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## BRIEF COMMUNICATIONS

## Knowledge of correct dosages of misoprostol in reproductive health

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The prostaglandin E1 analog misoprostol is a powerful uterotonic that is effective for labor induction, uterine evacuation, and prevention and treatment of postpartum hemorrhage [1]. Its low cost and ease of storage/administration make it ideally suited to use in low-resource settings. The patent holder has never applied to get a license for any of these indications and, consequently, misoprostol is used off-label in most countries. Furthermore, dosage regimens are complex because they vary by indication, gestation, and route of administration; there is therefore potential for the dangerous use of incorrect doses. To address this issue, a WHO-convened expert group met in Bellagio, Italy, in 2007 to create dosage guidelines [2] (Table 1), which were adopted by FIGO in 2009.

The aim of the present study was to identify the range of misoprostol dosage regimens used by a sample of clinicians worldwide and to compare it with the dosages recommended by the Bellagio expert group.

A survey was conducted between May and October 2008 using the online survey tool SurveyMonkey (SurveyMonkey, Portland, OR, USA). The snowball technique was used, whereby the survey was first sent to all clinicians known by the authors to be working in reproductive health. These recipients were asked to complete the survey and forward the request to other clinicians who they thought would be suitable. In addition, the survey was advertised in a newsletter sent out by the Royal College of Obstetricians and Gynaecologists, and the Society of Obstetricians and Gynaecologists of Canada.

In total, there were 271 respondents, of whom 211 (78%) completed all questions of the survey. The geographic spread of responses was: 46% from Canada; 14% from the USA; 17% from the UK; 5% from Brazil; 5% from Uganda; 3% from India; and 10% from other countries (each comprising

1%–2%). Of the respondents, 177 (65%) worked mainly in public hospitals, 21 (8%) worked in private hospitals, and the rest were from academic institutions. In total, 249 (92%) were specialists in obstetrics and gynecology; the rest were non-specialists providing obstetrics and gynecology care. When asked about the source of their information regarding correct dosages, 134 (49%) listed their hospital protocol or guidelines. The most commonly used doses are listed in Table 2.

Although most practitioners used appropriate dosages of misoprostol in the first trimester and for induction of labor at term, there was a considerable difference among the dosages used for the remaining indications—particularly for intrauterine fetal death (IUFD). Although the data were not strictly comparable, lower dosages for labor induction were reported in the present study than in the survey

Table 1

Recommended dosages of misoprostol by indication, per Bellagio group.<sup>a</sup>

Indication	Dosage	Notes
Induced abortion (0–12 wk)	800 µg vaginally every 12 h (3 doses)	Ideally used 48 h after mifepristone 200 mg
Missed abortion (0–12 wk)	800 µg vaginally every 3 h or 600 µg sublingually every 3 h	Give 2 doses and leave to work for 1–2 wk (unless heavy bleeding or infection)
Incomplete abortion (0–12 wk)	600 µg orally stat	Leave to work for 2 wk (unless heavy bleeding or infection)
Induced abortion (13–22 wk)	400 µg vaginally every 3 h (5 doses)	Use 200 µg only in women with cesarean scar. Ideally used 48 h after mifepristone 200 mg
Intrauterine fetal death	13–17 wk: 200 µg vaginally every 6 h 18–26 wk: 100 µg vaginally every 6 h >27 wk: 25–50 µg vaginally every 4 h	Reduce doses in women with previous cesarean delivery
Induction of labor	25 µg vaginally every 4 h; 50 µg orally every 4 h; or 20 µg oral solution every 2 h	Do not use in cases of previous cesarean delivery
PPH prophylaxis	600 µg orally or sublingually stat	Not as effective as oxytocin or ergometrine; exclude second twin before administration; do not repeat within 2 h
PPH treatment	600 µg orally or sublingually stat	Limited evidence of benefit; use conventional oxytocics first
Cervical ripening	400 µg vaginally 3 h before procedure	Use for insertion of intrauterine device, surgical termination of pregnancy, dilatation and curettage, and hysteroscopy

Abbreviations: PPH, postpartum hemorrhage; stat, single dose taken immediately.

<sup>a</sup> Permission to reproduce table from Ref. [2] granted by the International Federation of Gynecology and Obstetrics (FIGO).

