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Case Report

Intravenous paracetamol-related loss of consciousness at induction of anesthesia: A case report

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ABSTRACT

Paracetamol (Acetaminophen) is an analgesics, antipyretic, and non-steroidal anti-inflammatory drugs. It is known to be one of the commonly used analgesics globally. Intravenous paracetamol has been frequently used in patients as analgesics and antipyretics. In therapeutic doses, paracetamol is well-tolerated and devoid of severe adverse reactions. However, significant adverse reactions associated with intravenous paracetamol may occur rarely. Nausea, vomiting, and constipation are known to be the common side effects of paracetamol. Other side effects include pain and reaction at the site of injection. The adverse reactions of paracetamol are as follows; hypotension, malaise, hypersensitivity reaction, elevation of liver enzymes, and thrombocytopenia. In our center, we found a case of intravenous paracetamol-related loss of consciousness at induction of anesthesia in a patient booked for myomectomy.

Keywords: Induction of anesthesia, Intravenous, Loss of consciousness, Paracetamol

INTRODUCTION

Paracetamol (Acetaminophen) is an antipyretic, non-opioid analgesic, and non-steroidal anti-inflammatory drugs. It was first synthesized in 1878 from its precursor and its use was not widespread initially due to early reports of a link to methemoglobinemia.[1] After this association was discredited, paracetamol was initially marketed in the 1950s as a safer drug to phenacetin, which was found to have carcinogenic property.[2] As early as 1980s, paracetamol was superior to other agents as the most widely used over-the-counter analgesic in the United Kingdom and it is one of the drugs in the first step of the World Health Organization analgesic ladder for the management of pain.

The severe adverse reactions associated with intravenous paracetamol such as severe hypotension and loss of consciousness are extremely rare. The incidence of these adverse reactions is 1/10,000. The reported adverse events include; hypotension, malaise, hypersensitivity reaction, liver enzyme elevation, and thrombocytopenia.[3]

In our center, we found a case of bolus intravenous paracetamol-related loss of consciousness. To the best of our knowledge, there was no previous case of bolus paracetamol-related loss of consciousness in our center and that is why we are reporting the case for publications.

Paracetamol is a non-opioid analgesic and antipyretic agent used in the treatment of pain and fever. It can be used as a single agent for mild to moderate pain or in combination with an opioid

analgesic for severe pain. In our center, we use intravenous paracetamol as part of intravenous analgesics in balance anesthesia. It can also be used for post-operative pain management.

CASE REPORT

The patient was a 28-year-old woman who came to our clinic with 3 months history of on and off lower abdominal pain, dysmenorrhea, and menorrhagia. Physical examination revealed moderate anemia and abdominopelvic ultrasound findings showed multiple uterine fibroids. The laboratory investigations revealed a hemoglobin of 7.2 g/dL and other investigations were essentially normal. An assessment of multiple uterine fibroids was made and she was prepared for myomectomy under general anesthesia. An informed consent for both the anesthesia and surgery was obtained.

Intraoperatively, baseline vital signs were stable and at induction, she was given IV atropine at 0.02 mg/kg and IV paracetamol at a dose of 15 mg/kg. At about 5 min after bolus IV paracetamol was given, her general condition deteriorated and the blood pressure was 60/40 mmHg. The patient's oxygen saturation was found to be <80% despite being given 100% oxygen. The patient lapsed into unconsciousness and not responding to verbal commands. She was immediately intubated with size 7.5 cm endotracheal tube and connected to anesthetic machine for mechanical ventilation. After intubation, the vital signs were stable. She was maintained on inhalational anesthetic agent isoflurane, at 1.0 minimum alveolar concentration.

At about 45 min after intubation, she started making spontaneous respiratory efforts and was given intravenous pancuronium at 0.1 mg/kg to achieve muscle relaxation for the surgery. After the surgery, the residual effect of muscle relaxants was reversed with intravenous neostigmine and atropine at 0.07 mg/kg and 0.02 mg/kg, respectively. She was extubated, fully conscious, and obeying commands. She was transferred to post-anesthesia care unit for observation and finally transferred to the ward for close monitoring. Postoperatively, her general condition was satisfactory.

The anaphylactic shock was then treated with antihistamine and steroids. The patient general condition was satisfactory and was discharged from the hospital 1 week postoperatively.

The patient presented in clinic for follow-up, her general condition was normal, and there was no any neurological deficit.

DISCUSSION

The efficacy and safety of paracetamol is well documented in different literatures.[1,3] It has been reported that intravenous paracetamol is effective and safe for both pre-operative, intraoperative, and post-operative analgesia. The mechanism of action of paracetamol remains unclear; however, it was postulated to inhibit the cyclooxygenase, cannabinoids, and nitric oxide pathways in the central nervous system (CNS) and activate descending serotonergic inhibitory pathway.[4]

After several literature searches, we have found that intravenous paracetamol causes severe hypotension, especially in critically ill patients. These patients required prompt intervention to prevent morbidity and even mortality.

