Journal of Obstetrics, Gynecology and Cancer Research | ISSN: 2476-5848

Response Letter to Professor Hemida regarding a Published Article with the DOI of 10.30699/jogcr.4.3.111

Soheila Aminimoghaddam[*1], Afsar Ahmad[2], Setare Nassiri [1]

1. *Department of Gynecology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran*
2. *Iran University of Medical Sciences, Tehran, Iran*

10.30699/jogcr.7.4.358

Received: 2022/01/27; **Accepted:** 2022/03/02; **Published Online:** 14 Mar 2022;

Corresponding Information:
Soheila Aminimoghaddam, Department of Gynecology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.
Email: dr_aminimoghaddam@yahoo.com

Dear Editor in Chief

I am writing this letter to respond to the letter entitled "Misoprostol for Cervical Ripening Prior to Molar Evacuation: A letter to the editor." **(1)** written by Professor Reda Hemida from Mansoura University, Egypt, regarding a publication of Soheila Aminimoghaddam *et al.*, entitled "The Association of Gestational Trophoblastic Neoplasia and Misoprostol Administered Before Suction Curettage of Molar Pregnancy," published in 2019 in Journal of Obstetrics, Gynecology and Cancer Research (J Obstet Gynecol Cancer Res) **(2)**.

First, I want to thank Professor Hemida for reading my paper carefully and sharing comments. I highly believe that sharing comments and raising scientific questions could benefit our society. I hope that the responses that the co-authors have provided be helpful and to the point. As he suggested, I am willing to let the journal publish the responses in the next issue.

On the first page of the letter is stated that "Misoprostol is a proven induction agent in the first and second trimester for termination of pregnancy or fetal death." Neither the literature nor any guideline did not list Misoprostol as a proven induction agent, and it is just recommended to be used. In this regard, WHO recommended using Misoprostol for induced abortion and cervical preparing in pregnancies over 12 weeks to reduce the number of deaths and severe disabilities in patients who tried unsafe abortions **(3)**. The FDA approves using this pill to prevent and treat gastric ulcers induced by non-steroidal anti-inflammatory drugs (NSAID) **(4)**, which is not related to our study, so there might be a misunderstanding about the context of our paper.

Professor Hemida also questioned the effectiveness of Misoprostol for "cervical ripening prior to gynecologic procedures in postmenopausal women." I should state that the target group of this study is premenopausal patients, not postmenopausal women, which was mentioned in the question, so the question could not be asked about this study. Moreover, the literature confirms the effectiveness of Misoprostol for the gynecologic procedure in premenopausal patients **(5-8)**.

In the second paragraph, he stated that "there is theoretical concern over the routine use of potent oxytocic agents because of the potential to embolize and disseminate trophoblastic tissue through the venous system." This statement needs more information to become more transparent, so I explain the rationale. In practice, there is no evidence that we should have any concerns. On page 11, section 7.2 of RCOG Green-top guideline No.38 published in September 2020, it is mentioned that "preparation of the cervix immediately before evacuation is safe" **(9)**.

He also stated that "data from the management of molar pregnancies with mifepristone and misoprostol are limited." Flam *et al.* in 1991 **(10)** clearly said that we are allowed to use Misoprostol. This paper stated that "in a case-control study of 219 patients, there was no evidence that the ripening of the cervix prior to uterine removal is linked to a higher risk of needing chemotherapy." This paper was cited in two guidelines of RCOG and New Zealand College of Obstetricians and Gynecologists (RANZCOG) **(9)**, which proves the validity of its statements.

Then, he stated that "evacuation of complete molar pregnancies with these agents should be avoided at present since it increases the sensitivity of the uterus to prostaglandins." This sentence is not always true, as a statement for the management of gestational trophoblastic disease published by the Royal Australian and New Zealand College of Obstetricians and Gynecologists (RANZCOG) states that "use of prostaglandins to ripen the cervix before uterine evacuation is appropriate" **(11)**. Moreover, using Misoprostol has some benefits, such as facilitating cervical canal dilation and simplifying surgery procedures without increasing the post molar GTN rate **(3, 12)**.

