Title
Patterns of ecstasy-associated hyponatremia in California.

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Ecstasy-associated hyponatremia: Gender difference in California 2000 - 2005.

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ABSTRACT

Study objective: To describe the clinical characteristics of patients with Ecstasy (MDMA)-associated hyponatremia (serum sodium less than 130 mmol/L) reported to the California Poison Control System (CPCS) over a five-year period and to determine if a gender difference exists among patients with Ecstasy-associated hyponatremia.

Methods: We performed a retrospective review of cases involving Ecstasy intoxication reported to the CPCS and recorded in its computerized database from January 1, 2000 through October 9, 2005 We excluded all "information only" calls, cases managed at home, cases with no gender specified and cases in which the outcome was coded as "no effect", "unrelated – probably not responsible", "confirmed non-exposure", "judged as non-toxic- expect no effect", and "minimal clinical effects possible". Confirmation of exposure to MDMA was based on the history of use and, when available, urine toxicology screen testing positive for MDMA or amphetamine derivatives. Hyponatremia was defined as a measured serum sodium less than 130 mmol/L.

Results: A total of 1,436 cases involving Ecstasy were reported to the CPCS over the 5-year study period, of which 891 were excluded based on the criteria described above. Of the 545 cases that met inclusion criteria, 296 (54.3%) were females and 249 (45.7%) were males. There were 188 cases (34.5%) with a documented serum sodium, including 73/188 (38.8%) with hyponatremia (Na < 130 mmol/L). Of the 73 subjects with hyponatremia, there were 55 (75.3%) females and 18 (24.7%) males; of the 115 non-hyponatremic subjects 50 (43.5%) were female and 65 (56.5%) male. There was no observed gender difference in the ascertainment of serum sodium levels. Among patients with a documented serum sodium level, female gender was

associated with increased odds of hyponatremia by univariate analysis (OR 3.97; 95% CI 2.08 – 7.59).

Conclusion: Female gender was associated with increased odds of hyponatremia among persons with Ecstasy intoxication and a documented serum sodium level reported to CPCS from 2000 - 2005. Multiple potential study confounders, including spectrum bias, incomplete laboratory data and individual differences in subject characteristics prevent determination of causality regarding gender differences in the incidence of Ecstasy-associated hyponatremia and its complications.

Ecstasy-associated hyponatremia: Gender difference in California 2000 - 2005.

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Introduction

Background

Ecstasy (MDMA, 3,4-Methylenedioxymethamphetamine) has been a popular drug of abuse for several decades. A ring-substituted variant of methamphetamine, Ecstasy has gained popularity as a “club drug” in the United States (1, 2), Europe (3, 4, 5), Australia (6) Asia (7) and the Middle East (8), particularly among adolescents, young adults and attendees of “rave” parties (9). Ecstasy has anxiolytic, stimulant and hallucinogenic effects (10); its widely reported property of facilitating interpersonal communication and social interactions has led to its description as an “entactogen” (11) and, anecdotally among its users, as “the love drug”. Despite its widespread popularity, Ecstasy has been associated with a number of serious adverse effects, including life-threatening rhabdomyolysis (12), hyperthermia (13, 14), cardiac arrhythmias (15), hepatotoxicity (3), renal failure (16), disseminated intravascular coagulopathy (3), seizures (7), serotonin syndrome (17) coma (18) and death (2).

Importance

The occurrence of clinically significant hyponatremia has been reported in a number of cases of Ecstasy ingestion over the past two decades (1, 4, 5, 7, 19, 20, 21). The association between Ecstasy, female gender and hyponatremia has been raised (4, 7, 22) but no study has formally addressed this question. The largest prior published case series of Ecstasy-associated hyponatremia included 18 cases, with 17 females (94%) (4). A 28-month retrospective review of Ecstasy associated hyponatremia conducted by the National Poisons Information Service (NPIS) in London contained 17 patients, including 10 females (58.8%), with two fatalities, both female (5). A 3-month retrospective case series of 32 patients presenting to emergency services at a municipal hospital in Israel after Ecstasy ingestion included 3 patients (9.3%) with Ecstasy-

