“ICE” – A rare cause for coagulopathy in a case of massive post-partum hemorrhage

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ABSTRACT

A case of massive post-partum hemorrhage in East-Malaysia, associated with 3-4 methylene-dioxy-methamphetamine (MDMA) abuse otherwise known as Ecstasy or locally as “ICE”, injected by the patient as a means to suppress labor pains prior to hospital presentation. We report a rare case of substance abuse that lead to life threatening hemorrhage in a maternal patient of productive age group. Presenting to the labor suite in second stage of labor in breech presentation, exhibiting active neuropsychiatric symptoms of intoxication like euphoria, drowsiness, mydriasis but able to obey commands. A rapid response by the Obstetric on-call team proceeded with an assisted-breech delivery. Post-delivery, a baby girl with poor Apgar score was born and intubated. The mother was then posted for an Examination Under Anesthesia as she was noted to have slow blood oozing per-vaginally using a single shot spinal as she exhibited features of difficult intubation and high risk of aspiration. During the procedure, she tipped into massive PPH complicated with DVC, and was rushed into the intensive care unit for stabilization and back into the operation theatre, needing a total abdominal hysterectomy (TAH) as definitive bleeding control. She required large scale resuscitative efforts peri-operatively including continuous veno-venous hemofiltration (CVVH) as well as regional intensive care consultation. We describe, chronologically the anesthetic challenges faced in managing a patient in acute substance intoxication at presentation to our district hospital during twilight hours. We then explain the pharmacodynamics of MDMA in provoking coagulopathy. No reports of similar cases in the South-East Asia region.

INTRODUCTION

Recent data extracted from the Malaysian Drug Information 2015 census by the National Anti-Narcotics Agency (AADK), the Sarawak state drug addicts contributed 2.47% from the total registered number of drug addicts in Malaysia. Based on type of drug abuse, MDMA accounted for 29.61%.There are limited cases reported on MDMA abuse in pregnancy and its association with post-partum hemorrhage. As this case is being reported for purposes of widening field experience, patient agreement was sought after.

CASE REPORT

A 31 years old female parturient, active intravenous MDMA user, without antenatal screening presented to the labor room for contraction pains. She was estimated to have a BMI of 36 kg/m². An initial working diagnosis of breech in labor with high suspicion of substance abuse was made as she displayed active neuropsychiatric symptoms like occasional drowsiness, euphoria and tachycardia, mydriasis, and an acidic venous blood gas. Her delivery was facilitated via assisted breech technique due to foot presentation. A baby girl was born with an Apgar score of 1 in 1st minute and 3 in 5th minute, a suspicion of acute MDMA toxicity and intubated. Post instrumental delivery, the obstetric team noted a suspicion of acute MDMA toxicity and intubated. Although having neuropsychiatric symptoms, she was obeying commands and warm to touch. Airway assessment revealed a large protruding tongue, Mallampati score of 3, tyro-mental distance > 6.5cm, and mouth opening of 3 finger breadths and pendulous breasts. In the OR, standard ASA monitors appropriate for her weight were applied without struggle from the patient. In view of high risk of aspiration and anticipated difficult airway, we decided to proceed with Regional Anesthesia. Therefore, a single shot spinal technique was performed for spinal anesthesia totaling to 2.1 milliliters at L4-L5 intrathecal space administered over a duration of 2 minutes. No long acting opioids were given intrathecally due to risk of respiratory depression and exacerbation of patient’s
Post-operatively, she was kept ventilated in the intensive care unit (ICU), put on continuous minimally invasive hemodynamic monitoring and started on early continuous veno-venous hemofiltration (CVVH) in a form of renal supportive therapy in view of severe metabolic acidosis. The trend of her hematological and coagulation profile is shown in Table 1. Echocardiography done post ICU admission showed, severe global hypokinesia, with an ejection fraction of 8%. Repeated echocardiography after extubation revealed only septic hypokinesia and improved systolic function with an ejection fraction of 40%. Septic parameters were within physiological limits with cultures displaying no growth. Urine toxicology taken prior surgery tested positive for amphetamine, methamphetamine and opioid. Soon after, her overall clinical conditions improved and she was extubated and transferred out of intensive care unit (ICU).

