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**Case Report**

# Severe morbidity with sublingual misoprostol in a post-partum patient: a case report

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## ABSTRACT

Misoprostol is highly useful in preventing and treating postpartum hemorrhage. However, it may be associated with side effects like fever, chills and vomiting. Rarely may it cause severe morbidity and even death. We witnessed a case of 30 year old female, who developed postpartum hemorrhage immediately after her delivery. Patient was administered various uterotonics including 800 mcg sublingual misoprostol, with which her PPH was finally controlled. However, she developed hyperthermia, hypotension, tachycardia and fall in saturation of $O_2$, after few hours of misoprostol administration. Patient was managed by strict monitoring in ICU setting and mechanical ventilation. She gradually recovered over a period of 48 hours and was discharged in stable condition. Misoprostol should be carefully used as it has a potential to cause serious adverse effects in pregnant and postpartum phase.

**Keywords:** Misoprostol, Sublingual

## INTRODUCTION

Postpartum haemorrhage is a leading but preventable cause of maternal death in developing countries. Misoprostol, a PGE1 analogue has been found to have strong uterotonic action, thereby, allowing its use in Obstetrics cases for number of indications. In addition, it has many advantages including - cost effectiveness, ease of administration and storage. The present WHO guidelines allow the use of misoprostol for early termination of pregnancy, management of miscarriage, labor induction and management of postpartum hemorrhage.[1,2]

There have been various trials which experimented giving various doses of misoprostol via different routes, in controlling postpartum hemorrhage.[3,4] It has been shown that, this drug is significantly effective in terms of reduction in measured blood loss.[3,4] However, this benefit is not without side effects which mainly include chills and fever. Rarely, it may cause severe morbidity like hyperthermia, hypersensitivity reaction and even death.[5]

## CASE REPORT

We, hereby, present a case report, which had a severe morbidity and adverse reaction following administration of misoprostol. The patient, a 30 year old primigravida was admitted in a tertiary care hospital, at 40 weeks gestation in v/o decreased fetal movements. She was a fully booked patient and previously had regular antenatal visits. There was no associated high risk antenatal factor or medical co-morbidity.

On admission, her clinical findings were as follows: pulse: 80/minutes, B.P: 120/80 mmhg, temperature: 98. 4F and respiratory rate 16/minutes. On per abdomen exam: uterus was term size, relaxed with cephalic presentation and fetal heart rate 140/minutes. On per vaginum exam: cervix was 1 finger loose, soft, midposition, vertex at brim.

She was induced with 3 doses of dinoprostol gel at 6 hours interval. Following this, augmentation with oxytocin was started in escalating dose. She delivered a healthy female baby of weight 2830 gm on next day (18

hours post induction). Atonic postpartum hemorrhage occurred immediately post-delivery. This was initially managed by administering oxytocin, methergin (methylergometrin) and carboprost (PGF2α) injections. Subsequently misoprostol in the dose of 800mcg was given sublingually with which the PPH was finally controlled. After 1 hour, patient developed delirium and hyperthermia (temperature: 106F). Patient was immediately shifted to ICU for close monitoring and further management. After about 2 hours, patient developed tachycardia, hypotension and fall in oxygen saturation. She was intubated and put on mechanical ventilation. In addition, patient was resuscitated with vasopressors. Also, relevant investigations were sent. Her TLC count, at this point, was 29000/cumm. Other investigations including liver function test, kidney function test, chest X ray and 2D echocardiography were normal. Patient was started on broad spectrum antibiotics. Her temperature gradually settled in 3-4 hours with Injection paracetamol and vitals also stabilized. Over next few hours (after 12 hours), her TLC reduced. Other important investigations which were done included MRI and MR venography brain, USG whole abdomen and lumber puncture and all of these were normal. In addition, blood culture, urine culture and vaginal swab cultures were normal. Patient gradually improved and was weaned off the ventilator on 3rd day of ICU stay. Patient was subsequently shifted towards and discharged in stable condition.

## DISCUSSION

Incidence of hyperthermia has varied in different studies, in association with misoprostol administration ranging between 18-71%.[6,7]

The temperature elevations associated with misoprostol appear to be associated with shift in the hypothalamic set point as prostaglandins have been known to be associated with endogeneous fever mechanisms.[7]

High fever reported in our patient appears to be related to misoprostol rather than infection despite the fact there was leukocytosis. This may be explained due to the fact that there were no further spikes of fever and total leucocyte count dropped down to normal within next few hours. In addition, rise in total leucocyte count could be attributed to stress of labor and hyperthermia.

There may also be a correlation between ethnic origin and incidence of high fever with misoprostol. In a large clinical trial conducted to study the efficacy and safety profile of misoprostol in treating post-partum hemorrhage, patients were recruited from various regions across the world- Ecuador, turkey, Egypt, Burkina Faso and Vietnam.[8] It was seen that incidence of hyperthermia was unusually high among Ecuadorian women (36.5%) as compared to other populations (9.5%). This might be due to variation in environment and genetic factors among different ethnic groups. In our case, patient was of Indian origin belonging to north eastern belt.

In the same study, delirium and altered sensorium were also reported in about 20% of the patients with high fever. Similar symptoms were also noticed in our patient who necessitated requirement of ICU care.

In addition, it has been noticed in number of trials, that side effects are more frequent when ≥600 mcg of misoprostol is used.

Regarding its pharmacokinetics, misoprostol has a very rapid onset and prolonged duration of action along with greatest bioavailability when given sublingually. On the other hand, its rectal administration is associated with slower uptake and lesser duration of action.

There have been studies and case reports in which severe morbidity/mortality has been reported specifically in relation with orally/sublingually administered misoprostol.[3,9] Chonget al reported severe hyperthermia after administration of oral misoprostol in a post-partum patient.[9] In another study, unusually high fever of>40F was recorded in women, who were administered 800mcg of sublingual misoprostol for control of PPH.[10] In the present case also, severe morbidity was noticed with 800 mcg of sublingual misoprostol.

However, there are no studies involving direct comparison of adverse effects with relation to route of administration of misoprostol.

In a systemic review of trials, analyzing safety profile of misoprostol, when used in control of post- partum hemorrhage, over 40000 women were studied.[11] Out of these, 11 maternal deaths were reported. In 6 of them, cause was related to excessive bleeding (postpartum). However, in rest of the cases, no obvious cause of death could be explained. In all these cases, there was history of misoprostol administration via oral, sublingual or rectal route.[3,4,12,13] However, no direct relation with misoprostol administration could be established in these cases. Nonetheless, these findings do point out that misoprostol may have unexplained adverse effects on homeostatic mechanisms specifically thermoregulation of the body, especially during pregnant and post- partum phase.

## CONCLUSION

To conclude, misoprostol is extremely beneficial in preventing and controlling post- partum hemorrhage, but, its potential to cause side effects is a matter of concern. More research is warranted to establish its safest dose and route of administration.

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