associated hyponatremia, 2 of which (66%) were female (8). Some evidence points to a possible gender difference in the long-term degenerative effects of Ecstasy on brain serotonin neurons in heavy users of Ecstasy, with women more likely to suffer this type of neurotoxicity (23). Given the continued popularity of Ecstasy, especially among teenagers and young adults, determination of a gender difference in morbidity and mortality associated with Ecstasy use may assist in identifying individuals at increased risk of adverse outcomes.

Goals of this Investigation

The objective of this study was to describe the clinical characteristics of patients with Ecstasy-associated hyponatremia (defined as a serum sodium less than 130 mmol/L) reported to the California Poison Control System during a five-year period. In particular, we sought to determine whether a gender difference exists among these patients and whether females are at greater odds for hyponatremia and associated adverse outcomes.

Materials and Methods

Study Design and Setting

We designed a non-concurrent, prospective observational case series involving Ecstasy (MDMA) intoxication reported to CPCS and recorded in the Visual Dotlab (VDL) computerized database from January 1, 2000 through October 9, 2005. We obtained approval from the CPCS Research Committee and the University of California, San Francisco Committee on Human Research (CHR). The CPCS is a 24-hour emergency telephone consultation service. All data in CPCS case records are collected by CPCS staff in accordance with American Association of Poison Control Centers (AAPCC) criteria (24). CPCS staff uses the VDL database to record patient information in database fields for demographic information, substances involved in the exposure (free text and coded values) and standardized codes for presenting symptoms, treatments, and medical outcome.

CPCS staff also document case details regarding history, physical exam, laboratory data, medical treatments and poison center recommendations within a free text field.

Selection of Cases

We initially included searched for all cases where the substance exposure recorded in the database (generic code or free text) code indicated was “Ecstasy” or “MDMA” or “methylenedioxymethamphetamine” or “XTC”. We also searched the free text field for the search terms “Ecstasy”, “MDMA”, “methylenedioxymethamphetamine”, and “XTC”. We eliminated all duplicate cases using the CPCS case record number. Because our intent was to capture all cases in which a true exposure had occurred, we excluded all “information only” calls, all cases managed at home, and all cases in which the VDL database outcome code indicated was coded as “no effect”, “unrelated – probably not responsible”, “confirmed non-exposure”, “judged as non-toxic- expect no effect”, and “minimal clinical effects possible”. Confirmation of exposure to MDMA was based on the history of use and, when available, urine toxicology screen positive for MDMA or amphetamine derivatives. There was no age limit for subjects included in the study and patients with all co-ingestions were included.

Data Collection and Processing

Two of the study authors (JR and CS) served as abstractors and independently reviewed each case and excluded cases that were miscoded (i.e. when review of the text field revealed that the exposure was to a drug other than MDMA). They selected for further detailed review all cases in which a documented serum sodium concentration appeared in the case record (including those in which the sodium concentration was recorded by the poison center staff as “normal”) and all cases in which the patient had a documented seizure. A standardized abstraction form was then used by three study authors (JR, CS, and KO) to collect detailed data from the text field regarding the history of exposure, presenting symptoms, clinical course, laboratory testing, ICU admission, and death. These data were entered into a Microsoft Excel (Version 11.0, 2004) database. If data

was missing it was recorded as “not available”. After collection of the data the study authors met to review the findings and to resolve any differences in the interpretation of chart information. There were no instances in which such discrepancies could not be resolved.

Methods of Measurement

Sodium concentrations were measured at the referring hospitals and were recorded by CPCS staff as reported during their telephone consultation. No effort was made to confirm these values by obtaining medical records from the specific hospitals involved.

