REVIEW ARTICLE

MISOPROSTOL IN OBSTETRICS AND GYNAECOLOGY- A CLINICAL REVIEW

ISHRAT S[1], ISLAM F[2]

Abstract:
Although misoprostol is widely used in Obstetrics and Gynaecology it is not officially approved for these uses. The literature review shows its efficacy and safety in most of its indications. Misoprostol is effective in cervical priming and inducing uterine contraction and so used in termination of pregnancy. Its use at term can be complicated with serious side effects on uterine contractility and fetal heart rate , rarely causing uterine rupture and fetal death. But review of the studies finds limited reports of these life-threatening complications. Misoprostol is also effective in prevention of postpartum haemorrhage but the effect is not more than combination of oxytocin and ergometrine.

Key words: *Misoprostol, prostaglandin, clinical use.*

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Introduction:

Misoprostol is a synthetic analogue (methyl ester) of natural prostaglandin E1[1]. It produces dose related inhibition of gastric acid and pepsin secretion and enhances mucosal resistance to injury. It has been marketed for prevention of gastritis and peptic ulcer disease associated with the use of non-steroidal anti-inflammatory drugs [2]. Because of its ability to produce cervical ripening and uterine contraction misoprostol has been effectively used in termination of first and second trimester pregnancy, induction of labour as well as in active management of third stage of labour [2].

Misoprostol is not approved for obstetric use by Food and Drug Adminstration, so it is an off-label drug without an official approval [3]. But safe and effective use of the medication has been documented world wide. Various doses, routes and protocols have been investigated. The optimal dosage and route of administration have yet to be defined.

Methods of review:

Evidence based publications were collected by extensive hand and electronic searching. We searched the Medline under MeSH 'misoprostol' and retrieved the randomized controlled trials with valid end points and meta-analysis.

Prostaglandins and Misoprostol:

Prostaglandins are ecosanoids, a group of 20 carbon unsaturated fatty acids derived principally from arachidonic acid in cell walls. They are short lived and potent and are formed in almost every tissue of the body. The effects of prostaglandins are multitude and varied. They are particularly important in female reproductive cycle in particular, in cardiovascular system, in inflammatory response and in the causation of pain [4].

Systemic analogues of prostaglandins that are being used in obstetrics and gynaecology [5] include

i) PGE1 analogue: gameprost (termination of first trimester of pregnancy with or without antiprogesteron)
ii) PGE2 analogue: Dinoprostone (vaginal/ cervical gel for late therapeutic abortion and induction of labour)
iii) PGF2 alpha analogue: Dinoprost (termination of pregnancy), Carboprost (postpartum haemorrhage, resistant to oxytocin and ergometrine)

Pharmacokinetics of Misoprostol:

Although formulated for oral administration, misoprostol is effectively absorbed through vaginal wall as well as rectal, buccal and

1. Assistant Professor, Department of Obstetrics & Gynaecology, Dhaka Medical College & Hospital, Dhaka.
2. Professor & Head, Department of Obstetrics & Gynaecology, Dhaka Medical College & Hospital, Dhaka.
Correspondence: Dr. Shakeela Ishrat.

sublingual mucosa. Zeimen et al [6] showed that systemic bioavailability of vaginally administered misoprostol is three times higher than than that after oral administration. Vaginal misoprostol is absorbed more slowly than oral misoprostol reaching peak serum concentration within 1 hr compared to 30 minutes for oral administration. In addition vaginal misoprostol is eliminated more slowly than oral misoprostol > 4 hrs compared to 2-3 hrs respectively. This is perhaps because of the pre-systemic gastrointestinal bypass. In addition vaginal misoprostol may have direct effect on the cervix, initiating the physiologic events of increased uterine contractility. Misoprostol adminstered through sublingual and buccal (between birth and cheek) route.has higher efficacy than oral misoprostol because it bypasses the gartrointestinal and hepatic first pass metabolism. It can be discarded any time in the event of excessive uterine stimulation. The inconvenience of serial vaginal examination can be avoided while effective drug absorption can be provided[7,8].

