Fever and Acute Confusion in a Postpartum Patient Following Sublingual Prostaglandin E1 Administration: A Case Report

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Postpartum hemorrhage due to uterine atony is a condition that may be life-threatening unless immediate intervention is made. Oxytocin, ergot derivatives, and prostaglandin (PG) E_1 are first-line medical treatment options besides an effective uterine fundal massage. If the patient is unresponsive to the medical management approach, surgical intervention is required. All medications have potential side effects.

We present a case that developed uncontrolled tonic body movements and mild disorientation accompanying fever after sublingual PG E_1 administration for treatment of uterine atony.

Key Words: Uterine atony, Prostaglandin E_1, Postpartum hemorrhage, Fever, Disorientation, Sublingual

Gynecol Obstet Reprod Med 2013;19:119-121

Introduction

Misoprostol, a synthetic PG E_1 analogue, has been proven to be effective in preventing and treating postpartum hemorrhage (PPH) resulting from the failure of the uterus to contract fully after delivery.[1] While oxytocin is the gold standard drug for use in PPH treatment, PGs can be used for intractable PPH as a last resort when other measures failed.

The most common side effects related to misoprostol administration are fever and shivering.[2] Misoprostol may be administered in different routes. Fever is more common with oral and sublingual routes, which provide faster maximum serum concentrations, compared to rectal and vaginal routes.[3] Side effects after misoprostol treatment have been reported as transient, manageable by providers, and in vast majority of cases, women have found them tolerable.[4] There are rare cases reported of hyperpyrexia (>40 °C).[5] However, these fevers were transient and did not result in further complications and could be easily managed with simple antipyretic medications.

We present a case with acute confusion in a patient with temperature of 42 °C after misoprostol treatment for uterine atony.

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Submitted for Publication: *10. 05. 2013*
Accepted for Publication: *19. 07. 2013*

Case Report

A 20-year-old primiparous patient, with 41 weeks of gestation, was admitted in active labor to the delivery room of Zekai Tahir Burak Women Health Care, Education and Research Hospital. She had an obstetric history of normal antenatal visits and no proven risk factors. Ultrasound performed in the delivery room revealed a vertex-presenting fetus with 37-38 weeks of biometric measurements and normal amniotic fluid volume. At her admission, the vital signs were all in normal ranges, blood pressure; 110/80 mmHg, heart rate; 90 bpm, and body temperature; 36.3°C. Because urine test was consistent with a mild urinary tract infection, urine culture was obtained and empiric antibiotic treatment was started. She had also moderate anemia, hemoglobin level at her admission was 9.2 g/dl.

After 5 hours of active labor, the patient delivered a female newborn with a birth weight of 3.280 gram vaginally. The basic examination and APGAR scores of the infant were normal. Within approximately half an hour following birth, the patient had a profound bleeding of uterine origin. Besides bimanual fundal massage, intravenous fluid administration with crystalloids and treatment with oxytocin (40 IU of I.V.) bleeding continued and 800 mcg sublingual misoprostol was applied next. After 30 minutes of this treatment, the patient had shivering, fever (42 °C, tympanic), mild hypotension (90/60 mmHg), and severe tachycardia (180 bpm). At that time, uterine tonus was normal, there was no apparent bleeding, abdominopelvic ultrasound revealed a normally-involuted uterus with no demonstrable hematomas. Clinical diagnosis was misoprostol related fever which was possibly aggravated by the urinary tract infection and wide-spectrum antibiotic (1st

generation cephalosporin and clindamycin) treatment was administered. Paracetamol (Perfalgan®, 1 gm, I.V. infusion) and ice application have been started. Suddenly the patient presented hallucinations, uncontrolled tonic body movements and mild disorientation. Complete blood count revealed anemia (hemoglobin; 7.2 g/dl) and leukocytosis (white blood cell count 40.000/ml), renal function tests and coagulation panel were normal, electrocardiogram was consistent with sinus tachycardia. This neuropsychological state lasted about 3 hours and resolved as the patient's body temperature decreased. Consultant physicians from internal medicine and neurology also evaluated the patient and their examinations revealed no significant pathology. At approximately 6th hour of the delivery, the patient's vital signs were as following; blood pressure, 100/50 mmHg, heart rate; 114 bpm, body temperature; 37°C. Since hemoglobin level at that time was 6.2 g/dl and the patient was stabilized, 2 units of packed-red blood cell were transfused.