Outcome Measures

The primary outcome measure was hyponatremia, defined as a serum sodium less than 130 mmol/L, in subjects with Ecstasy exposure. Secondary outcomes included the occurrence of seizures, tachycardia, agitation, hyperthermia, coma and death among subjects with documented serum sodium values. Toxicology testing results, co-ingestions, site of ingestion, and ICU admission among subjects with Ecstasy intoxication were also investigated.

Primary Data Analysis

We present descriptive data for our study population in frequencies without statistical analysis. For comparisons of clinical characteristics and outcomes with respect to gender and the presence of hyponatremia univariate analysis was used to calculate odds ratios with 95% confidence intervals.

Results

Subject Inclusion

Our initial database search identified 1,436 cases, of which 545 remained after applying our exclusion criteria. 883 cases were excluded from the study (29 were coded as “no effect”, 63 as

"unrelated", 2 as "confirmed non-exposure", 3 as "judged as nontoxic", 167 as "minimal clinical effects possible" and 352 were coded as "unable to follow – potentially toxic". An additional five cases were eliminated after review revealed no exposure to MDMA (i.e. miscoding), and 3 cases in which gender was not specified. A flow diagram summarizing our database search is provided in Figure 1.

Toxicology Data

Urine toxicology screening was documented in 103 of the 188 (54.8%) cases with documented serum sodium levels. 68 (66%) patients were positive and 35 (34%) patients negative for amphetamines or amphetamine derivatives. The 35 patients with urine screens negative for amphetamines or amphetamine derivatives were considered to be true cases of MDMA intoxication based on documented history of MDMA ingestion. 35 (34%) patients had urine toxicology screening positive for a drug in addition to amphetamines. The most commonly detected drugs other than amphetamines were cocaine, THC, and benzodiazepines. Of the 73 cases of hyponatremia, there were 43 (58.9%) documented urine drug screens, 39 of which were positive for amphetamines or amphetamine derivatives and 4 of which were negative.

Case Characteristics

Table 1 summarizes the clinical characteristics associated with gender among all 545 cases included in the study. Of these 545 patients there were 296 (54%) females and 249 (45.4%) males. The most commonly coded clinical signs and symptoms were tachycardia (42.6%), agitation (31.9%), and seizures (11.2%). One hundred fifty three (28.1%) of all patients were admitted to the ICU and there were a total of 13 (2.4%) deaths. Of the 545 study cases, 50 (9.1%) had "Rave party" reported as the site of ingestion, including 3/73 (4.1%) of the hyponatremia cases.

When analyzed by gender, univariate analysis revealed no difference in the odds of developing any of the observed clinical characteristics with the exception of tachycardia. Females were less likely to develop tachycardia (OR 0.68; 95% CI 0.48 – 0.95). Both females and males were equally likely to be admitted to the ICU or to have died. A serum sodium ascertainment was documented in 188 (34.5%) patients. Among these, the exact quantification was specified for 134 (71%), whereas values were documented qualitatively as within the normal range without specifying an exact level in 54 (29%). There was no observed gender difference in the ascertainment of serum sodium levels.

Gender in Relation to Hyponatremia and Other Adverse Outcomes

There were 74/188 (39.4%) cases of hyponatremia (serum sodium < 130 mmol/L) among patients with a documented serum sodium. Among these cases, the median serum sodium concentration was 122 (25th to 75th percentile 119 - 124 mmol). Table 2 summarizes the relationship between gender and selected clinical characteristics, including our main outcome measure of hyponatremia, in the subset of 188 patients with a documented serum sodium. Within this subset, females had increased odds of developing hyponatremia compared to males (univariate OR 3.97; 95% CI 2.08 – 7.59).

Figure 2 is a set of univariate plots of all quantified serum sodium values (excluding those reported qualitatively as within normal limits) separated by gender. Median serum sodium values for women and men were 124 mmol/L and 137 mmol/L, respectively. There was, however, little gender difference in the absolute level of serum sodium within the hyponatremic group (mean gender difference 0. 07 mmol/L; 95% CI -2.2 to 2.1 mmol/L).

