Ecstasy (MDMA) Ingestion Related with Severe Hyponatremia in Patients with Mild Head Injury

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The occurrence of severe hyponatremia is an unusual complication in patients with a mild head injury. Between December 2001 and January 2003, 1147 patients with a mild head injury were reviewed. Only patients who presented with deterioration of consciousness or seizure due to hyponatremia, confirmed by serum investigation, were further evaluated, presenting features and clinical courses. The results revealed only 3 patients developed severe hyponatremia following a mild head injury. Surprisingly, all of them had a recent history of ecstasy (MDMA) use, as well as hyponatremia which didn't develope until the episode of a mild head injury. In the present report, the associated mechanisms of both conditions of severe hyponatremia are discussed and the literature is reviewed.

Keywords: *Ecstasy, MDMA, Hyponatremia, Mild head injury*

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"Ecstasy" (3, 4-methylenedioxymethamphetamine, MDMA) is a psychoactive amphetamine derivative, which is increasing in popularity, especially among teenagers. There has been an interest in the adverse effects of MDMA use, and with the neurotoxic effects and fatalities related to is use[1-8]. The mechanisms of MDMA are still doubtful. Moreover, various adverse effects related to MDMA dosage are also unpredictable. However, several papers have reported that hyponatremia and hyperthermia are the most significant acute adverse effects. Although hyponatremia and hyperthermia could be found in association with a small number of cases of MDMA ingestion, these complications are the principal causes of mortality.

Hyponatremia is also a common complication associated with various neurosurgical conditions. Several mechanisms of hyponatremia have been well described, particularly in association with severe and moderate head injury. Until now, they have been reported in only a few cases of hyponatremia related to a mild head injury. The association between the MDMA ingestion and head injury, which precipitated hyponatremia, is still doubtful while there has been no report on this synergistic effect, whether that results in the occurrence of hyponatremia.

In the present report, three patients, with a history of MDMA use, developed hyponatremia after a mild head injury, are presented. The association between MDMA and head injury are hypothesized whether MDMA is a precipitating factor of hyponatremia in patients with a mild head injury. The literature and mechanisms of the adverse effects of MDMA in association with a mild head injury are discussed.

Material and Method

Between December 2001 and November 2003, patients with a mild head injury, Glasgow Coma Scale (GCS) Score $\geq$ 13, who were admitted to the Neurosurgical Division, Thammasat University Hospital, Patumthani for neurological observation or some other indications, were reviewed in those with deterioration of consciousness or seizure due to hyponatremia. Only patients with severe hyponatremia (serum $Na^+ < 120$ mmol/l) were retrospectively reviewed. History and presenting features were re-analyzed. In addition, serial examinations of blood and urine biochemistry and computerized tomography were also re-evaluated.

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Results

Among the 1147 patients with a mild head injury (983 males and 164 females), only 3 male patients developed alteration of consciousness and/or seizure due to hyponatremia (serum sodium concentration < 120 mmol/l). Surprisingly, these 3 patients had a history of MDMA ingestion. Urine samples were investigated in 2 of the 3 patients for analytical confirmation of MDMA and the results showed positive reaction for MDMA. The other patient was only documented by history of MDMA ingestion. The clinical courses of all patients are illustrated as follows.

Patient 1

A 20-year-old man was admitted to the hospital with transient unconsciousness following a motorcycle accident. He drank alcohol and used one tablet of "ecstasy" at midnight of the previous night.

On presentation, neurological examination revealed no abnormal findings. No fracture was demonstrated in the plain skull x-ray. Computerized tomography (CT) scan demonstrated no abnormal findings. Initial biochemical examination showed normal serum electrolyte (Na+ 132 mmol/l, K+ 3.8 mmol/l, Cl- 102 mmol/l, HCO3- 20 mmol/l). He had a 6-month history of continuous MDMA ingestion, 2-3 tablets per week on average.

After conservative treatment, he gradually improved, but on the second day before discharge, deterioration of consciousness developed. At that time, the CT scan still demonstrated no abnormal findings, while blood chemistry analysis revealed hyponatremia (120 mmol/l).

Patient 2

A 21-year-old man was admitted to the hospital with a traumatic head injury due to falling from a 3-meter height. He had 5-minute unconsciousness and retrograde amnesia.

