

Management of pain associated with first trimester medical termination of pregnancy (MToP) using mifepristone-misoprostol regimens

A systematic literature review

Bombas T¹, Fiala C^{2,10}, Agostini A³, Cameron S⁴, Lertxundi R⁵, Lubusky M⁶, Parachini M⁷, Saya L⁸, Trumbic B⁹, Gemzell-Danielson K¹⁰

¹ Obstetric Service, Centro Hospitalar e Universitário de Coimbra. Portugal; ² Gynmed Clinic, Vienna, Austria; ³ Obstetric and Gynecology Department, La Conception hospital, Marseille, France; ⁴ Chalmers Centre, NHS Lothian, Scotland; ⁵ Clínica Euskalduna, Bilbao, Spain; ⁶ Department of Obstetrics and Gynaecology, Palacky University Hospital, Olomouc, Czech Republic; ⁷ San Filippo Neri Hospital, Rome, Italy; ⁸ Altius Pharma CS, Paris, France; ⁹ Cap Evidence, Paris, France; ¹⁰ Department of Women's and Children's Health, Division of Obstetrics and Gynaecology, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden.

INTRODUCTION

- Medical methods are widely spread for induced abortion.
- The most frequently used drug combination in Europe is mifepristone followed by a prostaglandin analogue, mainly misoprostol. This combination is associated with few adverse events, including the occurrence of pain.
- However, most reports of clinical trials fail to describe pain associated with first trimester medical termination of pregnancy (MToP). In addition, no specific and comprehensive guidelines regarding first trimester medical abortion pain management was found in the literature.

OBJECTIVE

- This systematic literature review was performed to provide data to a group of experts for an expert consensus regarding the management of pain associated with first trimester MToP.

METHODS

- A group of experts working in the field of MToP was identified across Europe (Austria, Czech Republic, France, Italy, Portugal, Spain, Sweden, United Kingdom).
- This group wrote a list of clinically important questions regarding pain associated with first trimester MToP. This list was established before performing the literature analysis.
- A systematic bibliographic search was performed looking at publications in English up to end of March 2015. The PubMed search looked at pain treatment / pain assessment and medical termination of pregnancy.

RESULTS

- The search allowed for finding responses to most questions.

EPIDEMIOLOGY

- The **frequency and the intensity** of pain associated with MToP are rarely reported and discussed in the literature. Few studies either mention pain directly, through recorded levels of pain or report of pain as an adverse event, or indirectly via the amount of analgesics.
- For pregnancies up to 9 weeks of amenorrhea, mean pain score measured on a 10-level scale (0=no pain, 10=worst possible pain) varied from 5 to 8 following misoprostol intake [Singh 2005; Shannon 2006; Livshits 2009]. It was 2.5 in a study using a 0 to 5 scale [Ojha 2012]. The pain was considered as severe by 20% [Svendsen 2005] to 30% [Bygdeman 1895; Lokeland 2014] to 80% [FIGO 2011] of women.
- Looking at pain defined by the amount of analgesic consumption in women who underwent ≤9 weeks of amenorrhea medical abortions, large differences were evidenced, mainly depending upon the local abortion service clinical practice regarding analgesic provision. [Ojha 2012, Westhoff 2000]
- **Onset of pain** after mifepristone administration and before misoprostol administration has been reported to occur in between 11%, [De Nonno 2000] to around 40% of patients. [Shannon 2005; Schaff 2000] Following misoprostol administration, time to onset of cramping was around 1 to 2 hours. [Bygdemann 1985; FIGO 2011; Shannon 2006]
- For gestations below 9 weeks of amenorrhea, the **duration of pain** was reported to be at least 1 day (median duration: 3 days). [Westhoff 2000]
- There are multiple **predictive factors** for first-trimester associated pain (Table 1).

Table 1

Factors associated with increased/decreased risk for pain and/or analgesic use as reported during clinical studies

Parameter	Increased risk for pain/analgesic use	Decreased risk for pain/analgesic use
Increased woman'age		Westhoff 2000 Abdel-Aziz 2004 Suhonen 2011 Kapp 2013
Increased parity		Westhoff 2000 Abdel-Aziz 2004 Teal 2007 Lokeland 2014
Increased number of previous pregnancies		Suhonen 2011
Increased number of previous deliveries		Suhonen 2011 Kapp 2013
Increased number of living children		Abdel-Aziz 2004
Increased gestational age	Westhoff 2000 Teal 2007 Suhonen 2011	
Important menstrual pain/dysmenorrhea	Suhonen 2011 Avraham 2012 Kapp 2013	
Retroverted uterus	Kapp 2013	
Married		Westhoff 2000 Abdel-Aziz 2004
Increased available financial support		Abdel-Aziz 2004
Asian women		Westhoff 2000
Indian women		Elul 1999
Provision of full preliminary information		Kruse 2000

PAIN ASSESSMENT

- WHO recommends pain assessment in all cases of pain. [WHO 2007]
- No specific recommendations are available regarding pain assessment during MToP.