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**Table 2**  
The most common initial dose, frequency, and route of administration of misoprostol.

Indication	Respondents administering misoprostol, %	Most commonly used route of administration <sup>a</sup>	Most common initial dose, µg <sup>b</sup>	Most common subsequent dose, µg <sup>b</sup>	Most common frequency <sup>c</sup>	Percentage who used higher or lower than recommended initial doses
<i>First trimester</i>						
Induced abortion	47	Vaginal (76)	800 (58)	400 (42)	Stat (37)	42 (range, 200–600 µg) <sup>d</sup>
Missed abortion	86	Vaginal (81)	800 (55)	800 (42)	Stat (33)	45 (range, 200–600 µg) <sup>d</sup>
Incomplete abortion	75	Vaginal (66)	800 (46)	800 (40)	Stat (39)	42 (range, 200–400 µg) <sup>d</sup>
<i>Second trimester</i>						
Induced abortion	58	Vaginal (79)	400 (44)	400 (70)	Every 4 h (44)	35 (range, 600–800 µg) <sup>e</sup>
Fetal death	90	Vaginal (83)	400 (35)	400 (55)	Every 4 h (42)	63 (range, 400–800 µg) <sup>e</sup>
<i>Third trimester</i>						
Induction of labor	27	Vaginal (88)	25–50 (92)	25 (50)	Every 4 h (39)	7 (range, 100–600 µg) <sup>e</sup>
Fetal death	68	Vaginal (89)	25–50 (40)	50 (29)	Every 4 h (40)	60 (range, 100–800 µg) <sup>e</sup>

Abbreviation: stat, single dose taken immediately.

<sup>a</sup> Values are given as route (percentage).

<sup>b</sup> Values are given as dose (percentage).

<sup>c</sup> Values are given as frequency (percentage).

<sup>d</sup> Used lower than recommended dose.

<sup>e</sup> Used higher than recommended dose.

by Clarke et al. [3]. However, there was no difference in the dosages used for the induction of labor in women with IUD. Clinicians often consider the risks to be lower with induction for IUD, and it is true that less fetal supervision is needed. However, with reduced monitoring, a greater tolerance of vaginal bleeding and hyperstimulation, and the lack of electronic fetal monitoring (which may show the first warning signs of uterine rupture), women in this situation are at increased risk of uterine rupture. Therefore, we believe that it is inappropriate to increase the dose above that used for labor induction with a live infant. In the present survey, 63% and 60% of clinicians used initial doses that were higher than those recommended for second- and third-trimester fetal death, respectively, despite the fact that 77% of respondents were from the USA, Canada, or the UK—where there is easy access to dosage guidelines. In resource-poor settings, the risk of incorrect dosage is increased and there is less monitoring available.

The potentially serious maternal and fetal complications of inappropriate misoprostol dosage—particularly uterine rupture in the second and

third trimesters—indicate an urgent need to disseminate international evidence-based guidelines more widely. The recent decision by FIGO to adopt and publicize the Bellagio group guidelines will contribute to the safer use of misoprostol worldwide and is, therefore, to be welcomed.

#### Conflict of interest

AW was one of the WHO experts at the Bellagio conference at which the guidelines were drafted.

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## Consequences of delay in obstetric care for maternal and perinatal outcomes

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The timing of medical interventions for obstetric emergencies is vital to prevent maternal and neonatal morbidity and mortality. A principal model of maternal mortality is the “3 delays model” – delay in seeking care; delay in identifying and reaching medical facilities; and delay in receiving adequate and appropriate treatment [1]. Recognized causes of these delays in low-resource countries are transport availability, the costs involved, and accessibility to health facilities.

The present study was conducted in a tertiary hospital in Lucknow, India, from April 2007 to January 2008. Institutional ethical clearance for the study was obtained. Pregnant women presenting at the hospital with hemodynamic instability or loss of consciousness were considered eligible for inclusion. After informed consent had been provided, the patients completed a questionnaire examining demographic profile, nature of illness, and educational status of the couple. The time taken for each woman to reach the hospital from when a problem had been recognized was recorded. A delay was analyzed in terms of maternal and perinatal

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