On presentation, the neurological examination revealed no abnormal findings. Plain skull x-ray was normal. He had a stable fracture of the midshaft of the right radius. His arm was immobilized by a long arm cast. On admission, blood chemistry and serum electrolyte revealed normal (Na+ 139 mmol/l, K+ 3.9 mmol/l, Cl- 104 mmol/l, HCO3- 21 mmol/l). He had a 4-month history of MDMA use, 1-2 tablets per week. The last ingestion was 2 days previously.

After 36-hours observation, deterioration of consciousness and seizure developed. Cerebral CT scan revealed no cerebral edema, hematoma or cerebral contusion, while blood chemistry analysis showed severe hyponatremia (113 mmol/l).

Patient 3

A 19-year-old man was admitted to the hospital with multiple laceration wounds of the face and scalp and a closed fracture of the mandible due to a motorcycle accident after a night party.

On presentation, neurological examination revealed no abnormal findings. He had no history of loss of conciousness. Plain skull x-ray was normal. Initial biochemical examination showed normal serum electrolyte (Na+ 136 mmol/l, K+ 3.5 mmol/l, Cl- 110 mmol/l, HCO3- 24 mmol/l). He had a history of 8 tablets of MDMA use during the last 2 months. He also ingested 2 tablets of MDMA at the night party.

After 48 hours of admission for mandibular fixation, he had deterioration of consciousness. CT scan revealed no cerebral edema, hematoma or cerebral contusion, while blood chemistry analysis showed hyponatremia (116 mmol/l).

The 3 patients with MDMA ingestion was obtained after the onset of alteration of consciousness or seizure, informed by their friends or families. The clinical courses of the 3 patients are summarized in Table 1.

Clinical Management and Outcome

After hyponatremia was detected, the 3 patients were treated with intravenous hypertonic saline solution (3% NaCl) at a rate between 60-80 ml/

Table 1 Clinical courses of patients with hyponatremia following mild head injury

Patient	Age and Sex	GCS[a]	Cause of Mild Head Injury	Previous Use of MDMA[b]	Serum Na^+ (mmol/l)		
					< 24 hr*	24-48 hr*	48-72 hr*
1	20 M	14	Motorcycle accident	1 tablet 1 d	132	120	135
2	21 M	15	Falling from 3-meter height	1 tablet 2 d	139	113	133
3	19 M	14	Motorcycle accident	2 tablets 6 hr	136	116	138

[a] Glasgow Coma Scale: on admission; [b] Previous use before admission; *Hours after admission

hr in conjunction with fluid restriction. The level of serum sodium returned to normal after 72 hours. The mental status and consciousness of the 3 patients improved within 48 hours after the onset of alteration. There was no evidence of hyperpyrexia during the admission. After 72 hours, the 3 patients were asymptomatic. They were discharged without any other complications within 1 week after medical management.

Discussion

Hyponatremia is a common complication in patients with severe and moderate head injury, but it is rarely reported in those with a mild head injury. In the present paper, the author reports 3 patients with mild head injury who presented with data of syndrome of inappropriate secretion of antidiuretic hormone (SIADH). Astonishingly, these 3 patients also had a history of MDMA ingestion. Although several reports showed that MDMA alone could induce hyponatremia, it did not often occur after ingestion of MDMA[9,10]. In the present retrospective review, it showed remarkably that all of the patients, with the previous ingestion of MDMA, did not develop hyponatremia until onset of the head injury. The author hypothesizes whether head injury has a synergistic effect on the occurrence of hyponatremia in patients with MDMA ingestion. However, there have been no reports on this association until now. The author, therefore, reviewed the literature and discussed on the likelihood of those related mechanisms.

For MDMA-induced hyponatremia, a number of recent reports demonstrated a rapid rising in antidiuretic hormone (ADH) concentrations after the ingestion of MDMA and supported the theory that MDMA-induced hyponatremia was due to SIADH[11,12]. One report demonstrated an increase of serum ADH after 8 normally hydrated healthy male volunteers ingested MDMA[13]. Additionally, in some animal experiments, the reports supported that ADH secretion is mediated by serotonergic transmission[14]. For the etiology of SIADH following cerebral injury, the mechanism is also caused by an increase of ADH concentration. Because of this identical mechanism, the increase of ADH secretion might occur more likely in the combination of a head injury and MDMA ingestion.