In the next paragraph, he mentioned that he did not use Misoprostol according to a guideline; however, as referenced before, this guideline **(9)** didn't question the use of this drug in such cases. Moreover, he reported the adverse effect of this drug by running an experiment on only seven patients, so it is a must to run a prospective study with a large sample size to approve/ disapprove such a hypothesis and evaluate an exposure/ outcome.

Then, he listed five questions and numbered them from one to four, then six by skipping question number five. I put the questions in quotations and respond to each of them separately, and keep the original numbering as he put in his letter:

1. "The authors did not justify the scientific rationale of the use of Misoprostol prior to molar evacuation. The cited articles discussed misoprostol use in labor induction and missed abortion, not molar evacuation. Till now, there is no international guideline, society recommendation, or FDA approval for the use of Misoprostol before molar evacuation."

In response to your comment, I should share an international guideline of the Royal College of Obstetricians and Gynaecologists (RCOG) Gestational Trophoblastic Disease (Green-top Guideline No. 38) published in September 2020, which discusses the use of Misoprostol before molar evacuation. On Page 11 of this guideline, it is recommended that preparation of the cervix immediately prior to uterine removal is safe **(7)**. I copied the following content from this guideline for your consideration:

"Ripening of the cervix with either physical dilators or prostaglandins prior to uterine removal is not associated with an increased risk of developing GTN. In a case-control study of 219 patients, there was no evidence that the ripening of the cervix prior to uterine removal is linked to a higher risk of needing chemotherapy."

Based on this guideline, I suggest you revise your practice and consider following this guideline. I should also note that a published article in 1991 **(8)** confirms our approach, so I have to refute the explanations you provided to question our approach. I copy the content below from this reference for your consideration:

"Medical methods, today mainly treatment with prostaglandins, can safely be used to evacuate molar pregnancies. Despite the wide-spread use of medical induction in Sweden, there is a low incidence of post-molar trophoblastic disease (< 10%)."

Moreover, there is another guideline **(9)** published by the Royal Australian and New Zealand College of Obstetricians and Gynecologists (RANZCOG), in a statement titled *the management of gestational trophoblastic* disease, that says "use of prostaglandins to ripen the cervix is appropriate."

2. "The dose, route of administration, and duration of the drug were not mentioned."

This suggestion could have been easily implemented in the paper during the review process, which was not asked at that time, so we thank you for bringing this up. For your information, we administered Misoprostol 200µg sublingual two hours before evacuation.

3. "The results showed that progression and pulmonary metastases are less in the misoprostol group which couldn't be understood."

Our result and discussion do not say anything about pulmonary metastases, and I copied the following sentence from our result section for your consideration: "we observed no case of trophoblastic embolism in the misoprostol group" so this comment is not related to our study.

4. "It is strange that consent was obtained from 150 cases although it is a retrospective study involved files of patients along many years from 2006 to 2013."

We thank him for this comment. We hope to understand the idea of the reviewer. It was rather vague for us. We conducted this study at a research-educational center and got informed consent from all patients at the time of admission to use their information anonymously in future publications. Additionally, we excluded patients who were lost to follow-up from our study.

6. "From the statistical aspect, when the effect of Misoprostol is nullified, the incidence of GTN progression should be nearly similar in both groups. However, the authors reported a statistically significant difference which may point to "a protective effect" of Misoprostol which is not logic."

We thank him for this intelligent comment. In the paper, we said that "use of misoprostol was correlated with a lower rate of persistent disease," which wouldn't be translated as "a protective effect" of Misoprostol. However, cervical ripening facilitates a complete uterine evacuation from molar tissue, followed by decreasing persistent GTN. Tidy *et al.* **(12)** assessed the influence of stimulation of uterine contractility by prostaglandins on the development of trophoblastic disease, and they concluded that "The cervix may be prepared by prostaglandins for a short duration before surgical evacuation."

