Case Report

Hyperpyrexia After Rectal Misoprostol Administration-A Rare Side Effect of Misoprostol: Case Report

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Abstract

Background: Misoprostol is a safe drug that is one of the prostaglandins analogs. It has uterotonic solid potential and is good for postpartum hemorrhage (PPH). Misoprostol has some side effects; hyperpyrexia is a rare side effect after misoprostol administration.

Cases Report: A 21-year- woman, Gravid 1 Parity 1, 18 hours after cesarean section, suffered from uterus atony and vaginal bleeding that rectal misoprostol was administered. Her PPH was managed with misoprostol and other uterotonics. She developed a fever, and because of the Coronavirus disease (covid-19) pandemic, we suspected it and assayed it, but it was negative.

Conclusion: In this rare case, hyperpyrexia occurred after rectal misoprostol administration because of dose and prostaglandin effect on the hypothalamus. In this critical situation that covid-19 is pandemic, we suggest to specialists that keep in mind fever and hyperpyrexia may occur consequently the misoprostol administration.

Keywords: Misoprostol, Hyperpyrexia, Temperature, Covid-19, Case report

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Introduction

One synthetic prostaglandin E1 analogue is misoprostol, which has Food and Drug Administration (FDA) approval and is administered orally for peptic ulcer treatment[1]. Misoprostol has an essential use in gynecology and obstetrics such as elective medical abortion, cervical ripening before the surgical abortion, depletion of the uterus in cases of embryonic or fetal death, and induction of labor, and one of the critical use is in treatment and prevention of postpartum hemorrhage[1]. Compared to another prostaglandin analog, misoprostol has good options: low price, availability, stability at room temperature, and low side effects. Misoprostol has different routes for administration: oral, sublingual, vaginal, rectal, and buccal routes[2]. Misoprostol increases the uterus tone, and the regular uterus tone arrives 1-2 hours after administration[3]. Misoprostol is a very safe drug that has a few side effects[4], but death after multi organs failure occurs in overdose[5].

The primary cause of maternal mortality and morbidity is postpartum hemorrhage (PPH) all over the world[6], half of million women die as a consequence of pregnancy worldwide[7] that estimated a quarter of them are caused by hemorrhage[8], so it is an emergency in obstetrics and gynecology that should be treat as soon as possible.

In some cases reported that misoprostol is a good choice in PPH treatment but in high doses in the third trimester can induce fever and chill[2] and in some cases, after misoprostol administration, hyperpyrexia (>40°C) and ICU (intensive care unit) admission is reported [(9)]. Now we report the rare case that she had hyperpyrexia after rectal misoprostol administration, and because of the coronavirus pandemic, we first became suspicious of covid-19 (coronavirus disease).

Case Report

In the coronavirus pandemic period, a 21-year-woman, Gravid 1 Parity 1 with gestational age (GA) 39 weeks and 6 days, presented herself in hospital with a membrane rupture. She had the fever (T:37.5 C) and tachypnea, so we suspected covid-19, and then the chest HRCT (High-resolution computed tomography), coronavirus PCR (polymerase chain reaction) was ordered. The cesarean section was performed because of membrane rupture, thick meconium, and non-reassuring NST (Nonstress Test) with complete protection of the mother, newborn, and the medical team. The result of the delivery was a boy neonate, with a 1-min Apgar score of 9 and 5-min Apgar score of 10, and a weight of 4050 gr. After 8 hours, she was out of bed, and the uterus, blood loss, and vital signs were normal (blood pressure 100/65, pulse rate of 98 beats/min, and the temperature was normal). Eighteen hours after C/S, she complained of dizziness and increased bleeding, so she was visited by the gynecologist; the uterus atony and postpartum hemorrhage were diagnosed, the second IV line was fixed, and the CBC, coagulation tests, and the cross-match test was requested, and oxytocin (Syntocinon), rectal misoprostol (800 μg), tranexamic acid (1 gr) and methergine was administered. The patient was transferred to CCU (the ICU was isolated, and there was no empty bed) to control the vital sign. The abdomen and pelvic ultrasonography was done, its report was: the uterus is larger than normal size and hyperechoic mass (110 CC) was seen in the uterus that it may be hematoma or clot because of the atony and does not need surgical intervention.

In CCU she had tachycardia (Pulse Rate 140), tachypnea (Respiratory Rate 30), and the body temperature was 38°C. A unit of packed red blood cells was transfused due to low hemoglobin (8), and urinary catheterization was performed to control the urine output.

O2 saturation was 93%, and the fine crackle (Rales) was heard at the lung base, so our first differential diagnosis was postpartum cardiomyopathy or embolism. A chest X-ray was done on the cardiologist, and an internal specialist consulted that a little central lung congestion was diagnosed and the cardiac size was normal. Electrocardiography showed sinus tachycardia, and in the Echocardiography report, the cardiomegaly and cardiomyopathy were rejected, and movement of the septum was normal. Despite this situation, the Lasix was administered due to fine lung crackle.

Because of continuing tachycardia and tachypnea and decreasing the O2 saturation until 93%, our second differential diagnosis was COVID-19, so Hydroxychloroquine 400 mg, Kaletra, and serum therapy were administered. The other differential diagnosis was a postoperative infection, so Vancomycin and Meropenem were administered.

Due to the patient's thirst, the temperature was checked again, the body temperature was 40.5-41°C, Apotel (1g) was administered immediately that did not affect

Table 1: The laboratory tests results.