Misoprostol and Pospartum Haemorrhage

Misoprostol administered in the third stage of labour can reduce postpartum blood loss in vaginal deliveries [9] as well as in caesarean section [10]. The efficacy is similar to intravenous or intramuscular oxytocin [11] but less than that of oxytocin and methylergometrine combined [12,13]. Misoprostol has specific side effects like shivering, transient pyrexia, nausea ,vomiting and diarrhea [14]. But the adverse effects are less when administered rectally or vaginally than orally [15]. So misoprostol may be a cheap alternative to oxytocin and ergometrine when their use is contraindicated and facilities for their storage and parenteral administration are limited [16]. Misoprostol has greater potential for use in third stage of labour in developing countries especially if it is administered orally and as it is thermo-stable in tropical countries [17].

Misoprostol and Induction Of Labour

Misoprostol effectively induces labour. Studies with different dose regimens (100 microgram orally or 25-50 microgram vaginally every 6-8 hours for maximum 5 doses) have shown that misoprostol leads to shorter induction delivery interval, less likely to require a repeat dose or oxytocin administration, but more incidence of hyper-stimulation and caesarean section for fetal distress [18,19]. Sublingual and buccal administration are also effective but have more side effects [8]. Other routes have more acceptability than vaginal route but there is risk of self administration and overdose with life-threatening complications for both the mother and foetus.

The trials to induce labour with misoprostol among women with history of caesarean delivery were terminated because of concern of patients safety. The American College of Physician and Surgeons has recommended the discontinuation of misoprostol use among women with a history of caesarean delivery [20].

Misoprostol and Second Trimester Termination of Pregnancy

Misoprostol can be used with caution for induction of second trimester abortion. A regimen of 200-400 microgram intra-vaginal or oral misoprostol every 6-8 hrs is a convenient alterative to the conventional methods of mid-trimester abortion [21]. The induction abortion interval is significantly shorter, the number of doses required are less and maximum Bishops scores reached are higher [22]. Misoprostol administered vaginally is significantly more effective then when administered orally as judged by induction to delivery interval and also the need to otherwise augment therapy with a syntocinon infusion [23]. High dose intravagiinal misoprostol doe not alter the maternal cardiac function as measured by transthoracic electrical bioimpedence [24].

A review of 38 RCT's involving 3679 women reveals that the use of vaginal misoprostol in the termination of second and third trimester pregnancy is as effective as other prostaglandins and more effective than oral administration of misoprostol. However important information regarding maternal safety, in particular the occurrence of rare

outcomes such as uterine rupture remains limited [25].

Misoprostol and First Trimester Termination of Pregnancy

Vaginal and sublingual misoprostol offered prior to surgical termination of pregnancy through manual vacuum aspiration facilitates cervical dilatation. It provides an alternative to mechanical dilatation of cervix. Use of misoprostol significantly decrease the time of surgical evacuation and minimize blood loss during the procedure. However there is a higher incidence of side effects including pre-evacuation vaginal bleeding, lower abdominal pain, nausea and vomiting. Sublingual misoprostol can be self administered and has a good patient acceptability rate for those who do not like repeated vaginal administration [26].

Vaginal misoprostol 0.4-0.6 mg is an effective alternative to surgical evacuation or expectant treatment in many cases of incomplete abortion and missed abortion in first trimester [27,28].

Misoprostol and Hysteroscopy

Vaginal or oral misoprostol administered hours before hysteroscopy reduces the need for cervical dilatation, facilitates hysteroscopic surgery and minimizes cervical complications. So a diagnostic hysteroscopy can be converted from a hospital procedure to a office one [29,30].

However the effect is not that apparent in postmenopausal women with tight cervical o[31].

Misoprostol and Myomectomy

A single preoperative dose of vaginal misoprostol is a simple, reliable method for reducing intra-operative blood loss and need for postoperative blood transfusion after abdominal myomectomies [32].

Conclusion:

Misoprostol has several advantages over other cervical ripening and oxytocic agents. They are low cost (10-15 tk per tab) , stable at room temperature—a potential for more extensive use in tropical developing countries. It is easy to administer and carries favourable side effect profile compared to other prostaglandins , which makes it acceptable to both health care provider and patients alike.

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