**DISCUSSION**

Substance abuse has been increasing in trend in the past few years. The most recent national substance abuse report compiled by the National Anti-Narcotics Agency (AADK), indicated, that the most commonly abused substance is methamphetamine or 3-4 methylenedioxyamphetamine (MDMA). Its actions in common as well as the pregnant population states are well documented and commonly associated with its cardio-stimulant and neuropsychiatric effects. MDMA abuse doubles the risk of post-partum hemorrhage. The National Obstetric Registry of Malaysia 2012 showed major cause of massive PPH as uterus atony at 9.52% compared to genital trauma at 0.04%. In this case report, we discuss a case of postpartum hemorrhage leading to devastating impacts on the patient's hemodynamics as her hemorrhage which lead to coagulopathy was compounded by methamphetamine abuse. Her last dose of methamphetamine, also commonly known as "ICE" in laymen terms, was one hour prior to admission which explained her acute intoxication symptoms accompanied by hypoxemia and acidosis. Despite acute intoxication, a low dose single shot spinal anesthesia was administered as per local guidelines of obstetrics anesthesia in her management as patient was still able to obey commands at post-partum and had a high risk of aspiration with features anticipated difficult airway. Features of chronic substance abuse were also noted in this patient whereby, difficulty in obtaining intravascular access and multiple puncture spots were noticed on her upper limbs. In view of limited recent evidence on this subject, few similar case reports whereby methamphetamine or even amphetamine intoxication contributing to neuropsychiatric symptoms. Post spinal, no hypotensive episodes were observed. We encountered a major difficulty in intravenous cannulation of the bilateral upper limbs possibly due to sclerosis and calcification of vessels after repeated punctures for substance abuse over period of few years. Using ultrasonography, we noted even her major vessels were severely constricted, further complicating venous access. We also encountered difficulties in achieving a firm grip using the standard “tegaderm” plasters in effort to secure our lines due to constant sweaty skin contributed by MDMA abuse which was overcome using the “durapore” medical adhesive plaster. During intraoperative obstetric examination, it was noted by obstetric surgeon and anesthesia team, patient had increased tendency of bleeding. She subsequently developed a post-partum hemorrhage (PPH) complicated with disseminated intravascular coagulation (DVC) despite multiple attempts to secure bleeders and continuous fluid resuscitation. At this point, we decided to convert her to General Anesthesia using Rapid Sequence Induction technique in view of hemodynamic instability as patient was pale, increasing tachycardia with occasional hypotensive episodes, arterial blood gas displaying worsening metabolic acidosis. Induction was done using intravenous fentanyl of 80mcg, sodium thiopentone 325mg at 4mg/kg in view of patient borderline hemodynamic parameters and suxamethonium 100mg. Intubation was uneventful, single attempt, obtaining a Cormack-Lehane 1 view with cricoid pressure. Post induction, we inserted a Right neck intrajugular venous catheter line (IJC) and arterial blood pressure monitoring (IABP) in the OR using ultrasound guidance under aseptic technique. This patient went into a stage IV hypovolemic shock, requiring activation of massive transfusion protocol including disseminated intravascular coagulopathy (DVC) regimes and recombinant factor VII administration, needing inotropic support to maintain blood pressure and end-organ perfusion. However, she had to be rushed into the intensive care unit for hemodynamic stabilization and back into the operation theatre. She eventually had to undergo a trans-abdominal hysterectomy (TAH) as a definitive means to stop life threatening hemorrhage.

### Table 1 Hematological Trend & Coagulation profile

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (gr/L)</td>
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<td>6.3</td>
<td>7.3</td>
<td>9.8</td>
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<tr>
<td>Platelet</td>
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<td>178</td>
<td>118</td>
<td>158</td>
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<tr>
<td>PT (sec)</td>
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<td>17.7</td>
<td>15.3</td>
<td>15.4</td>
</tr>
<tr>
<td>PTT (sec)</td>
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<td>45.9</td>
<td>50.3</td>
<td>48.9</td>
</tr>
<tr>
<td>INR</td>
<td>1.22</td>
<td>1.52</td>
<td>1.26</td>
<td>1.27</td>
</tr>
</tbody>
</table>

