The Cochrane Column

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Cochrane Column: Best Evidence from The Cochrane Library

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External Beam Radiotherapy (EBRT) Should Be Avoided in Stage 1 Endometrial Cancer Patients with No High-Risk Factors

Endometrial cancer is one of the most common gynecologic cancers in the West and 75% of affected women are postmenopausal. Most endometrial cancers are diagnosed with stage 1 disease. About 10% of women with stage 1 endometrial cancer treated with surgery alone are at risk for recurrence. This risk is significantly higher for some women with high-risk factors (the stage of the disease, depth of myometrial invasion, grade of the tumor, lymphovascular invasion and the patient’s age). The initial treatment for stage 1 disease is usually surgery including total abdominal hysterectomy and bilateral salpingo-oophorectomy. The chances of first relapse (usually in the upper vagina) can be reduced by adjuvant postoperative radiotherapy.

Several postoperative treatment options for stage 1 endometrial cancer currently available which include a surveillance policy, adjuvant pelvic external beam radiotherapy (EBRT), and adjuvant vaginal intracavitary brachytherapy. Both EBRT and vaginal intracavitary brachytherapy (to a lesser extent) carry the risks of acute toxicities and long-term complications. There is no clear consensus guideline on the relative merits of these three approaches for patients with early stage endometrial cancer after hysterectomy.

Four randomized controlled trials (RCTs) with 1,770 patients suffering from stage 1 endometrial cancer [870 in the treatment group (additional pelvic EBRT) and 900 in the control group (no additional EBRT)] were included in the present meta-analysis. The addition of pelvic EBRT to surgery reduced locoregional recurrence [relative risk (RR): 0.28, 95% CI: 0.17 – 0.44, P<0.00001], which is a 72% reduction in the risk of pelvic relapse and an absolute risk reduction of 6% (95% CI of 4 to 8%). The number needed to treat to prevent one locoregional recurrence: 17 patients (95% CI: 13 to 25).

The data from this review show that adjuvant EBRT greatly reduced locoregional recurrence in stage 1 endometrial cancer (RR reduction: 72%). This reduction in locoregional recurrence, however, did not translate into either a reduction in the risk of distant recurrence or death from all causes or endometrial cancer death. External beam radiotherapy carries an inherent risk of damage and toxicity and should be avoided in stage 1 endometrial cancer patients with no high-risk factors. However, in patients with multiple high-risk factors (at least grade 3 and stage 1c), there may be a trend towards a benefit in survival, as well as a reduction in locoregional recurrence. The results of ongoing trials are needed to tell us whether EBRT can improve survival in those women with stage 1 endometrial cancer with only one high-risk factor (e.g., grade 3 or stage 1c).


Oral Erythromycin May Be Effective in Treating the Rash and Decreasing the Itch in Pityriasis Rosea

Pityriasis rosea (PR) is a scaly rash that mostly affects young adults (10 to 35 years old) and is described by a sudden appearance of discrete plaques, usually on the trunk. It is relatively common and affects about 170 out of every 100,000 people in the community each year. A generalized eruption then follows and all lesions
disappear within two to 12 weeks spontaneously without treatment. Girls and women are more likely to have PR (female to male ratio is about 1.4:1). About 50% of all people with PR have moderate to severe itching. The quality of life of people with PR is significantly affected. Parents of children with PR also have significant anxieties about the cause, nature, and possible infectivity of the eruption. Currently, both topical (emollients and corticosteroids) and systemic treatments (oral antihistamines, sunlight and artificial ultraviolet radiation, systemic corticosteroids, oral antibiotics and antiviral agents) are used to treat PR.

The importance of the present review is due to experiencing moderate to severe itch by about 50% of people with PR. It is not known whether the current treatments are useful and whether the benefits outweigh the risk of adverse effects. The aim of present review was to assess the effects of interventions for PR.

Three RCTs were included in the study involving 148 participants. One small poor-quality trial compared licorice root with an anesthetic injected intravenously (23 subjects), a fair-quality trial compared an antihistamine with a steroid taken orally (85 subjects), and a good-quality trial that compared an antibiotic with placebo tablets (40 subjects).

The poor-quality trial found no significant difference between licorice and anesthetic for resolving symptoms or rash. The fair-quality trial found no significant difference in itch resolution between the antihistamine and the corticosteroid. However, the antihistamine and the corticosteroid on their own were both found to be better at clearing rash than a combination of antihistamine and corticosteroid. The small good-quality trial found that oral erythromycin was better than placebo in improving the rash and alleviating the itch. No serious adverse effects were reported for any intervention.

