Pharmacokinetic Analysis of Hourly Oral Misoprostol Administration – A Pilot Study

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Objective

To conduct a pilot study of optimal misoprostol dosing to induce moderate labor among woman and to understand the pharmacokinetic parameters of moderate labor induction or augmentation.

Method

We administered high doses of oral misoprostol (200μg) hourly to nine mid-trimester pregnant women who had requested termination of gestation to determine whether misoprostol metabolites (misoprostol acid, MPA) accumulated in the blood plasma. We then chose five pregnant women at term to receive individual hourly oral misoprostol administration program and measured plasma concentrations of MPA at various stages of labor including the beginning of misoprostol solution administration, the initial response of regular uterine contractions, and full cervical dilation.

Results

The concentration of MPA, which is responsible for misoprostol's clinical activity and toxicity, had no obvious accumulation after high-dose hourly oral misoprostol administration (Figure). Furthermore, the five moderate dosing programs of hourly oral misoprostol administration ripened the cervix with very low concentrations of MPA detected in the plasma (Table).

Figure . Pharmacokinetic profile of hourly oral misoprostol administration with 200 μg/hr

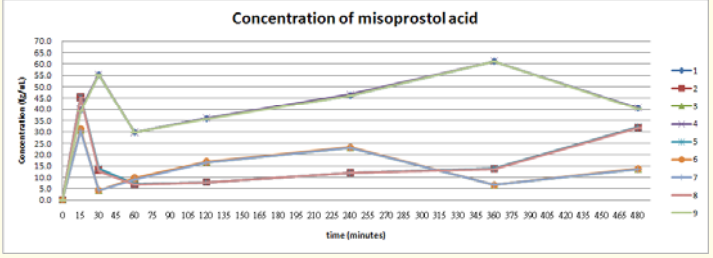

Table. Pharmacokinetic analysis of five regimens of hourly oral misoprostol administration

Case No	Age	Body Height (cm)	Body Weight (Kg)	Para	Bishop Score*	Concentation of misoprostol acid (fg/μL)			Dosing Regimen
						Time 0	Time 1	Time 2	
1	24.0	159	74.0	3	5	N.D.	N.D.	N.D.	20μg→20μg→20μg
2	25.9	158	78.0	1	3	N.D.	N.D.	N.D.	20μg→20μg→20μg→20μg→20μg
3	30.7	158	60.0	2	4	N.D.	N.D.	N.D.	20μg→20μg→20μg→20μg→40μg→40μg→20μg
4	32.5	18	70.0	4	8	N.D.	7.7	8.8	20μg→20μg→20μg→20μg→40μg→40μg→40μg
5	24.8	165	67.0	3	4	N.D.	4.7	N.D.	20μg→20μg→20μg→20μg→40μg→40μg→40μg →40μg→60μg→40μg→40μg

*: Bishop score on admission before labor induction or augmentation
N.D.: non-detectable
Time 0: immediately after initial misoprostol administration.
Time 1: at the start of regular uterine contractions.
Time 2: at full cervical dilatation.

Conclusion

The preliminary results show that the five defined programs in labor induction or augmentation are promising dosing regimens that avoid uterine hyperstimulation, shorten the labor course, and prevent the risk of potential toxicity from excess MPA.