(140) An updated review on herbal medicine and their effects on procedures

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With an increasing popularity for patients' use of herbal supplements, there is a greater need to understand the interactions that these herbal medications may have on the body. Some of these postprocedural complications include prolonged bleeding, inflammation, and hypertension. Since many patients do not disclose their use of such herbs, physicians are unaware of the potential for increased adverse effects postprocedurally. The MEDLINE and Cochrane Collaboration databases were searched for articles published between January 2000 and June 2012 using the search term herbal medicine and the names of 10 commonly used herbal medications. We selected studies, case reports, and reviews addressing the safety and pharmacology of the 10 commonly used herbal medications for which safety information pertinent to perioperative adverse effects was available. We extracted safety, pharmacodynamic, and pharmacokinetic information from such selected literature and reached consensus about any discrepancies. Feverfew, garlic, ginger, vitamin E, and echinachea are all known to prolong bleeding and should be discontinued 1 week prior to procedures. Ginkgo biloba is also known to prolong bleeding and should be discontinued for at least 36 hours. Ephedra is known to cause hypertension and should be discontinued at least 24 hours. Ginseng is known to prolong bleeding and worsen hypertension and should be discontinued for at least 1 week. Licorice is known to worsen hypertension and inflammation and should be discontinued for at least 24 hours. Finally, goldenseal is known to worsen inflammation and hypertension and should be discontinued 1 week preprocedure. Physicians need to be become more aware of the potential effects of such commonly used herbal medications to prevent, recognize, and treat potentially serious problems associated with their use and discontinuation. Overall, the understanding of the complications that herbal medications may have could assist to decrease postprocedural adverse effects and improve patient outcomes.

(141) Systematic review and meta-analysis of pharmacological therapies for pain associated with post-herpetic neuralgia

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A systematic review and meta-analysis was conducted to estimate of the relative efficacy of pharmacologic therapies for the treatment of post-herpetic neuralgia (PHN). The published literature was searched through June 2011 for randomized, blinded, controlled clinical trials of pharmacologic treatments for PHN reporting predefined efficacy and safety outcomes. Bayesian mixed-treatment comparison (MTC) methods were used to determine the relative efficacy and harms for all therapies. Data from 29 studies including 26 interventions across 4,375 patients were identified and included in the MTC. Most treatments were effective vs. placebo in reducing PHN pain however several treatments were studied in very few patients, contributing greater uncertainty to model estimates. Among guideline-recommended treatments studied in &ge50 patients, aggregated results of opioids (morphine and methodone) reported in one study was most effective on the numeric pain rating scale (0-none to 10-worst), (mean reduction = -1.70, 95% credible interval [CrI] = -2.22, -1.80). On the visual analog scale (0-none to 100-worst), only tramadol (-9.40, CrI: -11.54, -7.26) and gabapentin (-6.46, CrI: -7.25, -5.65) were more effective than placebo. Pregabalin &ge300mg/day was the most effective treatment in reducing pain by 50% and 30% (relative risk [RR] vs. placebo = 2.44 and 2.13, respectively). Mixed evidence was seen with discontinuation rates of tricyclic antidepressants vs. placebo. A study reporting aggregate results of nortriptyline and desipramine demonstrated more discontinuations than placebo (4.07, CrI: 1.37, 6.41); however, estimates of nortriptyline (0.66, CrI: 0.06, 2.17) obtained from other studies did not show statistically different discontinuations. All treatments had more adverse events than placebo except lidocaine 5% plaster (0.93, CrI: 0.52, 1.32), tramadol (0.95, CrI: 0.63, 1.27), and amitryptyline (1.38 CrI: 0.89, 1.69). These indirect comparisons of PHN treatments can help decision makers better understand the relative benefit of a given choice of therapy. This research was supported by Pfizer, Inc.

(142) A systematic review of the sensitivity of efficacy endpoints TOTPAR and SPID in acute pain

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The effect size of an analgesic investigation is influenced by three factors: (1) the inherent efficacy of the study medication, (2) study conduct, and (3) study design. A key study design component is the choice of primary endpoint. The purpose of this retrospective review was to compare the assay sensitivity of pain intensity endpoints (SPID) to pain relief endpoints (TOTPAR). This was accomplished by performing a systematic review of the literature using PubMed, summary basis of approvals, the Cochrane library and manual searches to identify acute pain studies that calculated both SPIDs and TOTPARs. Studies were included in this review if: (1) they were randomized, double-blind placebo controlled investigations involving study medication for post-surgical acute pain, (2) enough data was provided to calculate both a pain intensity and pain relief effect size for a single time point, and (3) the data was provided for a single dose time interval (e.g., single-dose studies or multiple-dose studies where data were captured for the first dose). A determination was made as to whether a greater effect size was demonstrated utilizing SPID or TOTPAR for a single time point within each study. Of the 10 studies examined, 8 studies showed greater effect sizes using TOTPAR as the efficacy outcome compared to its corresponding SPID. The magnitude of the differences between the two outcomes ranged from 4-40%. Conversely, 2 studies revealed SPID to produce a greater effect size. This review comparing effect sizes from multiple randomized studies suggests that TOTPAR may have better assay sensitivity than SPID. Although a more exhaustive literature search may lead to a definitive conclusion, our data underscores the importance of choosing the proper primary endpoint in the design and planning of clinical trials.

(143) The role of Embeda (morphine sulfate-naltrexone hydrochloride) in opioid abuse: a systematic review of literature

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The struggle to balance the analgesic needs of the patient and reduce public health concerns of prescription opioid abuse have led to the development of abuse resistant opioid formulations. Embeda is a novel abuse resistant opioid formulation consisted of extended release morphine sulfate with sequestered naltrexone hydrochloride. The method of abuse deterrence involves a release of naltrexone to counteract the effects of morphine sulfate if the capsule is compromised by crushing. A systematic review of literature was conducted to evaluate whether Embeda reduces opioid abuse. A search from 2004-2011 was done using PubMed, OVID, Scopus, and National Library of Medicine Drug Information Portal using terms: Embeda, morphine/naltrexone, and opioid abuse. Twelve studies to date have been reviewed by the FDA in the evaluation of Embeda but only 3 studies evaluated the abuse potential. In a randomized double-blinded study 32 subjects were evaluated for subjective effects of Embeda whole, Embeda crushed, morphine sulfate solution, & placebo. Results produced statistically significant ($p<0.01$) degree of increased euphoria in morphine sulfate solution population than crushed Embeda at similar plasma concentrations. A second randomized double-blinded study evaluated the effect of dose ranging naltrexone on morphine induced euphoria in 27 subjects. Results from the second study showed that only naltrexone at 4.8mg dose produced statistically significant reduction in morphine induced euphoria. The third study was a randomized double-blinded study that evaluated euphoric effects of intravenous morphine alone versus combination with naltrexone in 28 subjects. The results of the study showed statistically significant 71% reduction in euphoria compared to IV morphine alone. All three studies were conducted in non-opioid dependent subjects. In conclusion all three studies showed statistically significant reduction in euphoric effects of crushed Embeda but there is no evidence to prove a reduction of abuse in opioid-dependent individuals.