The patient's physical examination was completely normal on day two and she was discharged from the hospital with routine postpartum recommendations. The condition was assessed as a side effect of sublingual administration of misoprostol.

Discussion

Postpartum hemorrhage is a potentially fatal condition, encountered both with vaginal and cesarean births. It is a leading cause of maternal morbidity and death in both developed and less developed countries. Uterotonic agents are administered prophylactically in most medical centers immediately following birth, since they reduce the risk of bleeding and the need for transfusion. WHO, based on reproductive health guidelines, recommends misoprostol for induction of labor, prevention and treatment of postpartum hemorrhage, and management of spontaneous and induced abortion.[6] There is obviously no sufficient data to define the most effective dose and the choice of administration route in different patient populations. However, researches have shown that a single dose of misoprostol 800 µg administered sublingually is a safe and effective treatment for PPH due to uterine atony in women who received oxytocin prophylaxis, as well as those who have received no oxytocin prophylaxis, during the third stage of labor .[7,8] The sublingual route is recommended because it is the only treatment route tested in randomized controlled studies (RCT). To date, all published studies and case reports on misoprostol for treatment of PPH have been reported on rectal or sublingual route.[9] However, evidence on rectal administration is limited because no double-blind RCT has assessed the efficacy of administering misoprostol via this route to treat PPH.

Women who receive misoprostol postpartum are at risk for shivering and transient pyrexia. In several studies, misoprostol has been associated with fever of above 40°C.[2,10-13] It has been reported that such effects were dose related, transient (which subsided spontaneously within 8 h of delivery), self-limiting, and did not result in additional health complications.[4,5,10] Only one case was reported peak temperature of 41.9 °C following 800 micrograms of oral misoprostol given prophylactically.[13] Nevertheless, some women can develop a temperature of ≥ 40.0 °C and may need therapeutic interventions as in our case.[5] The temperature elevations associated with misoprostol are compatible with a shift in the hypothalamic set point, and do not appear to be cases of hyperthermia which may be fatal, but rather of pyrexia.[5] The most common side effects of fever and shivering are considered as dose- and route-dependent. These conditions are usually self-limiting and can be easily managed with simple antipyretic medications. Oral and sublingual administration provide faster plasma maximum concentration (at approximately 8-10 minutes following administration), which is essential for immediate intervention in case of postpartum bleeding, but the risk of side effects increases as well.[3] In our case, the patient has been administered 800 mcg sublingual misoprostol, and within about 30 minutes, hyperpyrexia and acute confusion developed. Anemia and mild urinary tract infection could also have aggravated the clinical state. Lower dosages or different routes of administration may minimize the occurrence of such events. Currently, however, no data support other routes of administration or lower doses of misoprostol for treatment of PPH. Until definitive relationships between genetic or environmental variation and drug response can be established, the questions of why some women develop high body temperature will not be answered. Further and larger studies are required to establish the smallest effective dose in various routes of administration as well as prediction and prevention of potential side effects of misoprostol.

Postpartum Bir Hastada Sublingual Prostaglandin E1 Verilmesinin Ardından Gelişen Ateş ve Akut Konfüzyon: Bir Olgu Sunumu

Uterin atoniye bağlı postpartum kanama, acil müdahale edilmezse, yaşamı tehdit edici bir durumdur. Etkili uterin fundal masajın yanında, oksitosin, ergot deriveleri ve prostaglandin E1 ilk medikal tedavi seçenekleridir. Hasta medikal tedaviye cevap vermezse, cerrahi girişim gereklidir. Tüm tedavilerin belli yan etkileri mevcuttur.

Uterin atoni tedavisi için sublingual PG E1 verilmesinin ardından ateşe eşlik eden kontrolsüz tonik vücut hareketleri ve hafif dezoryentasyon gelişen bir hastayı vaka olarak sunmaktayız.

Anahtar Kelimeler: Uterin atoni, Prostaglandin E_1, Postpartum kanama, Ateş, Dezoryantasyon, Sublingual

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