

Maintenance tocolysis. Still unsolved problem

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Preterm birth (PTB) is a major cause of neonatal mortality and morbidity. Few RCTs evaluated the effectiveness of the main tocolytics as maintenance tocolysis. Oral ritodrine and oral nifedipine were not effective in reducing the recurrence of preterm labor (PTL) or in prolonging pregnancy. An individual patient data meta-analysis including 6 studies (787 women) found no significant differences in the incidence of perinatal death, neonatal morbidity and prolongation of pregnancy in women treated with oral nifedipine compared with placebo/no treatment. Subcutaneous continuous atosiban was tested as maintenance tocolysis in one RCT. A significant prolongation of 5 days in time to first recurrent labor episode was reported in treatment group. Magnesium has no effect compared with placebo/no treatment or other therapies in preventing preterm birth. The role of vaginal progesterone (P) and 17-alpha-hydroxyprogesterone caproate (17P) is still debate. A recent meta-analysis by Palacio et al shows a reduced risk of PTB<37 weeks and a significant prolongation of pregnancy in patients treated with progestogens compared with placebo/no treatment. However, analyses including only five high-quality studies found no significant differences. Last year, we published a RCT comparing P and 17P. We found no differences in PTB<37 weeks. Stratifying according to cervical length, there was an increased risk of PTB<37 and <35 weeks in women receiving P respect with controls. Given the inefficacy of common tocolytics, we tested alpha-lipoic acid (ALA) and published a pilot RCT on vaginal ALA effects on cervical length after primary tocolysis. Nulliparous women with singleton pregnancies between 24-30 weeks after a PTL episode were enrolled and randomly allocated to vaginal ALA 400 mg/day, or placebo. We evaluated changes in pro-(IL1, IL2, IL6, IL8, TNF?) and anti-inflammatory (IL4, IL10) cytokines in cervical fluid in 17 and 15 patients respectively in ALA and placebo group. Baseline cytokines were similar. After treatment a significant increase in anti-inflammatory cytokines was detected in ALA group. Cervical length remains stable in ALA group, while it significantly shorten in placebo group. Stratifying for cervical length (<20mm or ?20mm) the same changes were observed. Vaginal ALA treatment is associated with stabilization of cervix, probably due to stimulation of anti-inflammatory cytokines. Since this was a pilot study, such findings have to be confirmed by larger trials.

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