PAIN TREATMENT

- WHO recommend to offer all women appropriate pain management before medical abortion. [WHO 2014]
- NSAIDs were demonstrated not to decrease the efficacy of MToP. [Creinin 1997]
- WHO 2014 guidelines recommend the use of ibuprofen 400-800 mg, and recalls the absence of efficacy for paracetamol in this indication. [WHO 2014]
- However, there are no precise recommendations for a specific analgesic protocol especially in terms of timing.
- Non-pharmacological strategies should not be forgotten:
 - Detailed information on the procedure [Kruse 2000]
 - Presence of a partner or friend [Kopp-Kallner 2012]
 - Use of hot water bottle or heating pads [WHO 2014]

CONCLUSION

- Additional work is currently ongoing from the expert group to provide consensus guidelines for management of pain associated with first-trimester MToP.

REFERENCES

• Abdel-Aziz E, Hassan I, Al-Ta'her HM. Assessment of pain associated with medical abortion. International Journal of Gynecology and Obstetrics 2004; 84: 264-265. Avraham 2012

• Bygdeman M & Swahn ML. Progesterone receptor blockage. Effect on uterine contractility and early pregnancy. Contraception 1985; 32: 45-51

• Creinin MD, Shulman T. Effect of nonsteroidal anti-inflammatory drugs on the action of misoprostol in a regimen for early abortion. Contraception. 1997;56:165-168

• De Nonno LJ, Westhoff C, Fielding S, Schaff E. Timing of pain and bleeding after mifepristone-induced abortion. Contraception 2000; 62: 305-309

• Elul B, Ellertson C, Winkoff B, Coyaji K. Side effects of mifepristone-misoprostol abortion versus surgical abortion. Contraception 1999; 59: 107-114

• FIGO Working Group on Prevention of Unsafe Abortion and Its Consequences; International Federation of Gynecology and Obstetrics. The combination of mifepristone and misoprostol for the termination of pregnancy. Int J Gynaecol Obstet. 2011;115:1-4

• Kapp N, Whyte P, Tang J, et al. A review of evidence for safe abortion care. Contraception. 2013;88:350-356

• Kopp Kallner H, Fiala C, Gemzell-Danielsson. Assessment of significant factors affecting acceptability of home administration of misoprostol for medical abortion. Contraception 2012; 85: 394-397

• Kruse B, Poppela S, Creinin MD, Paul M. Management of side effects and complications in medical abortion. Am J Obstet Gynecol 2000; 183: S65-S75

• Livshits A, Machtinger R, David LB, et al. Ibuprofen and paracetamol for pain relief during medical abortion: a double-blind randomized controlled study. Fertil Steril. 2009;91:1877-1880

• Lokeland M, Iversen OE, Engeland A, et al. Medical abortion with mifepristone and home administration of misoprostol up to 63 days' gestation. Acta Obstet Gynecol Scand 2014; 93:647-653

• Ojha K, Gillot DJ, Wood P, et al. Clinical outcomes form a prospective study evaluating the role of ambulation during medical termination of pregnancy. Contraception 2012;85:398-401

• Shannon CS, Winkoff B, Hausknecht R, et al. Multicenter trial of a simplified mifepristone medical abortion regimen. Obstet Gynecol 2005; 105: 345-351

• Shannon C, Wiebe E, Jacot F, et al. Regimens of misoprostol with mifepristone for early medical abortion: a randomised trial. BJOG 2006; 113:621-628

• Singh KC, Umrat S, Rajaram S, Goel N. First trimester abortion with mifepristone and three doses of sublingual misoprostol: a pilot study. Australian and New Zealand Journal of Obstetrics and Gynaecology 2005; 45: 495-498

• Suhonen S, Tikka M, Kivinen S, Kaupilla T. Pain during medical abortion: predicting factors from gynecologic history and medical staff evaluation of severity. Contraception. 2011;83:357-361

• Svendsen PF, Rotbye C, Vejborg T, Nilas L. Comparison of gemeprost and vaginal misoprostol in first trimester mifepristone-induced abortion. Contraception 2005; 72: 28-32

• Teal SB, Dempsey-Fanning A, Westhoff C. Predictors of acceptability of medication abortion. Contraception 2007; 75: 224-229

• Westhoff C, Dasmahapatra R, Schaff E. Analgesia during at-home use of misoprostol as part of a medical abortion regimen. Contraception 2000;62:311-314

• Westhoff C, Dasmahapatra R, Winkoff B, et al. Predictors of analgesia use during supervised medical abortion. Contraception 2000;61:225-229

• WHO. Comparison of two doses of mifepristone in combination with misoprostol for early medical abortion: a randomised trial. British Journal of Obstetrics and Gynaecology 2000; 107: 524-53

• WHO. Normative guidelines on pain management. June 2007. Accessed on 9th April 2015 at http://www.who.int/medicines/areas/quality_safety/delphi_study_pain_guidelines.pdf

• WHO. Clinical practice handbook for Safe abortion. 2014. Accessed on 21st January 2016 at http://apps.who.int/iris/bitstream/10665/97415/1/9789241548717_eng.pdf?ua=1

