



CASE REPORT

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Oxytocin induced itching in a 37 week primigravida with meconium stained liquor

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ABSTRACT



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Introduction: Oxytocin is the most frequently used medication for labour augmentation in obstetrics. One of the known benefits of its use is the improvement of uterine contractions. An injectable form of oxytocin is administered intravenously as an infusion. Adverse drug reactions at this stage may distress the baby and worsen the outcome of the pregnancy.

Case details: A 19-year-old female with a history of nine months gestation presented in labour. She was administered oxytocin infusion in ringer lactate to augment labor. She developed itching all over her body and was immediately administered Inj. hydrocortisone intravenously. As the foetus was in distress, she was taken for an emergency lower segment cesarean section (LSCS).

Conclusion: The administration of IV oxytocin was considered the possible cause of the development of rashes in this case. We suggest adopting preventive strategies to avoid ADRs in emergencies to avoid deleterious consequences. The preventive strategies may include screening in the antenatal period for previous history of sensitivity to oxytocin, latex, etc. In addition, other strategies are discussed in this article.

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Introduction

Oxytocin was the first oligopeptide peptide hormone with an amino acid sequence Cysteine–Tyrosine– Isoleucine– Glutamine–Asparagine–Cysteine–Proline–Leucine– Glycineamide (CYIQNCPLG-NH₂) which was purified, synthesized and made available in the 1950s for pharmacological studies (MacDonald et al., 2011; Viero et al., 2010). The antepartum indications for oxytocin use are inactive uteri, preeclampsia, maternal diabetes, and premature rupture of the membranes. In all these cases, it is given to strengthen the uterine contractions with the aim of a successful vaginal delivery of the fetus. It is also used in second-trimester abortions that are unavoidable or

incomplete. Oxytocin is also indicated in the postpartum period to deliver the placenta during the third stage of labour and control postpartum hemorrhage. Non-approved indications of oxytocin use include delayed orgasm, inducing sexual arousal, and treating autism. Further research is going on in these areas (Osilla et al., 2022).

Adverse drug reactions (ADRs) are noxious and unintended reactions to drugs that occur at doses normally used in humans for disease prevention, diagnosis, therapy, or the modification of physiologic function. Up to 0.3 % of non-hospitalized and 30 % of hospitalized pregnant women were reported to experience ADRs, respectively. The majority of the drugs' ADR profiles for pregnant



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women are not yet published because pregnant women are often excluded from clinical trials (de Oliveira-Filho et al., 2017).

The publication of ADRs associated with drugs used to treat various diseases is an integral part of pharmacovigilance signal detection activities. They also provide information to understand the etiology, pathogenesis, natural history, and treatment of the disease in a natural, real-life context (Murthy et al., 2022; Joshi et al., 2014). Therefore, in this article, we attempted to present a case of intravenous oxytocin-induced adverse drug reaction in a full-term pregnant woman with meconium-stained liquor. Furthermore, an attempt will be made to present a brief review of the literature on ADRs caused by oxytocin.

Case Report

A 19-year-old female reported to the emergency department with a history of amenorrhea for 9 months with discharge per vagina. She also had pain abdomen since 4:30 am. She was admitted to the hospital at 7:40 am on July 18, 2022. She was a primigravida with 37 weeks and 4 days of gestation in active labour.

General examination revealed: a pulse rate of 60 beats per minute; respiratory rate of 20 per minute; SpO₂ of 99 %; and a blood pressure of 110/70 mm of Hg. A thorough systemic examination revealed the following: S1 and S2 heart sounds were appreciated; bilateral normal vesicular breath sounds were found; the uterus was at term size, 3C/20"10', with the cephalic presentation, and fetal heart sounds were present. Meconium-stained liquor (MSL) was discovered during a per speculum examination. The cervix was soft and dilated by 6 cm per vaginal examination, fully effaced, and the vertex at station +2 was noted.

Given MSL, to augment labour she was administered oxytocin 5 units in one pint of ringer lactate at a rate of 8 drops per minute intravenously. The patient started experiencing severe itching all over the body. On examination, her pulse rate was found to be 98 bpm, SpO₂ 99 %, and her blood pressure was found to be 100/70 mm Hg. The oxytocin was immediately stopped, and 100 mg of hydrocortisone was administered intravenously.

As the fetal heart deceleration was noted, the patient was taken for emergency lower segment cesarean section (LSCS). The patient delivered a single, live, term male baby weighing 3.1 kg under spinal anesthesia. The baby did not cry immediately. At 1 minute, the Apgar score was 2/10, and at 5 minutes, it was 5/10. The baby was shifted to the neonatal intensive care unit (NICU). The postoperative period for the mother was uneventful. The patient was treated with IV fluids, antibiotics, analgesics, and other supportive measures. Both mother and baby were discharged after a 7-day hospital stay.

The ADR induced by intravenous oxytocin, i.e., "severe itching all over the body," was considered to be severe, serious, probably related to oxytocin, and preventable.

