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Intravenous Use of Metoclopramide and Sustained Hypotension: A Case Report

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ABSTRACT

Introduction:
Transient hypotension has been commonly associated with metoclopramide hydrochloride, particularly with intravenous use. However, the risk of sustained hypotension that lasts for hours has not been previously associated with metoclopramide, except for one published case report. This case report is aimed at documenting the second case of unusual and serious sustained hypotension that lasted for more than six hours following rapid intravenous use of metoclopramide prescribed for the prevention of cesarean section delivery related intra/postoperative nausea and vomiting.

***Case Report*:**
A 33-year-old gravida III and para II woman was admitted to a hospital for an elective cesarean section delivery with normal baseline blood pressure. Following metoclopramide 10 mg intravenous push administration, over 5-10 seconds, the mother encountered sustained hypotension (60/40 mmHg) that lasted for 120 minutes. After resuscitation, her blood pressure raised to 105/60 mmHg. However, after spinal anesthesia with bupivacaine hydrochloride, her diastolic arterial blood pressure dropped back again to 40 mmHg which persisted for about six hours post-operation. Upon investigation, the sustained hypotension was found to be probably related to inappropriate and rapid administration of intravenous bolus dose of metoclopramide hydrochloride that could have been prevented since it should be administered slowly over at least three minutes.

Conclusion:
The risk of metoclopramide-induced hypotension should not be underestimated as it sometimes might be much severe than the risk of nausea and vomiting that warrants immediate attention from healthcare professionals and program managers.

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Introduction

Metoclopramide hydrochloride, a class of benzamides, has been associated with cardiovascular disorders in general and transient hypotension in particular (1-3). Hypotension that usually lasts for few minutes has been particularly associated with overdose of intravenously administered metoclopramide (1,4). In the summary of product characteristics of metoclopramide hydrochloride injection that was approved by the Medicines and Healthcare products Regulatory Agency of the UK and European Medicines Agency, the manufacturers advise healthcare professionals that intravenous doses should be administered slowly at least over three minutes (1).

To the best of the authors' knowledge, there is only one published case report of sustained hypotension that lasted for about 90 minutes and was associated with intravenous injection of metoclopramide though transient hypotension has been frequently reported in this regard (5).

This case report is therefore aimed to document an unusual case of serious sustained hypotension that lasted for about six hours following rapid administration of intravenous metoclopramide injection prescribed for the prevention of intra/postoperative nausea and vomiting. Metoclopramide hydrochloride is indicated for the prevention of intra/postoperative nausea and vomiting, intractable nausea and vomiting, and prevention of radiotherapy-induced nausea and vomiting (1,2).

Case Report

A 33-year-old gravida III and para II woman was admitted to a hospital for an elective cesarean section delivery. The weight and height of the mother were 58 kg and 170 cm, respectively. She had a regular antenatal care follow-up in a nearby health center and visited our hospital three times for general check-ups.

She reported that she was healthy before admission and denied any history of labor pain, dizziness, and fatigue. The mother also reported that she had a history of cesarean section two times before due to a narrow pelvis; however, she experienced no other past medical and surgical history. In addition, she denied any pre/ intra/postoperative complications on her previous cesarean section. Upon admission to Tesseney Hospital, Eritrea, East Africa, in September 2020, she was generally stable with normal vital signs of blood pressure (BP) (100/60 mmHg), pulse rate (98 beats per min), temperature (36.8°C), and oxygen saturation (SPO2) (98%). Baseline investigation, such as complete blood count, blood group, urinalysis, and ultrasonography that was made upon admission were all also normal. The trans-abdominal sonography showed that she had a pregnancy of 39 weeks by femoral length

After obtaining the informed consent, she was prepared for a cesarean section, and two units of blood were prepared for possible need of blood transfusion. Before she was transferred to the operating room, two large-bore cannulas were inserted, and a 1000 mL of normal saline 0.9% infusion was given as part of her preoperative preparation which raised her BP to 105/60 mmHg after 30 minutes. It should be mentioned that no other medications were administered, and she was transferred to the operating room on foot which was about 200 meters away. Following that, she sat on the theater for spinal anesthesia, and metoclopramide 10 mg intravenous push, over 5-10 sec, was administered as part of the hospital's routine practice. The mother started to experience dizziness, lassitude, and sweating two minutes later; moreover, she was unable to speak and support her body. Immediately, she was put on left lateral decubitus position, and three minutes following the administration of metoclopramide, her blood pressure was recorded to be 60/40 mmHg, which showed a 42.9% drop of systolic arterial blood pressure from baseline. In addition, SPO2 was estimated at 99%, and her pulse rate increased to 117 beats per min. The extremities became cold and started air hunger with somnolence. The mother denied any history of medication use or substance intake before admission. Urgent resuscitation efforts were made with oxygen 5 liters/minute via nasal prong and bolus of 1000 mL ringer's lactate, as well as normal and rapid saline 0.9%. After 80 minutes and