Yaman *et al.*[5] reported a case of paracetamol infusion-related severe hypotension and cardiac arrest in a 2-year-old child who presented in their accident and emergency unit as a case of febrile neutropenia. Intravenous paracetamol infusion was administered to the patient and her general condition deteriorated after about 5th min of infusion. The paracetamol infusion was stopped immediately; the value of blood pressure could not be measured. The patient developed severe hypotension and cyanosis. He finally developed cardiac arrest. Cardiopulmonary resuscitation (CPR) was immediately commenced. After 15th min of CPR, the patient's circulatory system was reactivated. She was intubated and was admitted to pediatric intensive care unit (ICU) for mechanical ventilation using synchronous intermittent mandatory ventilation mode. She was extubated on 4th day and was discharged on 11th day of admission. Her general condition was normal and there was no neurological deficit.

Duncan *et al.*[6] studied the CNS effect of intravenous paracetamol and they have found that paracetamol reduces the incidence of post-operative nausea and vomiting (PONV) by affecting serotonergic pathways in the CNS.

And again, Duncan *et al.*[6] reported a retrospective observational study in intensive care setting. This study demonstrated the hemodynamic effect of centrally administered paracetamol. They studied 122 patients. About 17% of patients were found to have significant blood pressure reduction and all of these patients received intravenous paracetamol. They concluded that intravenous paracetamol-related hypotension occurred more than the oral-administered paracetamol.

De Maat *et al.*[7] study the effect of intravenous paracetamol. This study showed a significant decrease in systolic blood pressure following administration of intravenous paracetamol. The reduction in blood pressure causes loss of consciousness with associated hypoxia, which may lead to cardiac arrest and may increase morbidity and mortality. In this their study, it was also found that those that had intravenous paracetamol developed hypotension compared to those that received paracetamol through oral route.

Boyle *et al.*,[8] however, provided evidence that intravenous paracetamol can cause reduced blood pressure up to 60 min after infusion.

Recently, Needleman[9] investigated the safety of rapid infusion of paracetamol. In a retrospective review, the paracetamol was found to cause statistically significant decreases in both the systolic and diastolic blood pressure. In their study, it was found that patients had severe hypotension and cardiac arrest due to paracetamol infusion. The patient's hypotension might have developed due to the rapidly administered paracetamol infusion. Hypovolemia is a common cause of hypotension. The paracetamol-induced hypotension may be clinically important, especially in the setting of critical illness where it is most frequently reported.[10] This finding of hypotension associated with paracetamol is commonly seen in critical and emergency department due to close monitoring of vital signs in these critical settings where vital signs of patients are closely monitored.

Picetti *et al.*[11] carried out a prospective observational study in 32 patients in neurosurgical ICU to explore the cerebral and hemodynamic effect of intravenous paracetamol in patients with acute brain injury. Those patients with hypovolemic were excluded from the study. In their study, it was found that paracetamol was very effective as an antipyretic in patients with acute brain injury. However, it causes significant hypotension which requires prompt management to prevent further damage to the injured brain.

Again, a 4-year narrative review of 4771 patients by Lee *et al.*[12] showed a significant proportion of patients with significant hypotension as adverse drug reaction following administration of intravenous paracetamol.

The hemodynamic effect of intravenous paracetamol in healthy volunteers were reported by Chiam *et al.*[13] It was concluded that intravenous paracetamol caused transient decrease in blood pressure immediately after infusion when compared with its excipients (mannitol) and placebo (normal saline). It was discussed that the physiological mechanism of hypotension was consistent with systemic vasodilation rather than the reduction of cardiac index.

Cruz *et al.*[14] in a comparative study of metamizole and propacetamol (which is a brand of paracetamol). They compared the hemodynamic and antipyretic effects of these two drugs in critically ill patients with fever. It was found that propacetamol is an effective antipyretic and also has adverse hemodynamic effects which may be poorly tolerated especially in critically ill patients.

Young[15] carried out a narrative review of 27 articles and all these articles concluded that significant relationships between intravenous paracetamol administration and hypotension exist.

CONCLUSION

Intravenous paracetamol-related loss of consciousness is a rare complication. Therefore, close monitoring of patients receiving intravenous paracetamol is crucial to prevent morbidity and mortality especially in critical care settings.

This incident of loss of consciousness related to intravenous paracetamol administration thought us lessons as follows: close monitoring of hemodynamic status of all patients receiving intravenous paracetamol especially in critical care setting and also prompt management to prevent morbidity associated with severe hypotension, loss of consciousness, and cardiac arrest.

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