Finally, we examined the univariate odds of developing various clinical findings in patients with Ecstasy-associated hyponatremia stratified by gender. The results are summarized in Table 3.

Females with hyponatremia (n=55) compared to those without (n=50) had approximately four times the univariate odds of coma or seizure. In contrast, males with hyponatremia (n=18) compared to those without (n=65) had no increased univariate odds of coma and only a doubling of seizure odds, with wide confidence intervals (univariate OR 2.11; 95% CI 0.69 - 7.07).

Case Fatalities

There were 13 fatalities in the study population of 545, with an incidence of death of 2.4%. There were 4 fatalities in the hyponatremia group. Of these fatalities, 3 were female and 1 was male. All hyponatremia fatalities had a urinalysis positive for amphetamines or amphetamine derivatives, with one subject having a urinalysis specifically positive for MDMA. All fatal hyponatremia cases experienced hypotension requiring pressors and all four developed cerebral edema confirmed by CT scan. Two of the hyponatremia fatalities had seizures. One of the hyponatremia fatalities presented initially with significant hypothermia (34.4 C). Two of the hyponatremia fatalities manifested pulmonary edema on chest radiographs. Of the non-hyponatremia fatalities, there were 6 females and 3 males, with 5 toxicology screens positive for amphetamine derivatives, including one specifically positive for MDMA and one toxicology screen negative for amphetamines. Of the non-hyponatremia fatalities, 5 experienced asystole or ventricular fibrillation in the field, enroute to the hospital or in the ICU, three had hyperthermia, one had severe acidosis with subsequent brain death, and two experienced fatal intracranial hemorrhages. See Appendix A for a summary of study fatality data.

Limitations

Poison control center data collection is a passive surveillance source subject to reporting bias by the general public as well as health care professionals. As a retrospective observational case series, our study is further limited by the accuracy with which patient information is collected by poison center staff. By utilizing CPCS records rather than data obtained directly from hospital

charts, we may have missed cases of Ecstasy intoxication and Ecstasy-associated hyponatremia and underestimated the frequency of related events and complications. Clinical events such as seizures and lab data such as toxicology test results and serum sodium nadirs may not have been reported or entered correctly into the CPCS case report. Such limitations may have decreased the number of cases of Ecstasy intoxication and related complications captured by our computerized data base query. Many cases of Ecstasy intoxication in the community are likely not called in to CPCS, and some physicians may not have reported additional hospital cases to CPCS. This type of referral bias may lead to spectrum bias, resulting in our case series representing the more severe outcomes in the overall continuum of Ecstasy intoxications, possibly leading to overestimation of the frequency of Ecstasy-associated hyponatremia and associated adverse outcomes.

All cases of hyponatremia in our study had a positive history of Ecstasy exposure reported by the patient or a witness, however, this is anecdotal information and may have led to inclusion of cases resulting from intoxication by substances other than MDMA, such as other hallucinogens, phenethylamines, PMA, MDA or 2-CB, which may be used as adulterants in purported “Ecstasy” products (2). Our study may therefore overestimate the frequency of Ecstasy intoxication, Ecstasy-associated hyponatremia and other complications. In our study, only 54.8% of subjects with documented serum sodium levels also had documented urine toxicology screening, and of these, 34% were negative for amphetamines. Of the hyponatremia cases, only 58.9% had reported toxicology testing and 9.3% of these cases had urine toxicology tests reported as negative. Thus, a major limitation of our study is the lack of laboratory confirmation of MDMA ingestion a significant percentage of cases in our series. Gas chromatography coupled with mass spectrometry (GC/MS) is highly specific for MDMA but was not reported as performed in any of the study cases. Some commercial urine drug screens detecting amphetamines are not specific for MDMA and do not differentiate between different amphetamines and amphetamine derivatives –

such screens may lead to negative results when MDMA is in fact present. Data specifying the type of assay utilized were not available in the computerized data base record - our study may include subjects with tests positive for amphetamines other then MDMA leading to overestimation of MDMA intoxications and complications, and/or cases with negative toxicology screens that may in fact represent cases of actual MDMA intoxication.