Moreover, one of the consequences of the MDMA ingestion is profuse sweating as a result of both the pharmacological action on the thermoregulatory mechanism and energetic physical action. Sodium can be lost in sweat, and if the patients drink a large amount of water to reduce overheating, the result is hemodilution and inducing hyponatremia[14]. Evidence of water intoxication has been detected both in vivo[5] and post-mortem[10,15,16]. Because patients with a traumatic head injury are usually given nothing per oral (NPO) during the first 24 hours of neurological observation, intravenous hypotonic saline solution is therefore generally given to the patients. Hence, the relative hemodilution could occur as well as it might exacerbate hyponatremia. The mentioned instance might support previous reports which showed the incidence of hyponatremia related principally to the water consumption[12,13,17,18] while no association between dosage of MDMA and occurrence of hyponatremia has been documented. Because of the popular use of various recreational drugs, especially MDMA, a history of drug ingestion should be elucidated in most patients with traumatic head injury. When the patients have a history of MDMA use, management by using excessive fluid with hypotonic saline solution should be particularly cautioned.

In several mortality cases due to MDMA use alone, a number of patients developed severe hyponatremia in association with severe cerebral edema, which was demonstrated on the cerebral CT scan or pathological results[13,19,20]. This severe complication seems to be the principal cause of death. Fortunately, all 3 patients in the present report revealed no cerebral edema on the CT scan. However, in the author's opinion, cerebral CT scan should be performed, when the patient develops a seizure or alteration of consciousness during the neurological observation, in order to rule out any surgical conditions due to the head injury.

In summary, the presenting report supports that ingestion of MDMA could be associated with hyponatremia in patients with a mild head injury. The identical mechanisms of abnormal ADH secretion due to MDMA ingestion and cerebral injury, as well as the excessive water management could be a synergistic factor in the occurrence of hyponatremia. For the management of patients with a head injury presenting with alteration of consciousness or seizure, the history of any recreational drug, especially MDMA, should not be overlooked. After the exclusion of neurosurgical conditions and confirmation of hyponatremia, the restoration of electrolyte balance and, particularly, correction of hyponatremia, should be a priority. The aim of this review was to make clinicians recognize in obtaining the history of recreational drug use in patients with a head injury, because severe hyponatremia could be a severe complication and lead to be the

cause of mortality, especially in the era of recreational drugs.

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ความสัมพันธ์ของการใช้ยาอี (ecstasy) กับภาวะโซเดียมต่ำในเลือดในผู้ป่วยบาดเจ็บที่ศีรษะเล็กน้อย

ภัทรวิทย์ รักษ์กุล

การเกิดภาวะโซเดียมต่ำในเลือดเป็นภาวะแทรกซ้อนที่พบได้ไม่บ่อยนักในกลุ่มผู้ป่วยบาดเจ็บที่ศีรษะเล็กน้อย รายงานนี้เป็นการศึกษาย้อนหลังผู้ป่วยที่มีอาการบาดเจ็บที่ศีรษะเล็กน้อยที่ได้รับการรักษาในโรงพยาบาลในระหว่างธันวาคม ค.ศ. 2001 ถึง มกราคม ค.ศ. 2003 (จำนวนทั้งสิ้น 1147 ราย) ผู้ป่วยซึ่งมีอาการชักหรืออาการสับสนของสติสัมปชัญญะระหว่างนอนรักษาในโรงพยาบาล โดยได้มีการตรวจยืนยันผลเลือดแล้วพบว่ามีภาวะของโซเดียมต่ำในเลือดอย่างรุนแรง (< 120 มิลลิโมลต่อลิตร) ผู้ป่วยจะถูกคัดเลือกมาเพื่อศึกษาทบทวนประวัติ อาการทางคลินิก และการดำเนินโรคทางคลินิกทั้งหมดอีกครั้งหลังจากศึกษาย้อนหลัง พบผู้ป่วยเพียง 3 รายที่มีภาวะโซเดียมในเลือดต่ำอย่างรุนแรง ที่น่าประหลาดใจก็คือผู้ป่วยทั้ง 3 รายนี้มีประวัติเคยใช้ยาอี (ecstasy) มาก่อน โดยไม่เคยมีอาการของโซเดียมต่ำในเลือดจนกระทั่งเกิดอาการบาดเจ็บที่ศีรษะและเกิดภาวะโซเดียมต่ำในเลือดในเวลาต่อมา ในรายงานนี้จะอภิปรายถึงกลไกของสาเหตุที่ทำให้เกิดภาวะโซเดียมต่ำในเลือดจากความสัมพันธ์ของทั้งสองกรณี และทบทวนวรรณกรรมที่เกี่ยวข้อง