Test	Result	Test	Result
ESR	33	Urea	18
CRP	17.8	Cr	0.7
BILL	0.7	LDH	396
AST	20	Ca	8.1
ALT	11	P	4.9
K	4.3	Mg	1.5
Na	144	Total Protein	5.9

body temperature, then a rectal Diclofenac suppository was used, but body temperature stayed high. Eventually, putting a wet cloth on the patient's body reduced the fever. To definitively diagnose, CT-scan of the chest was performed and COVID-19 was rejected.

The last differential diagnosis was the misoprostol side effects because hyperpyrexia is rare after misoprostol, especially in rectal use. Besides, she was afebrile at first, and the body temperature went high after the misoprostol administration, so it can be suggested that the high temperature was an adverse effect of misoprostol, not sepsis. In the second 24 hours, the patient's vital signs became normal, and she was discharged. Table 1 shows the laboratory tests result.

Discussion

Misoprostol is a synthesized prostaglandin E1 analog that at first administered to peptic Ulcer induced because of NSAID (non-steroidal anti-inflammatory) drugs use, and then the effects of misoprostol on uterus and cervix were observed and became an important drug in obstetrics and gynecology[10]. Based on WHO reports, half of the millions of women died in year consequence pregnancy that PPH is the major mortality and morbidity caused in pregnant women[7], and between uterotonic drugs, misoprostol is inexpensive, available, stable at room temperature. It has a strong potential for treating PPH[11], therefore WHO suggests this drug for treatment and prevention of PPH[12]. One of the side effects of misoprostol is increasing the body temperature, in some cases more than 40°C that it is related to dose and route of administration, in oral and sublingual occur more than another router[12], it may happen because of quicker maximum plasma concentration[13] and on the other hand prostaglandins as endogenous factors effect on the hypothalamus and increase the body temperature and induce fever[14]. Based on many studies, this side effect is not very critical because it disappears near 12 hours after administration[14, 15], like our case. An important issue, in this case, was that it coincided with the covid-19 pandemic that fever is one of the important signs of it[16].

Conclusion

In this rare case, hyperpyrexia occurs after 800 μg rectal misoprostol administration because of dose and prostaglandin effect on the hypothalamus. In this critical situation that covid-19 is pandemic, we suggest to specialists that keep in mind fever and hyperpyrexia may occur consequently the misoprostol administration.

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References

1. Goldberg AB, Greenberg MB, Darney PD. Misoprostol and pregnancy. New England Journal of Medicine. 2001;344(1):38-47.
2. Tang O, Gemzell-Danielsson K, Ho P. Misoprostol: pharmacokinetic profiles, effects on the uterus and side-effects. International Journal of Gynecology & Obstetrics. 2007;99:S160-S7.
3. Aronsson A, Bygdeman M, Gemzell-Danielsson K. Effects of misoprostol on uterine contractility following different routes of administration. Human reproduction. 2004;19(1):81-4.
4. Kotsonis F, Dodd D, Regnier B, Kohn F. Preclinical toxicology profile of misoprostol. Digestive diseases and sciences. 1985;30(11):142S-6S.
5. Henriques A, Lourenço AV, Ribeirinho A, Ferreira H, Graça LM. Maternal death related to misoprostol overdose. Obstetrics & Gynecology. 2007;109(2):489-90.
6. Callaghan WM, Kuklina EV, Berg CJ. Trends in postpartum hemorrhage: United States, 1994–2006. American journal of obstetrics and gynecology. 2010;202(4):353. e1-. e6.
7. Organization WH, UNICEF. Maternal mortality in 2005: estimates developed by WHO, UNICEF, UNFPA, and the World Bank: Geneva: World Health Organization; 2007.
8. Organization WH. The World health report: 2005: make every mother and child count: World Health Organization; 2005.
9. Chong Y, Chua S, El-Refaey H, Choo W, Chanrachakul B, Tai B, et al. Postpartum intrauterine pressure studies of the uterotonic effect of oral misoprostol and intramuscular syntometrine. British Journal of Obstetrics and Gynaecology. 2001;108(1):41-7.
10. Allen R, O'Brien BM. Uses of misoprostol in obstetrics and gynecology. Reviews in obstetrics and gynecology. 2009;2(3):159.
11. Alfirevic Z, Blum J, Walraven G, Weeks A, Winikoff B. Prevention of postpartum hemorrhage with misoprostol. International Journal of Gynecology & Obstetrics. 2007;99:S198-S201.
12. Hofmeyr GJ, Gülmezoglu AM, Novikova N, Linder V, Ferreira S, Piaggio G. Misoprostol to prevent and treat postpartum haemorrhage: a systematic review and meta-analysis of maternal deaths and dose-related effects. Bulletin of the World Health Organization.

2009;87:666-77.
13. Khan R-U, El-Refaey H. Pharmacokinetics and adverse-effect profile of rectally administered misoprostol in the third stage of labor. Obstetrics & Gynecology. 2003;101(5):968-74.
14. Durocher J, Bynum J, León W, Barrera G, Winikoff B. High fever following postpartum administration of sublingual misoprostol. BJOG: An International Journal of Obstetrics & Gynaecology. 2010;117(7):845-52.
15. Patted SS, Goudar SS, Naik VA, Bellad MB, Edlavitch SA, Kodkany BS, et al. Side effects of oral misoprostol for the prevention of postpartum hemorrhage: results of a community-based randomised controlled trial in rural India. The Journal of Maternal-Fetal & Neonatal Medicine. 2009;22(1):24-8.
16. Jiang F, Deng L, Zhang L, Cai Y, Cheung CW, Xia Z. Review of the clinical characteristics of coronavirus disease 2019 (COVID-19). Journal of General Internal Medicine. 2020:1-5.