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MEDICAL ABORTION WITH MIFEPRISTONE AND MISOPROSTOL IN THE FIRST TRIMESTER:

Efficacy, side effects, women's perceptions and endocrine effects

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ACADEMIC DISSERTATION

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ABSTRACT

Aims

Medical abortion with a combination of mifepristone and a prostaglandin analogue, an alternative to surgical abortion in early pregnancy, has been studied since the early 1980s. In 2000, this procedure became available for routine use in several European countries. The purpose of this study was to evaluate the efficacy, side effects and duration of bleeding of oral versus vaginal administration of misoprostol combined with mifepristone, and of continued oral misoprostol, in termination of early pregnancy. Women's perceptions of medical abortion, and the kinetics of selected hormones and of insulin-like growth factor-binding protein-1 (IGFBP-1) were also assessed.

Methods

The efficacy, side effects and duration of bleeding were investigated in a multinational, double-blind, randomized controlled trial comprising 2219 women from eleven countries requesting medical abortion with ≤63 days of amenorrhoea. Mifepristone 200 mg was administered orally, followed two days later by 0.8 mg of misoprostol, either orally or vaginally. The oral group and one of the vaginal groups continued with 0.4 mg of oral misoprostol twice daily for seven days.

Women's perceptions were evaluated in the multinational trial and in more detail in a subgroup of 123 Finnish participants.

The kinetics of serum hCG, progesterone, oestradiol and cortisol were studied in a subgroup of 34, and those of serum and cervical IGFBP-1 in a subgroup of 16 Finnish women. Serum and cervical samples for measurement of IGFBP-1 were collected up to six weeks, and serum samples for measurement of the hormones and of mifepristone up to two weeks following the beginning of the treatment.

Results

The crude complete abortion rate was 92.3% in the oral plus continued oral misoprostol group, 93.5% in the vaginal-only group and 94.7% in the vaginal plus continued oral misoprostol group. In pregnancies with ≥57 days of amenorrhoea, the risk of failure was 2.8 times (CI 1.3 to 5.8) higher in the oral plus continued oral misoprostol group, and 2.2 times (CI 1.0 to 4.7) higher in the vaginal-only group, when compared with the vaginal plus continued oral misoprostol group. In pregnancies <57 days, the differences were not significant. Nausea, vomiting and diarrhoea were

more frequent after oral than after vaginal administration of misoprostol. Continuation of misoprostol had no effect on the duration of bleeding, but increased the frequency of diarrhoea by threefold, to 27%.

Should the need arise, the majority of women, 84%, would choose medical abortion again, and 70% would prefer clinic to home abortion.

Serum hCG, progesterone and oestradiol concentrations continued to increase until two days after administration of mifepristone. Following misoprostol, hCG and progesterone levels decreased by 70.5 $\pm$ 8.8% and 61.3 $\pm$ 16.3% (mean $\pm$ SD), respectively, in 24 hours. The decline in hCG correlated inversely with the time taken to abort. The kinetics of hCG and progesterone were similar irrespective of the route of administration of misoprostol.

In the cervix, the concentration of IGFBP-1, measured both with the assay detecting the amniotic fluid isoforms and with the assay preferring the phosphorylated, decidual isoforms, increased after administration of mifepristone. After misoprostol, the increase in IGFBP-1, measured by the assay preferring the amniotic fluid isoforms, was more pronounced. The increase in cervical IGFBP-1 after administration of misoprostol, measured by the assay preferring the decidual isoforms, correlated inversely with the time taken to abort. In serum, the highest concentrations of IGFBP-1 were reached after mifepristone but before administration of misoprostol. The serum levels of IGFBP-1, measured by the assay preferring the decidual isoforms, exceeded those in cervical secretion after administration of mifepristone.

Conclusions

In pregnancies with $\geq$57 days of amenorrhoea, vaginal administration of misoprostol was more effective than oral when continued with oral misoprostol for seven days. In this amenorrhoea group, continuation of misoprostol improved the efficacy compared with a single dose of vaginal misoprostol, but it did not shorten the duration of bleeding. In pregnancies <57 days of duration, no difference in efficacy was present between the treatment groups. Nausea, vomiting and diarrhoea were more frequent after oral administration of misoprostol.

The majority of women would choose medical abortion again and would prefer clinic to home abortion.

The kinetics of hCG and progesterone were similar with each other, and similar irrespective of the route of administration of misoprostol.

The kinetics of circulating and cervical IGFBP-1 differed, indicating different sources and regulation of serum and cervical IGFBP-1.