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Isonicotinic acid hydrazide (INH): A new agent for cervical ripening at term

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Induction of labor is frequently used when continuation of pregnancy is associated with greater risks for mother and/or fetus than intervention (e.g., diabetes, post-term pregnancy, eclampsia- preeclampsia, IUGR or fetal distress). Favorable cervix is a prerequisite for successful induction of labor. However, in many cases, there is an indication for labor induction in the absence of favorable cervix. At present, misoprostol is the prostaglandin of choice for induction of labor in a number of countries. However, it is associated with serious adverse effects such as uterine hyperstimulation or rupture. Several processes involved in cervical remodeling are similar in mouse and human and studies in murine pregnant cervix have shown that during pregnancy, increase in collagen solubility decreases tissue rigidity and results in cervical softening. Furthermore, it has been reported that isonicotinic acid hydrazine (INH), an anti-tuberculosis agent, increases collagen solubility due to inactivation of lysyl oxidase. This enzyme is responsible for initiating cross-link formation in collagen and it is proposed that INH may cause lysyl oxidase inhibition by competing for its obligatory cofactor, pyridoxal phosphate. Crosslinks between collagen molecules are essential for strength of collagen fibers and tissues and reduction in collagen cross-linking has been shown to decrease mechanical strength of the resulting tissue. We hypothesized that intravaginal INH could induce cervical ripening by increasing collagen solubility and in this randomized clinical trial we compared the efficacy and safety of intravaginal INH and misoprostol in pre-induction cervical ripening. In this randomized double-blind controlled trial, 150 pregnant women with term pregnancy who scheduled for labor induction with Bishop's score <5 were enrolled. They were assigned randomly to vaginal administration of isonicotinic acid hydrazide (INH) (900 mg) or misoprostol (25 mcg), which were repeated every 4 h up to 3 times as needed. Changes of Bishop's score and time from start of medication to labor and to delivery were assessed. There was a significant increase in Bishop's score in each group during the first 12 h of study. However, in INH group, changes of Bishop's score were greater at the end of 12 h after first drug insertion ($p=0.04$), labor induction was needed more frequently, and the time from start of medication to the beginning of active phase of labor and to the time of delivery were significantly longer ($p<0.001$). In conclusion, INH may be used as a ripening agent before induction of labor at term.

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