Case Report

SUBLINGUAL MISOPROSTOL ALLERGY: A CASE REPORT

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ABSTRACT

Misoprostol is being used in obstetrics especially during the first and third trimesters of pregnancy. It has become a good drug for prevention and treatment of postpartum haemorrhage. It is considered a safe drug with few side effects. However, we present a report of a rare severe hypersensitivity reaction in a patient who had sublingual misoprostol for prevention of postpartum haemorrhage.

KEYWORDS: Misoprostol; Sublingual, Postpartum Haemorrhage; Hypersensitivity.

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INTRODUCTION

Misoprostol is a synthetic analogue of prostaglandin E1. Its chemical (International Union of Pure and Applied Chemistry) name is Methyl 7-(1*R*,2*R*,3*R*)-3-hydroxy-2-(*S*,*E*)-4-hydroxy-4-methyloct-1-enyl)-5-oxocyclopentyl-heptanoate.[1] It is marketed as cytotec© by Pfizer. It was originally registered for preventing gastric ulcer as it binds to prostaglandin receptors at the parietal cells, stimulates G_i pathway, thereby decreasing intracellular cyclic AMP and gastric acid secretion.[1]

However, its property to induce contraction of smooth muscle of the uterus was exploited in women's reproductive health programs. Misoprostol is being used in obstetrics as a treatment of missed abortion, incomplete abortion, cervical preparation before surgical evacuation and induction of labor.[2] Misoprostol has proven to be effective in preventing and treating postpartum haemorrhage resulting from the failure of the uterus to contract fully after delivery.[2] It can be administered by oral solution, oral tablet, sublingual, rectal and vaginal routes.[1] The oral solution has been shown to produce the fastest and strongest uterotonic effect.[3] It is rapidly absorbed after oral administration and it is de-esterified to form misoprostol acid which is the active metabolite.[1] The therapeutic effect starts within 30 minutes and peaks at 60 to 90 minutes.[1] Its duration of action is up to 3 hours with an elimination half-life of 20 to 40 minutes.[1] The reported adverse effects of misoprostol include fever, shivering, diarrhea, abdominal pain and cramp.[4] It is excreted mainly in the urine.

Oxytocin with inherent property of uterine contraction is the standard for postpartum haemorrhage prevention and treatment. However, its use in augmentation of labour in the cases of prolonged labour has resulted in desensitization of its receptors at the uterus, thereby impairing the post-delivery effect of uterine contractility and increasing the risk of atonic postpartum haemorrhage.[5]

Therefore, the body of knowledge about efficacy of misoprostol resulted in the addition of misoprostol to the World Health Organization's (WHO) list of essential drugs for postpartum haemorrhage prevention and treatment in 2011.[6] The evidence on misoprostol for treatment of postpartum haemorrhage shows it curbs excessive postpartum bleeding where oxytocin has shown suboptimal effect.[2] However, we

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describe a rare case of hypersensitivity reaction to misoprostol so that we become much more careful in its administration and avoid its random usage.

CASE REPORT

A 30 year old woman, a trader, gravid 2, para 1^{+0}, 1alive was booked for emergency caesarean section on account of prolonged labour with previous caesarian section scar. She was referred from a maternity home where labour was augmented with oxytocin and admitted at gestational age of 39 weeks, 4 days with 30 hour history of labour pain. Her past medical history was remarkable of previous caesarean section on account of obstructed labour done in a private hospital with no clear cut knowledge of drugs she received then.

There was no history of allergy to misoprostol or any other drug. Her last meal was 8 hours prior to presentation. The clinical evaluation was remarkable for labour pain and laboratory result reviewed. The pack cell volume was 34% (only investigation result available) and she was assigned American Society of Anesthesiologist physical status I. She was counseled for subarachnoid block and general anaesthesia in case of subarachnoid block failure and she gave consent. Her vital signs at the time of review were stable. She was given intravenous metoclopramide 10 mg and ranitidine 50 mg.