Although there is inadequate evidence of efficacy for most treatments, but oral erythromycin (250 mg every six hours for two weeks) may be effective in treating the rash and relieving the itch. We should consider that the result is adapted from just one small study.


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**Intravenous Use of Magnesium in Acute Myocardial Infarction is Not Evidence Based**

Cardiovascular disease remains the leading cause of death in developed countries, and acute myocardial infarction accounts for a large proportion of these deaths. In some countries, intravenous (IV) magnesium is an inexpensive, easy-to-use supplemental treatment and administered to heart attack patients in order to limit damage to the heart muscle, prevent serious arrhythmias, and reduce the risk of death. Several small trials appeared to support the practice. But the authors of this review found that other trials went unpublished once they produced unfavorable results.

A controversy appeared in 1995, when a large well-designed trial with 58,050 participants did not demonstrate any beneficial effect to IV magnesium, contradicting earlier meta-analyses of the smaller trials. The aim of Li et al’s review was to examine the effect of IV magnesium versus placebo on early mortality and morbidity.

This review includes 26 clinical trials with more than 70,000 participants that had randomly assigned heart attack patients to receive either IV magnesium or an inactive substance (placebo). Their results were mixed: IV magnesium reduced the incidence of serious arrhythmias, but this treatment also increased the incidence of profound hypotension, bradycardia, and flushing. However, any apparent beneficial effects of magnesium may simply reflect various biases in these trials. Additionally, there was a lack of uniformity in these trials in terms of dosage and the timing of the IV magnesium regimen, which in some trials also included anticlotting drugs.

Owing to the likelihood of publication bias and marked heterogeneity of treatment effects, it is essential that the findings are interpreted cautiously. From the evidence reviewed here, the authors conclude that: 1) it is unlikely that magnesium is beneficial in reducing mortality both in patients treated early and in patients treated late, and in patients already receiving thrombolytic therapy; 2) it is unlikely that magnesium will reduce mortality when used at high dose (≥75 mmol); 3) magnesium treatment may reduce the incidence of ventricular fibrillation, ventricular tachycardia, and severe arrhythmia needing treatment or Lown 2 – 5, but it may increase the incidence of profound hypotension, bradycardia, and flushing; and 4) the areas of uncertainty...
regarding the effect of magnesium on mortality remain the effect of low dose treatment (<75 mmol) and in patients not treated with thrombolysis. The evidence produced by this review does not support continued use of IV magnesium. Other effective treatments (aspirin, beta-blockers) should be used to treat heart attack.


Omega-3 Fatty Acids (Fish Oil) Seem to Be Safe and Effective in Crohn's Disease for Maintaining Remission

Crohn's disease (CD) is characterized by chronic intestinal inflammation causing a varying spectrum of clinical symptoms. Some patients remain chronically active, while others have a pattern of clear exacerbations and remissions. Randomized controlled trials have suggested a positive effect of omega-3(Ω 3) in various disease states, including cardiovascular, inflammatory, immunologic, psychologic, and neurologic disorders. The beneficial effects of Ω 3 are thought to be secondary to an anti-inflammatory, antithrombotic, antiarrhythmic, hypolipidemic, and vasodilatory properties. The primary objective of this study was to systematically review the effectiveness of fish oil or Ω 3 for maintaining remission in CD. Fish oil contains Ω 3 fatty acids that may be beneficial in reducing inflammation, such as seen in the bowel of CD patients.

Four studies were included. There was not statistically significant benefit of Ω 3 therapy for maintaining remission (relative risk: 0.64; 95% CI: 0.4 – 1.03; P=0.07). However, the studies were both clinically and statistically heterogeneous (P=0.01, I2=72%). Three studies used enteric coated capsules and reported a significant reduction in the one-year rate of disease relapse in comparison with placebo (risk reduction: 31%). Subgroup analyses of studies, which used enteric coated capsules revealed a statistically significant benefit for maintenance of remission (relative risk: 0.49, 95% CI: 0.35 – 0.69); number needed to treat to prevent relapse in one year was three (95% CI: 2 – 5; I2=19%). There were no serious side effects in any of the studies.

The limited existing data suggest that daily oral therapy with enteric coated Ω 3 is safe and may be effective for maintenance of remission in pediatric and adult CD. Currently, however, the data are insufficient to make a recommendation for the routine use of Ω 3 fatty acids for this purpose.