Discussion

In our case report, the severe itching caused by oxytocin was thought to be probably drug-related (on the WHO scale for causality assessment of ADRs) (WHO 2018), because the event occurred immediately after the oxytocin intravenous drip was started. Re-challenge of the drug was not done. Therefore, we were not able to comment on the definite relationship with the drug. The ADR subsided after being treated with intravenous hydrocortisone 100 mg immediately after the initiation of the event.

According to the definition of SAE (Tang et al., 2015), this ADR was considered a serious adverse event as the hospital stay for the mother and baby was prolonged. In addition, ADR required immediate, specific remedial measures to avoid an adverse outcome. If the patient was not treated immediately, serious consequences would have affected the mother's and baby's clinical outcomes. The event was considered a severe-grade event (Hartwig et al., 1992), as it required advanced, specific treatments like LSCS for delivering the baby and supportive treatment to rescue the mother and baby from adverse outcomes.

Itching and hypersensitivity reactions are known ADRs of oxytocin. Theoretically, a test dose of oxytocin before starting the intravenous drip of oxytocin would have prevented the event. But such testing is not practically possible in mothers who are in full-term pregnancy and active labour. Since the patient was in labour, and the patient did not have any history of allergy to any drug or food products, she was administered oxytocin. The baby with MSL was already stressed and required immediate intervention. Therefore, the patient was taken for LSCS and appropriate management of the delivery of the baby. This is considered the limitation of the preventability assessment scale published by Schumock et al. (Schumock et al., 1992).

In a literature search, it was found that Guo J et al., in their preclinical studies, demonstrated the ability of oxytocin to induce transient hind-paw scratching behaviors in mice through spinal oxytocin receptors (OTRs). The stimulation of OTRs increases the expression of c-fos mRNA in spinal GRP neurons, which transmit spinal itch via the GRP/GRPR pathway (Guo et al., 2020). In another study, Li R et al. demonstrated that oxytocin plays a role in chloroquine-induced scratching behavior via vasopressin-1a receptor (V1AR) binding events. These findings provide novel evidence relevant to advancing the understanding of oxytocin-induced behavioral changes and related adverse drug reactions. These advancements will also aid in the development of oxytocin-based drugs to treat a variety of psychiatric disorders, as well as CQ-

induced itch relief via V1AR antagonists (e.g., Conivaptan, etc.) (Li et al., 2019).

Intravenous injection of oxytocin is known to induce a variety of other adverse reactions, like cardiac arrhythmias, tachycardia, bradycardia, nausea, vomiting, headaches, skin rashes, anaphylactoid reactions, water intoxication, and associated neonatal hyponatremia, erythema at the site of injection, intensified or frequent uterine contractions, stomach pain, loss of appetite, seizures, confusion, hallucinations, extreme increase in blood pressure, and blurred vision (MacDonald et al., 2011; Osilla et al., 2022).

G. Liccardi et al. reported that multiple pathways can be attributed to the development of various ADRs following oxytocin IV infusion. Allergic sensitization to latex may be an important risk factor for the development of anaphylaxis after the first oxytocin infusion during delivery. Oxytocin-induced release of pro-inflammatory cytokines similar to those released in asthma may lead to the contraction of smooth muscles and the narrowing of the airways. Parasympathetic neuromodulation, vasodilatation, negative cardiac inotropy, and chronotropy, etc. may lead to cardiac adverse events like cardiac arrhythmias, tachycardia, bradycardia, etc. (Liccardi et al., 2013).

Considering these aspects, the researchers suggested some preventive strategies for the ADRs induced by oxytocin. They are the identification of latex allergy and susceptibility to bronchial asthma during antenatal checkups. The use of a latex-free anesthesiological setting, the use of alternative agents to oxytocin, and drug premedications can be other preventive strategies (Liccardi et al., 2013).

In general, the majority of drugs' ADR profiles for pregnant women are not published because pregnant women are often excluded from clinical trials. Therefore, individual case safety reports (ICSRs), pharmacovigilance studies, and post-marketing phase IV studies play an important role in detecting and quantifying ADRs and identifying the safety of medications during pregnancy. In addition, epidemiological studies are required to assess the prevalence of these events in pregnant women, especially among patients at high risk for pregnancy complications.

Conclusion

Oxytocin is used as an inducing agent at the initiation of vaginal delivery. The development of ADRs at this moment can worsen the outcome of the pregnancy and put the baby in distress. In our case report, oxytocin is thought to be probably related to the development of severe itching all over the body. Immediately, a decision was made to save the mother and baby by conducting an emergency delivery through LSCS.

We suggest adopting preventive strategies to avoid such deleterious consequences. Preventive strategies may include antenatal screening for previous history of sensitivity to oxytocin, latex, and other substances, as discussed in this article. Various mechanisms are attributed to the development of ADRs due to the infusion of oxytocin. Further research in this area may lead to the development of a newer group of drugs for treating oxytocin/vasopressin-mediated neurological diseases and premedication for its hypersensitivity reactions (i.e., itching, etc.). Further research is required to study the ADRs produced by various drugs that are used in pregnancy, which may help in eliciting preventive strategies. This may help to improve the pregnancy outcome and the survival of newborn babies.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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