IOP) was elevated above 21 mmHg after discontinuation of corticosteroid eye drops at any follow-up visit. RESULTS: No significant operative or postoperative <P 38> complications </> (other than failure) were encountered in either group. At 2 years follow-up, the mean <P 0> intraocular pressure(IOP) </> level was statistically significantly decreased in the OloPhacovisco group (p = 0.02) and complete <P 0> success </> occurred in 23 eyes (59.0%) in the Phacovisco group and in 32 eyes (80.0%) in the OloPhacovisco group. There was a statistically significant higher <P 0> success </> rate regarding complete <P 0> success </> in patients that received Ologen(R) implant (p = 0.04). CONCLUSIONS: Ologen(R) implant improved the <P 0> success </> rate of phaco-viscocanalostomy. Larger studies with longer follow-up periods may be required to confirm these findings. TRIAL REGISTRATION: This trial was retrospectively registered on 20/12/2018 under the number ( NCT03782051 ).

30727989\_PD.txt

Title: Using physical education to promote out-of school physical activity in lower secondary school students - a randomized controlled trial protocol.

Publication Type: Randomized Controlled Trial

Journal-Name:BMC public health

Journal ID: 100968562

Publication date: 2019/02/08 06:00 [entrez]

BACKGROUND: Given the documented decline in levels of physical activity in early adolescence, promoting physical activity in young people is a priority for health promotion. School physical education (PE) is an important existing network in which participation in physical activity beyond school can be promoted to the captive young people. The objective of current article is to present the protocol for a PE teacher-delivered theory-based trial to promote secondary school students' <P 25> participation </> in physical activity out-of-school contexts. The intervention will be guided by the trans-contextual model explaining the processes by which PE teachers' support for autonomous motivation in the classroom promotes students' <P 28> motivation </> to engage in out-of-school physical activity. We hypothesize that school students receiving the teacher-delivered intervention to promote autonomous motivation toward physical activity will exhibit greater <P 25> participation </> in physical activities outside of school, relative to students receiving a control intervention. METHODS: The trial will adopt a waitlist-control design with cluster-randomization by school. PE teachers assigned to the intervention condition will receive a two-week, 12-h training program comprising basic information on how to promote out-of-school <P 25> physical activity </> and theory-based training on strategies to promote students' autonomous <P 28> motivation </> toward physical activity. Teachers assigned to the waitlist control condition will receive an alternative training on how to monitor physical functional capacity in children with special needs. PE teachers (n = 29) from eleven schools will apply the intervention program to students (n = 502) in PE classes for one month. <P 25> Physical activity participation </>, the primary outcome variable, and psychological mediators from the trans-contextual model will be measured at pre-trial, post-trial, and at one-, three- and six-months post-trial. We will also assess teachers' <P 32>(S1) autonomy-supportive techniques and <P 32> behaviours </> by observation. DISCUSSION: The study will make a unique contribution to the literature by testing a theory-based intervention delivered by PE teachers to promote school students' <P 25> participation </> in out-of-school physical activity. Information will be useful for educators, community stakeholders and policy makers interested in developing programs to promote students' out-of-school <P 25> physical activity </>. TRIAL REGISTRATION: ISRCTN39374060 . Registered 19.7.2018.

30727991\_PD.txt

Title: Promoting vaccination in the province of Quebec: the PromoVaQ randomized controlled trial protocol.

Publication Type: Randomized Controlled Trial

Journal-Name:BMC public health

Journal ID: 100968562

Publication date: 2019/02/08 06:00 [entrez]

BACKGROUND: Vaccination has a huge public health impact. Maintaining vaccine coverage is key to avoid the devastating consequences of resurgence. In the Province of Quebec, vaccine coverage in young children are sub-optimal, mostly due to ambivalence toward vaccine safety and efficacy. We previously conducted a regional study in the Quebec's Eastern Townships region, the PromoVac Study, to test a new educational intervention, based on motivational interviewing techniques, aimed at promoting <P 32> infant vaccination </>. This first study evidenced that the intervention led to a marked increase in mothers' <P 29> intention </> to vaccinate, and <P 32> vaccine </> coverage in their infants. The current study protocol aims at scaling up these results at a provincial level using a randomized controlled trial design. METHODS: This pragmatic, randomized, controlled, parallel-group clinical trial will compare the effectiveness of the motivational interviewing to an educational intervention, including the distribution of an information flyer as standard of care on vaccination coverage in four maternity wards across the Province of Quebec (PromovaQ). Adult mothers of children born in participating maternity wards were recruited between March 2014 and February 2015. Vaccination coverage will be assessed at 3-years of age, thus the trial is expected to be completed in March 2019. Statistical analyses will be conducted under the intention-to-treat principle. <P 32> Vaccine </> coverage will be analyzed using Chi-squared distribution testing and logistic regression to identify determinant factors. Secondary outcomes will include vaccine <P 29> hesitation </> and <P 29> intention </> scores, mother's <P 29> knowledge </>, <P 29> attitudes </> and <P 29> beliefs </> about immunization, and <P 26, 28> psychosocial </> determinants of intention to vaccinate. DISCUSSION: In the case results of this Provincial RCT be confirmed, serious consideration should then be given by Ministry of Health authorities to the possible implementation of MI-based strategies across provincial maternity wards. To ensure adequate input and secure implementation, study design and results will be reviewed with relevant stakeholders, including the children's families, and provincial and regional decision-makers. Results will be adapted and shared with all stakeholders. TRIAL REGISTRATION: ClinicalTrials.gov NCT02666872 (Retrospectively registered as January 28, 2016).