the injection of two boluses of intravenous crystalloids, her blood pressure raised to 84/48 mmHg; however, no improvement was observed in her general condition. As ephedrine was not available, another rapid infusion of 1000 mL of normal saline 0.9% was administered. After 120 minutes of resuscitation efforts, her blood pressure raised to 105/60 mmHg. It was diagnosed as 'sustained hypotension' secondary to the use of metoclopramide intravenous injection.

A decision was made to continue with the procedure, and ceftriaxone 1 g was administered intravenously given for prophylaxis of infection. Spinal anesthesia (bupivacaine hydrochloride) was administered, and delivery with cesarean section was made safely with blood loss of approximately 400 mL, followed by no intraoperative complications. Misoprostol 200 micrograms sublingual was taken for the reduction of postoperative bleeding. Following the procedure, the diastolic arterial blood pressure dropped back to 40 mmHg, which persisted for about six hours post-operation. After six hours, her condition improved and BP raised to 100/60 mmHg; moreover, the 24-hour urine output was recorded as 1100 mL. After two days of admission where her blood pressure was persistently recorded as that of the baseline, the mother was discharged from the hospital with a follow-up appointment. She was advised of the possible adverse effect of a metoclopramide intravenous bolus administration.

Discussion

According to Naranjo adverse drug reaction causality assessment scale, the unusual case of sustained hypotension that lasted for hours was found to be probably related to metoclopramide (6). The plausible temporal relationship, unavailability of other alternative explanations, a reasonable response to the withdrawal of the offending medication, and availability of objective evidence were among the main factors for the association of sustained hypotension with the intravenous use of metoclopramide. The 42.9% drop in systolic arterial blood pressure from baseline, following metoclopramide use, qualified the case for serious hypotension. The reaction abated approximately after two hours of resuscitation and recurred following spinal anesthesia with bupivacaine hydrochloride that lasted for another six hours. The hypotension might be aggravated by the spinal anesthesia and the inability to use prophylactic vasopressors of either ephedrine or phenylephrine (7-9).

Although transient hypotension has been frequently reported with intravenous use of metoclopramide (1,2,4), sustained hypotension is a new form of the known association that warrants immediate attention from healthcare professionals and programmers. Preventability assessment using the P-method (10) reflected that the sustained hypotension would have been possibly prevented for the following two reasons: 1) The intravenous bolus dose was administered rapidly though manufacturers advised that it should be administered slowly over at least three minutes and 2) The life-saving medication for the prevention of hypotension during spinal anesthesia was not administered for its unavailability, which might have complicated the case during post-operation.

It is not well known how metoclopramide could cause hypotension. However, there is a hypothetical mechanism through its antagonism with serotonin (5-hydroxytryptamine, 5-HT) (11). Serotonin 5-HT is a vasoconstrictor and can increase epinephrine release from the medulla in receptor-dependent and receptor-independent sympathomimetic mechanisms (12,13). Although it can be argumentative, it is hypothesized that metoclopramide might cause hypotension by blocking the effect of serotonin 5-HT that is showed to have central control of blood pressure in non-stressed rats by exerting a tonic inhibitory influence (11,14).

Availability of strict and updated treatment protocols, healthcare professionals' adherence to national or international guidelines and manufacturer's recommendations, and ensuring the continued availability of vital medicines are highly recommended to mitigate the potential risk.

Moreover, the application of a sequential mechanical pump to the lower limbs could have been useful to reduce the severity of the

hypotension by restoring the central blood volume (15).

This case report reflects that the risk of metoclopramide-induced hypotension should not be underestimated as it sometimes is much severe than nausea and vomiting that would be encountered with the intervention. Therefore, healthcare professionals, consumers, manufacturers, and regulators should be aware of the potential risk of sustained hypotension associated with intravenous use of metoclopramide hydrochloride.

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