She had emergency lower segment caesarean section under spinal anaesthesia and the surgery lasted 64 minutes. She was delivered of a life female baby who weighed 3.8 kg with APGAR scores of 6 at the first minute and 9 at the fifth minute. The estimated blood loss was 800 mls and intra-operative haemodynamic variables were stable with Oxygen saturation (SPO_2) range of 95-97 % at room air, Blood Pressure range of 106/68 - 146/93 mmHg, Respiratory Rate range of 16-20 cycle per minute, Pulse Rate range of 64-92 beat per minute and temperature range of 37.0-37.4°C. She received 2.5 litres of normal saline intra-operatively. The uterus was not adequately contracted despite oxytocin infusion. The patient was given sublingual misoprostol 600 µg and transferred to the recovery room.

It was observed 15 minutes later that the patient was in respiratory distress with respiratory rate (RR) of 26 cycles per minute, SPO_2 was 88-90% (room air), Blood Pressure (BP): 85/50 mmHg, Pulse Rate (PR): 142 beats per minutes and temperature was 37.7^0c. She was shivering and no significant bleeding per vagina. She was told to spit out the poorly dissolved 3 tablets of misoprostol (200µg each) under her tongue and immediately commenced on supplemental 100% oxygen at 4L/min via facemask. There was no history of pain or swelling on the lower limbs. Chest and lower limbs examination were unremarkable. She was given intravenous hydrocortisone 200 mg, promethazine 25 mg and transferred to intensive care unit. Emergency Chest Xray, clotting profiles and d-dimer assay were requested. Her vital signs after 15 minutes were BP: 90/54 mmHg, PR: 104 beats per minute, RR: 24 cycles per minute, SPO_2: 92 % and temperature: 37.6°c.

She was continued on intravenous normal saline 1 litre at 120 ml/min. There were improvement in her vital signs within 1 hour; BP: 102/63 mmHg, PR: 100 beats per minutes, RR: 24 cycles per minutes, SPO_2: 96%, temperature: 37.5°c and shivering stopped. Patient was observed for the next 8 hours and she was stable with RR dropped to 18 cycles per minute with SPO_2: 94 % (room air). Chest Xray revealed no significant findings and the clotting profiles within the limit of normal. The d-dimer assay was not done. She was subsequently transferred to the ward, seen 24 hours later by the team and was stable with adequate contraction of the uterus.

DISCUSSION

Anaphylaxis is a clinical syndrome that affects multiple organ systems especially cardiovascular and respiratory symptoms with compromised haemodynamic variables.[1] Clinically, there is always hypotension with attendant poor perfusion of vital organs as we witnessed in the index case. Respiratory system may witness poor gaseous exchange following bronchospasm and dyspnea with decrease in oxygen saturation. In the index case, there was early recognition of the decrease in the oxygen saturation, hence the immediate intervention.

At the molecular level, anaphylaxis involves degranulation of mast cells and basophils with release of immunoglobin E and pro-inflammatory mediators following re-exposure to the precipitating antigen[1]. In the index case, it is

probable that the patient received misoprostol during her first caesarian section and upon the second exposure, developed the anaphylaxis. Madaan et al[7] reported similar hypersensitivity reaction following administration of misoprostol through the vaginal route for management of missed abortion in a primigravida. However, when there is no prior antigen exposure, it becomes anaphylactoid reaction.[8] The allergy in the report by Madaan et al[7] might have been anaphylactoid reaction. However, the management of the patient was similar to our management in the index case. There was a similar reported of lichenoid eruptions caused by misoprostol according to Cruz et al[9] in their study.

On the contrary, some studies[10,11] showed the protective property of misoprostol in allergic diseases. Babakhin et al[10] demonstrated that misoprostol can inhibit basophil histamine release, indicating a potentially beneficial role of misoprostol as pharmacotherapy for allergic diseases. . Misoprostol might have suppressed the absorption of the allergen levels and outbreak of the allergic symptoms induced by aspirin in the patients with wheat dependent exercise induced anaphylaxis.[11] Despite these, misoprostol allergy still occurs. Hence, clinicians should be aware of the possibility of allergy as a rare adverse effect as the use of misoprostol in women's reproductive health programs continues to increase.

Therefore, early detection and immediate treatment of this rare drug allergy is vital to save life as was done in the index case. Immediate laboratory and radiological tests are paramount to rule out pulmonary embolism, especially d-dimer assay which unfortunately we had no facility for it. Documentation of the misoprostol allergy in the patient's case file and adequate clerking are very necessary steps to forestall such allergy.

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