30728061\_PD.txt

Title: Citrus Aurantium and caffeine complex versus placebo on biomarkers of <P 0> metabolism </>: a double blind crossover design.

Publication Type: Randomized Controlled Trial

Journal-Name:Journal of the International Society of Sports Nutrition

Journal ID: 101234168

Publication date: 2019/02/08 06:00 [entrez]

BACKGROUOND: The purpose of this study was to examine resting the metabolic response to the <P 0> ingestion </> of a complex containing Citrus Aurantium + Caffeine (CA + C) and if its consumption influences <P 0> metabolic recovery </> following a high-intensity anaerobic exercise bout in habitual caffeine users. METHODS: Ten physically active males (25.1 +/- 3.9 years; weight 78.71 +/- 9.53 kg; height 177.2 +/- 4.6 cm; body fat 15.5 +/- 3.13%) participated in this study. This study was performed in a double-blind, randomized crossover fashion consisting of two exhaustive exercise protocols. On each visit the participants consumed either a CA + C (100 mg of CA and 100 mg of C) or placebo (dextrose) capsule. After consumption, participants were monitored throughout a 45-min ingestion period, then completed a repeated Wingate protocol, and were then monitored throughout a 45-min recovery period. <P 0> Metabolic function </> was measured through blood <P 0> glucose </>, plasma <P 0> insulin </>, plasma <P 0> triglycerides </>, and plasma <P 0> catecholamines </>: <P 0> epinephrine (E) </> and <P 0> norepinephrine (NE) </>. Biomarkers were taken at four different time points; Ingestion period: baseline (I1), post-ingestion period (I2); Recovery period: immediately post-exercise (R1), post-recovery period (R2). RESULTS: A repeated measures ANOVA revealed significant time-dependent increases in plasma <P 0> epinephrine (E) </> and <P 0> norepinephrine (NE) </> at I2 only in the CA + C trial (p < 0.05), and a significant decrease in blood <P 0> glucose </> at I2 in the PLA trial (p < 0.05); however, no meaningful changes in <P 0> glucose </> was observed following CA + C ingestion. No changes in <P 0> insulin </> or <P 0> triglycerides </> were observed during the ingestion period. No trial-dependent differences were observed in the Recovery period. All biomarkers of <P 0> metabolic recovery </> were equivalent when evaluating R1 v R2. Participants recovered in a similar time-dependent manner in all markers of <P 0> metabolism </> following the PLA and CA + C trials. CONCLUSION: The findings of this study suggested that normal recommended dosages of 100 mg CA + 100 mg C is sufficient to promote <P 0> glucose </> sparing at rest, with modest increases in <P 0> SNS activity </>; however, the individual role of CA or C in this response cannot be determined.

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Title: The effects of Shilajit supplementation on fatigue-induced decreases in <P 25> muscular strength </> and serum <P 0> hydroxyproline </> levels.

Publication Type: Randomized Controlled Trial

Journal-Name:Journal of the International Society of Sports Nutrition

Journal ID: 101234168

Publication date: 2019/02/08 06:00 [entrez]

