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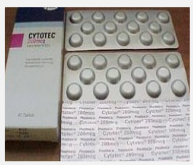
UPDATES ON MISOPROSTOL BY INTERNATIONAL FEDERATION OF GYNECOLOGY AND OBSTETRICS (FIGO) by PRP Nashreen & Ms Izyan

Misoprostol (Cytotec®) is synonym in the obstetrics and gynaecology practice. It was first developed and approved by the FDA in 1985 for the indication of reducing NSAIDs-induced gastric ulcers among patients at high risk of complications from gastric ulcer. It works by acting as an analogue to prostaglandin (PG) E1, hence binding to PG receptor in the stomach. This results in increase mucus secretion and inhibits gastric acid secretion thus protecting the stomach and small intestine from ulceration.[1]

Apart of its action in the gastrointestinal region, misoprostol also acts on the PG receptor in the uterus where it causes increase uterine contractile activity; hence accelerate physiological ripening of the cervix at all gestational ages in pregnant women. This mechanism of action is where misoprostol has its major role in pregnancy as it facilitates uterine evacuation. The clinical applications of this property include induced abortion, missed abortion, incomplete abortion, intrauterine foetal death, induced labour and postpartum haemorrhage (PPH).[2]

Nevertheless, the potency of misoprostol's effect primarily varies with gestational age and route of administration. Uterus sensitivity to misoprostol increases with gestational age. This means that lower dose of misoprostol is sufficient to cause an effect in older gestational age. Misoprostol was originally formulated in tablet form. However, its form of tablet can uniquely be given as orally, sublingually and vaginally. It is important to choose the correct dose for the chosen route and gestational age. But the question is; which route to choose? Oral route has the **fastest onset of action**, hence it is suitable to be used to induce labour. Sublingual route offers the **fastest time to peak concentration** and has the **highest peak**, which is suitable to be used in primary postpartum haemorrhage (PPH) or cervical priming. Consequently, this produces more side effects compared to the other routes. Nonetheless, vaginal route has **high bioavailability and offers sustained serum level** which is useful for indication that requires longest action and more regular contraction such as medical abortion. On top of all the properties mentioned above, patient's preference must also be taken into consideration as they are more likely to choose route which they are most comfortable with.[3]



The side effects associated with misoprostol are quite mild. This includes nausea and vomiting, headache, diarrhoea, abdominal cramp, transient hyperthermia and fever or chills. However, one of the dangerous adverse effects that causes clinicians hesitate to use misoprostol despite of its effectiveness is **uterine rupture**. This can be avoided by screening the patient first for the risk factor of having uterine rupture and exclude the patient where indicated. **The risk factors** are women with **prior caesarean delivery, advanced gestational aged (>24 weeks), high gravidity (≥3 pregnancies), uterine scar and high dose misoprostol (varies with gestation age).** [1,3-4]

Misoprostol usage has become more popular these days because of the low cost, ease of administration and storage plus its effectiveness. Therefore, included in this article is the dosage guideline proposed by The International Federation of Gynecology and Obstetrics (FIGO) as a guide for all clinicians in choosing the right dose for their patient.[2]

References:

1- Australian Government Department of Health and Ageing. Australian public assessment report for misoprostol. 2012 Oct 2 [2012]. Available from: www.tga.gov.au

2- FIGO. Misoprostol recommended dosages 2012. Available from: www.figo.org

3- Tang O.S, K. Gemzell-Danielsson, Ho. Misoprostol: pharmacokinetic profiles, effects on the uterus and side effects. Int Journal Gyne Obs. 2007; 99, s160-s167. Available from: ScienceDirect

4- Ministry of Health Malaysia. Health technology assessment: report on misoprostol inpregnancy. Available from: www.moh.gov.my

MISOPROSTOL RECOMMENDED DOSAGES BY FIGO (2012)

RECOMMENDED DOSAGES 2012

<table>
<tr><td rowspan="4">800µg</td><td rowspan="2">Induced abortion[1]
800µg pv or sl 3 hrly
(max x3 within 12hrs)</td><td></td><td></td><td rowspan="2">PPH treatment
800µg sl single dose</td></tr>
<tr><td rowspan="3">Missed abortion
800µg pv 3 hrly (max x2)
or
600µg sl 3 hrly (max x2)</td><td></td><td></td></tr>
<tr><td>600µg</td><td></td><td></td><td rowspan="2">PPH prophylaxis[2]
600µg po single dose</td></tr>
<tr><td rowspan="3">400µg</td><td></td><td></td><td></td></tr>
<tr><td rowspan="2">Incomplete abortion[2,3]
600µg po single dose
or
400µg sl single dose</td><td></td><td></td><td></td></tr>
<tr><td>Cervical Ripening pre-instrumentation
400µg pv 3 hrs or sl 2-3hrs before procedure</td><td>Induced abortion[1,4] / Interruption of pregnancy
400µg pv or sl 3 hrly
(max x5)</td><td></td><td></td></tr>
<tr><td>200µg</td><td></td><td>Intrauterine foetal death
13-17 wks
200µg pv 6 hrly (max x4)</td><td></td><td></td></tr>
<tr><td>100µg</td><td></td><td>Intrauterine foetal death
18-26 wks
100µg pv 6 hrly (max x4</td><td></td><td></td></tr>
<tr><td rowspan="2">25µg</td><td></td><td></td><td>Intrauterine foetal death[5]
25µg pv 6 hrly or
25µg po 2 hrly</td><td></td></tr>
<tr><td></td><td></td><td>Induction of labour[2,5]
25µg pv 6 hrly or
25µg po 2 hrly</td><td></td></tr>
<tr><td></td><td></td><td colspan="2">Care with previous uterine scar and caesarean section</td><td></td></tr>
<tr><td></td><td>1st Trimester</td><td>2nd Trimester</td><td>3rd Trimester</td><td>Post-Partum</td></tr>
</table>

NOTES:

1. Only use where legal and with mifepristone, where available
2. Included in the WHO Model List of Essential Medicines
3. Leave to work for 1-2 weeks unless excessive bleeding or infection
4. Halve dose if previous caesarean section or uterine scar
5. Make sure you use the correct dosage - overdose can lead complications. Do not use if previous C-section.

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