In this case report, we discuss a case of postpartum hemorrhage leading to devastating impacts on the patient’s hemodynamics as her hemorrhage which lead to coagulopathy was compounded by methamphetamine abuse. Her last dose of methamphetamine, also commonly known as “ICE” in laymen terms, was one hour prior to admission which explained her acute intoxication symptoms accompanied by hypoxemia and acidosis. Despite acute intoxication, a low dose single shot spinal anesthesia was administered as per local guidelines of obstetrics anesthesia in her management as patient was still able to obey commands at post-partum and had a high risk of aspiration with features anticipated difficult airway. Features of chronic substance abuse were also noted in this patient whereby, difficulty in obtaining intravascular access and multiple puncture spots were noticed on her upper limbs. In view of limited recent evidence on this subject, few similar case reports whereby methamphetamine or even amphetamine intoxication contributing to neuropsychiatric symptoms. Post spinal, no hypotensive episodes were observed. We encountered a major difficulty in intravenous cannulation of the bilateral upper limbs possibly due to sclerosis and calcification of vessels after repeated punctures for substance abuse over period of few years. Using ultrasonography, we noted even her major vessels were severely constricted, further complicating venous access. We also encountered difficulties in achieving a firm grip using the standard “tegaderm” plasters in effort to secure our lines due to constant sweaty skin contributed by MDMA abuse which was overcome using the “durapore” medical adhesive plaster. During intraoperative obstetric examination, it was noted by obstetric surgeon and anesthesia team, patient had increased tendency of bleeding. She subsequently developed a post-partum hemorrhage (PPH) complicated with disseminated intravascular coagulation (DVC) despite multiple attempts to secure bleeders and continuous fluid resuscitation. At this point, we decided to convert her to General Anesthesia using Rapid Sequence Induction technique in view of hemodynamic instability as patient was pale, increasing tachycardia with occasional hypotensive episodes, arterial blood gas displaying worsening metabolic acidosis. Induction was done using intravenous fentanyl of 80mcg, sodium thiopentone 325mg at 4mg/kg in view of patient borderline hemodynamic parameters and suxamethonium 100mg. Intubation was uneventful, single attempt, obtaining a Cormack-Lehane 1 view with cricoid pressure. Post induction, we inserted a Right neck intrajugular venous catheter line (IJC) and arterial blood pressure monitoring (IABP) in the OR using ultrasound guidance under aseptic technique. This patient went into a stage IV hypovolemic shock, requiring activation of massive transfusion protocol including disseminated intravascular coagulopathy (DVC) regimes and recombinant factor VII administration, needing inotropic support to maintain blood pressure and end-organ perfusion. However, she had to be rushed into the intensive care unit for hemodynamic stabilization and back into the operation theatre. She eventually had to undergo a trans-abdominal hysterectomy (TAH) as a definitive means to stop life threatening hemorrhage.

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coagulopathy in past literatures have been reported internationally in the last two decades. No similar cases were ever reported locally in Malaysia. Chatwick et al in 1991 reported a case mortality in 16 year old girl with a reported MDMA intoxication which lead to disseminated intravascular coagulation (DICV) that was confirmed via post mortem (normal muscle biopsy). There were also few instances of events in the past decades shown by Chadwick et al reporting which have been linked with adverse outcomes from MDMA abuse. MDMA is known as a semi-synthetic hallucinogen. Chatwick also highlighted the difficulty in choosing inotropes in hemodynamic support due to the central and peripheral sympathomimetic effects of MDMA which in this present case was complicated with hypovolemia, and suggested the management should be aggressive and not delayed.4 The exact pathophysiology of coagulopathy in MDMA abuse is largely unknown. Although not a sole contributing factor in this case, based on the literature we have gathered, high fever and neuro-psychiatric manifestation on presentation which are signs and symptoms of acute MDMA abuse, could have been among the multiple contributing factors triggering events that lead to this patient’s poor coagulating ability.5 Methamphetamine leads to altered serotonin 5HT-3 levels. In regards to serotonin effects centrally, Green et al quoted few studies in his article that demonstrated rats exhibiting the so-called serotonin behavioural syndrome. The rapid irreversible inhibition of tryptophan hydroxylase by MDMA, a rate- limiting enzyme in serotonin pathway synthesis is expected to have a sustained inhibition of tryptophan hydroxylase, an effect which can last for 2 weeks or longer after a single dose of MDMA, hence, would be expected to decrease 5-HT synthesis and function which can lead to psychiatric or other physiological consequences of methamphetamine abuse.5 Serotonin plays a dose dependent role in enhancing effects of ADP and thrombin as well functioning as a platelet agonist in clot aggregation in vivo. Li’s article in 1997 also stated that serotonin blocking agents demonstrated antithrombotic effects.6 Serotonin also influences clot retraction and platelet aggregating factors.7 Kathryn S. et al and Green in his article also quoted studies using rats injected with neurotoxic doses of MDMA, impairment of thermoregulation was observed as a result of impairment of serotonin function recording temperatures as high as 43 degrees Celcius.6 Hyperthermia also on the other hand, could have contributed towards coagulopathy by increasing fibrinolysis and reducing fibrinogen to very low levels as well as lowering platelets manifested by increased pro-thrombin times and reduced platelet counts.9 In a study done by Sakai et al 2 years ago in Japan, demonstrated methamphetamine as the most likely cause of death in a stillborn that received the substance from the mother who actively injected herself with MDMA during labour and delivery. Methamphetamine has low molecular weight and high lipophilic profile and also stay longer in infants due to immature metabolic capability. Also mentioned in his study, were animal studies that stated maternal administration of methamphetamine increased vascular resistance in the uterus and reduced oxygen partial pressure (PaO₂). Long term exposure to MDMA, resulted in behavioural changed and death in rats.10

CONCLUSION

Past studies have related methamphetamine towards being one of the causative agents in triggering massive detrimental responses like disseminated intravascular coagulation (DICV) necessitating large scale resuscitative efforts to ensure survival of our patients. Therefore, it is of utmost importance to have early suspicion of substance abuse in patients who continue to bleed despite multiple interventions and to manage them adequately throughout the duration of the intoxication and to provide critical care support early and as needed until they stabilize clinically.

REFERENCES


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