BACKGROUND: Shilajit is a safe, fluvic mineral complex exudate that is common to Ayurvedic medicine and is composed of fulvic acids, dibenzo-alpha-pyrones, proteins, and minerals. The purpose of this study was to examine the effects of 8 weeks of Shilajit supplementation at 250 mg.d(- 1) (low dose) and 500 mg.d(- 1) (high dose) versus placebo on <P 0> maximal voluntary isometric contraction (MVIC) </> strength, <P 0> concentric peak torque </>, fatigue-induced percent decline in <P 25> strength </>, and serum <P 0> hydroxyproline (HYP) </>. METHODS: Sixty-three recreationally-active men ([Formula: see text] +/- SD: 21.2 +/- 2.4 yr.; 179.8 +/- 6.3 cm; 83.1 +/- 12.7 kg) volunteered to participate in this study. The subjects were randomly assigned to the high dose, low dose, or placebo group (each group: n = 21). During pre-supplementation testing, the subjects performed 2 pretest MVICs, 2 sets of 50 maximal, bilateral, concentric isokinetic leg extensions at 180 degrees .s(- 1) separated by 2-min of rest, and 2 posttest MVICs. Following 8 weeks of supplementation, the subjects repeated the pre-supplementation testing procedures. In addition, the groups were dichotomized at the 50th percentile based on pre-supplementation MVIC and baseline HYP. Mixed model ANOVAs and ANCOVAs were used to statistically analyze the dependent variables for the total groups (n = 21 per group) as well as dichotomized groups. RESULTS: For the upper 50th percentile group, the post-supplementation adjusted mean percent decline in <P 0> maximal voluntary isometric contraction (MVIC) </> was significantly less for the high dose group (8.9 +/- 2.3%) than the low dose (17.0 +/- 2.4%; p = 0.022) and placebo (16.0 +/- 2.4%; p = 0.044) groups. There was no significant (p = 0.774) difference, however, between the low dose and placebo groups. In addition, for the upper 50th percentile group, the adjusted mean post-supplementation baseline <P 0> hydroxyproline (HYP) </> for the high dose group (1.5 +/- 0.3 mug.mL(- 1)) was significantly less than both the low dose (2.4 +/- 0.3 mug.mL(- 1); p = 0.034) and placebo (2.4 +/- 0.3 mug.mL(- 1), p = 0.024) groups. CONCLUSIONS: The results of the present study demonstrated that 8 weeks of PrimaVie(R) Shilajit supplementation at 500 mg.d(- 1) promoted the retention of <P 25> maximal muscular strength </> following the fatiguing protocol and decreased baseline HYP. Thus, PrimaVie(R) Shilajit supplementation at 500 mg.d(- 1) elicited favorable <P 0>(E1) muscle and <P 0> connective tissue </> adaptations.

30732134\_PD.txt

Title: Tobramycin/dexamethasone eye drops as a better choice for lacrimal duct probing in persistent congenital nasolacrimal duct obstruction: A consort study.

Publication Type: Randomized Controlled Trial

Journal-Name:Medicine

Journal ID: 2985248R

Publication date: 2019/02/27 06:00 [medline]

BACKGROUND: Congenital nasolacrimal duct obstruction (CNLDO) is common and. lacrimal duct probing is the major treatment. But persistent CNLDO in older children makes the success rate rapidly decreased due to long-term chronic inflammation. To improve the success rate, probing combined with tobramycin/dexamethasone ointment is considered effective. But in practice, we found a lot of problems in using the ointment. So we tried tobramycin/dexamethasone eye drops as a replacement. The results is surprising, so we hope to do some further research in order to prove it is worth to clinical application. OBJECTIVE: To evaluate the effect of lacrimal duct probing combined with tobramycin/dexamethasone eye drops or ointment on persistent CNLDO in children older than 1-year-old. METHODS: This randomized controlled study included 409 subjects (496 eyes) older than 1-year-old with persistent CNLDO in southwest China, and classified into 3 groups: 96 cases (123 eyes) were the tobramycin/dexamethasone eye drops group (drops group), 88 cases (104 eyes) were the tobramycin/dexamethasone ointment group (ointment group), and 225 cases (269 eyes) were control group which probing with normal saline (NS group). The data of age, sex, and laterality were analyzed through pairwise comparison. Then the 3 groups were divided into 2 subgroups by age, 12 to 24 months and 25 to 36 months. The <P 0> surgical findings </> and <P 0> success </> rate in two subgroups were compared. RESULTS: The <P 0> success </> rates in the tobramycin/dexamethasone eye drops group in both 2 age subgroups were significantly higher than that in the ointment group and NS group (P < .05). CONCLUSIONS: Probing combined with tobramycin/dexamethasone eye drops was effective and <P 32> easy-to-perform </> in the clinic, and it may be a better choice for persistent CNLDO.

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Title: Comparison of fit factors among healthcare providers working in the Emergency Department Center before and after training with three types of N95 and higher filter respirators.