Lastly, he raised a concern that using this treatment "increases the rate of postmolar gestational trophoblastic neoplasia and other serious complications." However, according to the literature, cervical preparation before a gynecologic procedure can decrease cervical injury and uterine perforation **(5-8)**. Misoprostol is an important innovation in the obstetrics and gynecology field. Our study showed no major

complication of using this drug or an increased incidence of post molar GTN.

I appreciate sharing your comments on behalf of all the authors, and I hope you find our responses helpful in your practice.

Conflict of Interest

The author declared no conflict of interest.

References

1. Hemida R, Misoprostol for Cervical Ripening Prior to Molar Evacuation: A letter to the editor. J Obstet Gynecol Cancer Res. 2022;7(4):356-7.
2. Aminimoghaddam S, Ahmad A, Nassiri S. The Association of Gestational Trophoblastic Neoplasia and Misoprostol Administered Before Suction Curettage of Molar Pregnancy. J Obstet Gynecol Cancer Res. 2019;4(3):111-6. [DOI:10.30699/jogcr.4.3.111]
4. World Health Organization, Safe abortion: technical and policy guidance for health systems. World Health Organization, 2012.
5. Krugh M, Maani CV. Misoprostol. [Updated 2021 Jul 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539873/
6. Saha M, Chakraborty A, Chattopadhyay S, Saha S, Paul J, Das A. Effect of misoprostol for cervical priming before gynecological procedures on nonpregnant premenopausal women. J Nat Sci Biol Med. 2015;6(Suppl 1):S123-7. [DOI:10.4103/0976-9668.166116]
7. Celik H, Sapmaz E. Use of a single preoperative dose of misoprostol is efficacious for patients who undergo abdominal myomectomy. Fertil Steril. 2003;79(5):1207-10. [DOI:10.1016/S0015-0282(03)00076-1]
8. Abdel-Hafeez M, Elnaggar A, Ali M, Ismail AM, Yacoub M. Rectal misoprostol for myomectomy: A randomised placebo-controlled study. Aust N Z J Obstet Gynaecol. 2015;55(4):363-8. [DOI:10.1111/ajo.12359]
9. Fiala C, Gemzell-Danielsson K, Tang OS, von Hertzen H. Cervical priming with misoprostol prior to transcervical procedures. Int J Gynaecol Obstet. 2007;99 Suppl 2:S168-71. [DOI:10.1016/j.ijgo.2007.09.005]
10. Tidy, J, Seckl, M, Hancock, BW, on behalf of the Royal College of Obstetricians and Gynaecologists. Management of Gestational Trophoblastic Disease. BJOG.2021; 128: e1- 27.
11. Flam F, Lundström V, Pettersson F. Medical induction prior to surgical evacuation of hydatidiform mole: is there a greater risk of persistent trophoblastic disease?. Eur J Obstet Gynecol Reprod Biol. 1991;42(1):57-60. [DOI:10.1016/0028-2243(91)90161-D]
12. Paul Duggan et al. The management of gestational trophoblastic disease. R. Aust. New Zeal. Coll Obstet Gynaecol. Mar. 2020.
13. Tidy JA, Gillespie AM, Bright N, Radstone CR, Coleman RE, Hancock BW. Gestational trophoblastic disease: a study of mode of evacuation and subsequent need for treatment with chemotherapy. Gynecol Oncol. 2000;78(3 Pt 1):309-12. [DOI:10.1006/gyno.2000.5839]

How to Cite This Article:

Aminimoghaddam S, Ahmad A, Nassiri S. Response Letter to Professor Hemida Regarding a Published Article with the DOI of http://dx.doi.org/10.30699/jogcr.4.3.111. J Obstet Gynecol Cancer Res. 2022; 7(4):358-60.

Download citation:
BibTeX | RIS | EndNote | Medlars | ProCite | Reference Manager | RefWorks