There was no statistically significant change from baseline HbA1c in either group during the study (treatment group: 6.5% baseline, 6.5% final, placebo group: 6.3% baseline, 6.1% final). The analysis of variance showed no significant differences between the groups ($P=.20$).

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The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the US Army Medical Department, the US Army at large, or the Department of Defense.

In patients undergoing induction for a second-trimester fetal demise, does the use of high-dose oxytocin reduce the incidence of retained placenta?

Evidence-Based Answer

Ten units oxytocin intramuscularly during the third stage of labor may decrease the incidence of placental retention, whereas a continuous oxytocin infusion (started with a misoprostol induction) does not appear to help. Third-stage oral misoprostol and oxytocin via umbilical vein postdelivery also do not appear to decrease the incidence of placenta retention (SOR: $B$, RCTs).

A 2009 RCT study of 251 women who had undergone induction with misoprostol for second-trimester termination were randomized into 1 of 3 treatment groups after delivery of the fetus (10 U intramuscular oxytocin, 600 mcg oral misoprostol, or no medication) to evaluate the incidence of placental retention. The presence of retained placenta was evaluated 60 minutes postdelivery.

Oxytocin was associated with a significantly lower rate of placental retention compared with no pharmacologic intervention (OR 0.24; 95% CI, 0.1–0.57; $P=.001$). Misoprostol was found to be similar to no intervention (OR 0.92; 95% CI, 0.47–1.80; $P=.813$).

A 2006 RCT compared 200 mcg intravaginal misoprostol followed by 100 mcg oral misoprostol with the same misoprostol regimen plus oxytocin 6 mU/min IV started at the onset of induction in second-trimester termination of pregnancy in 388 women. The primary outcome was failure rates, defined as retained placenta and/or incomplete/unsuccesful abortion. There was no difference in failure rates between the groups (18% vs 28%; $P=.32$).

A 1993 RCT evaluated the incidence of placental retention after injection of oxytocin into the umbilical vein in 50 women with midtrimester pregnancy losses. After delivery of the fetus (spontaneously or postinduction), the patients were randomized to receive either 100 U oxytocin or 20 mL normal saline injected into the umbilical vein. Placental retention was evaluated after 60 minutes. There was no difference in how many patients required operative removal of the placenta between the oxytocin group and control group (33% vs 29%; $P=.53$).

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Are antioxidants effective in preventing macular degeneration?

Evidence-Based Answer

Antioxidant supplements or minerals, such as vitamin E and beta-carotene, do not prevent or delay the onset of age-related macular degeneration (AMD) (SOR: $A$, meta-analysis of RCTs). Similarly, dietary intake of antioxidants does not appear to affect the development of AMD (SOR: $B$, meta-analysis of primarily cohort studies).

In 2012, a Cochrane review examined whether antioxidant supplements prevent AMD. This analysis included 4 RCTs of more than 62,000 subjects across the United States, Australia, and Finland. The minimum age included in any of the trials was 40 years. Two trials included male subjects only and 1 included female health professionals exclusively. These trials evaluated vitamin E (500 IU daily and 600 IU every other day), beta-carotene (20 mg daily
and 50 mg every other day), and alpha-tocopherol (50 mg daily) supplementation alone or in combination for 4 to 12 years (median 6.1 years).

There was no observed difference in the risk of developing AMD in patients taking any antioxidants compared with patients taking placebo (risk ratio [RR] 0.98; 95% CI, 0.89–1.1). Similar results were found when looking at advanced AMD (RR 1.1; 95% CI, 0.80–1.4). Additionally, results remained consistent when analyses were confined to beta-carotene alone (2 trials, N=21,589; AMD RR 1.0; 95% CI, 0.89–1.2; advanced AMD RR 0.97; 95% CI, 0.69–1.4) or alpha-tocopherol alone (3 trials, N=40,887; AMD RR 0.97; 95% CI, 0.85–1.1; advanced AMD RR 1.3; 95% CI, 0.84–2.1). The authors concluded otherwise healthy individuals will not benefit from antioxidant supplements to prevent or delay AMD.

A 2007 systematic review evaluated the effects of dietary antioxidant consumption on the development of early and late AMD in 12 trials with nearly 173,000 adults aged 40 years and older. Data from 9 prospective cohort trials (1 published only as an abstract) and 3 RCTs (1 published only as an abstract) were analyzed. The mean duration of follow-up in the cohort trials was 9 years. Follow-up ranged from 4 to 12 years in the RCTs.

Of the dietary antioxidants examined—including vitamins A, C, E, zinc, lutein, zeaxanthin, alpha- and beta-carotene, beta-cryptoxanthin, and lycopene—none provided a protective effect against AMD. In pooled data from the 2 highest quality trials, vitamin E demonstrated a protective effect (5,879 patients; OR 0.75; 95% CI, 0.59–0.94); however, this benefit was not seen when pooling the results of all included studies (OR 0.83; 95% CI, 0.69–1.0). Results regarding dietary antioxidants and late AMD could not be pooled as each of the studies evaluating this endpoint used a different antioxidant. The authors concluded that dietary antioxidants have minimal or no effect on the development of early AMD in well-nourished Western populations.

A 2004 Cochrane systematic review of 26 RCTs with 1,826 children, aged 4 months to 18 years examined the effectiveness of the second-generation antihistamine, ketotifen, in the long-term treatment of asthma. Use of other asthma control medications in addition to ketotifen was allowed in all trials, but there was no standardization of types of asthma-control medications among the RCTs.

Children were more than twice as likely to stop or decrease their use of inhaled bronchodilators when treated with ketotifen (risk ratio [RR] 2.4; 95% CI, 1.6–3.5). Ketotifen was associated with an increased risk of sedation (RR 1.7; 95% CI, 1.1–2.6) and weight gain (RR 1.4; 95% CI, 1.0–2.0). Despite these adverse events, there was no increased risk of stopping ketotifen due to adverse effects (RR 1.2; 95% CI, 0.30–4.9). A 2011 systematic review discussed 5 RCTs of second-generation antihistamines (desloratadine and cetirizine) in children and adult patients with both asthma and allergic rhinitis. A total of 1,637 patients were included, and most trials lasted only 4 weeks.

Do antihistamines improve asthma symptoms in patients with seasonal allergies?

Evidence-Based Answer
The first-generation antihistamine oxatomide does not relieve asthma symptoms, whereas certain second-generation antihistamines might. However, current consensus guideline recommendations are to not treat asthma symptoms with antihistamines (SOR: C, inconsistent systematic reviews, single RCT, and expert opinion).

A 2003 Cochrane systematic review of 6 RCTs with 494 patients examined the effectiveness of the first-generation antihistamine, oxatomide, in asthma treatment. The review was unable to pool pulmonary function tests or symptom scores.

None of the individual studies found a significant difference in peak expiratory flow between oxatomide and placebo. Measurements of FEV1 and FEV1/FVC showed variability among the studies. The review was able to analyze adverse events and determined significantly more patients receiving oxatomide had adverse effects such as drowsiness and weight gain (OR 3.0; 95% CI, 1.7–5.2) than patients receiving placebo. The number needed to harm was 7 for any adverse event and 8 for drowsiness.

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