Publication Type: Randomized Controlled Trial

Journal-Name:Medicine

Journal ID: 2985248R

Publication date: 2019/02/27 06:00 [medline]

INTRODUCTION: N95 or higher filtering respirators have been recommended in healthcare settings, although there is still a risk of infection due to the improper selection and wearing of respirators. We aimed to assess the effects of training with N95 or higher filter respirators on the <P 32> protection </> performance of respirators among healthcare providers in the emergency medical center (EMC). METHODS: This randomized crossover study evaluated 23 healthcare providers. Quantitative fit tests (QNFTs) were performed before and after training using three types of N95 or higher filter respirators (cup-type, fold-type, valve-type). Training was performed by lecture, real-time feedback, and fit check. The primary outcome was the <P 0> fit factor </>, and the secondary outcomes were <P 0> overall fit factor </>, adequate <P 32> protection </> rate, and respiratory <P 32> preference </>. RESULTS: <P 0> Fit factors </>, <P 0> overall fit factor </>, and <P 32> adequate protection </> rate were higher after training than before training for the 3 types of respirators (all P < .05). For normal breathing, <P 0> fit factors </> before and after training were 121 (10-185) vs 192 (161-200) for cup-type, 200 (39-200) vs 200 (200-200) for fold-type, and 85 (18-157) vs 173 (117-200) for valve-type. For normal breathing, the adequate <P 32> protection </> rates before and after training were 62 (0-100) vs 100 (90-100) for cup-type, 100 (0-100) vs 100 (100-100) for fold-type, and 19 (0-100) vs 100 (44-100) for valve-type (all P < .05). The most <P 32> preferred </> respirator type was the valve-type (10 persons, 45.5%). CONCLUSIONS: Training on wearing an N95 or higher respirator improved the <P 32> protection </> performance of respirators among healthcare providers working in the EMC. The selection of proper respirators and training would be beneficial to the safety of healthcare providers.

30732169\_PD.txt

Title: Comparison of the <P 0> immunogenicity </> and safety of 3 inactivated hepatitis A vaccines in Korean children aged 12 to 18 months: An open-label, randomized, prospective, multicenter study.

Publication Type: Multicenter Study

Journal-Name:Medicine

Journal ID: 2985248R

Publication date: 2019/02/27 06:00 [medline]

Several approved inactivated hepatitis A (HA) vaccines are available in Korea. These have been shown to be immunogenic and safe in European children; however, their immunogenicity and safety have not been investigated among Korean children. We aimed to compare the <P 0> immunogenicity </> and safety of the most commonly used HA vaccines in ethnic Korean children aged 12 to 18 months.In this open-label, randomized, prospective, multicenter study, 108 children were enrolled and randomized to receive a pediatric form of Avaxim, Epaxal, or Havrix. The 2nd dose was administered after an interval of 6 months. <P 0> Anti-HA virus (HAV) immunoglobulin (Ig) G </> was measured to assess geometric mean concentrations (GMCs) and seropositvity rates (>/=20 mIU/mL anti-HAV IgG). To assess safety, <P 38> local solicited adverse events (AEs) </>, <P 38> systemic solicited AEs </>, <P 38> unsolicited AEs </>, and <P 38> serious AEs (SAEs) </> were graded.Among the 108 participants enrolled, 37, 34, and 37 received Avaxim, Epaxal, and Havrix, respectively. After administration of 2 doses, the seropositivity rates in the Avaxim, Epaxal, and Havrix groups were all 100% (95% confidence intervals [CIs]: 99.0-100, 98.9-100, and 99.0-100, respectively; P < .001). The <P 0> anti-HAV GMCs </> in the Avaxim, Epaxal, and Havrix groups were 5868.4 (95% CI: 4237.2-8126.6), 1962.1 (95% CI: 1298.0-2965.9), and 2232.9 mIU/mL (95% CI: 1428.4-3490.4), respectively, after administration of 2 doses (P < .001). There were no significant differences in the proportions of participants reporting <P 38> local solicited AEs </>, <P 38> systemic solicited AEs </>, <P 38> unsolicited AEs </>, and <P 38> SAEs </> among the 3 vaccine groups after the 1st and 2nd doses. All <P 38> local solicited and unsolicited AEs </> were grade 1 or 2. Grade 3 <P 38> systemic solicited AE </> occurred in 5.4% and 2.9% of the participants in the Havrix group after the 1st and 2nd doses, respectively. <P 38> SAEs </> after the 1st and 2nd doses were reported in 2 participants and 1 participant, respectively, but none was assessed as being related to vaccination. The results indicate that these vaccines were safe and <P 0> immunogenic </> in ethnic Korean children. The results have contributed to the establishing of an HA vaccination policy in Korea and will be informative to countries that plan to initiate vaccination programs against HAV.