A major limitation of our study is the lack of a recorded serum sodium level in the majority (65.5%) of study cases, which may have led to underestimation of the frequency of Ecstasy-associated hyponatremia. Subjects may have had asymptomatic or mildly symptomatic hyponatremia without a serum sodium level being drawn, contributing to both underestimation of hyponatremia frequency and under-recognition of clinical presentations accompanying this disorder. Additionally, the initial serum sodium levels used in our study may be misleading regarding the natural history of Ecstasy-associated hyponatremia, as the timing of collection of these sodium levels may not have been consistent across cases and thus not representative of the progression of the disorder. Ecstasy-associated hyponatremia may be a relatively benign, self-correcting process in some cases, with certain individuals predisposed to development of adverse outcomes – the prospective computerized data base used in our study did not allow us to adequately evaluate this possibility. Finally, multiple potential confounders such as differing subject body habitus, renal function, hydration, co-ingestions and behavioral factors limit the ability of the study to attribute causality and draw conclusions about the likelihood of a given population to develop hyponatremia or other adverse outcomes related to Ecstasy intoxication.

Discussion

Previous reports have raised the possibility that gender differences might exist with regards to the risk of Ecstasy-associated hyponatremia, hypothesizing that females may be at increased risk of

developing this condition (4, 7, 22). Our study, which was intended to specifically test this hypothesis, provides support that such a gender difference does indeed exist. This gender difference may involve a number of physiological factors, including metabolic and hormonal interactions and other mechanisms of homeostatic regulation (20, 27, 28, 32, 36, 38). This presumes that any female-associated risk of adverse outcomes associated with Ecstasy is mediated entirely through hyponatremia. Our data suggest that this may not entirely be the case, at least insofar as some neurological adverse events are concerned. Multiple possible confounders and other limitations of our study, however, preclude any definitive statement on the nature and mechanisms of the observed gender differences in this case series.

Ecstasy-associated hyponatremia has been hypothesized to involve several mechanisms and is likely multifactorial. In the past, Ecstasy users have been advised via “word of mouth” and the alternative media to drink copious amounts of water and/or non-alcoholic “energy tonics” to prevent dehydration and hyperthermia (1, 5, 21). However, excessive hydration can contribute to hyponatremia (25) and has been reported in cases of Ecstasy-associated hyponatremia (4). Rave parties and dance clubs typically involve high ambient temperatures and sustained dancing and physical exertion which may lead to excessive sweating, electrolyte loss and dehydration, all factors in the development of hyponatremia.

There is also evidence of Ecstasy-induced secretion of antidiuretic hormone (ADH, or vasopressin). MDMA administration stimulated ADH release from rat hypothalamus in vitro (26) and in healthy, normally hydrated human male volunteers, with a drop in serum sodium accompanying the rise in serum ADH (27). Additional evidence for MDMA-induced ADH secretion has been provided by determination of elevated levels of ADH in a patient with hyponatremic coma after Ecstasy ingestion (20). Several case reports of Ecstasy-associated hyponatremia reported low plasma osmolality and elevated urine osmolality, characteristics of the

syndrome of inappropriate ADH (SIADH) in euvolemic patients (5, 19). ADH secretion is mediated by serotoninergic neurons, with serotonin causing ADH release in conscious rats (28). In humans, serotoninergic medications such as the selective serotonin reuptake inhibitors (SSRI's) have also been linked to SIADH, supporting the association between increased serotonin and ADH secretion in humans (29). MDMA has been noted to strongly stimulate release and inhibit reuptake of serotonin in humans (30, 31).

Our study raises the possibility of a gender difference in the incidence of Ecstasy-associated hyponatremia, with women more likely than men to develop this condition. We also noted increased odds of seizure or coma among hyponatremic women in our study, whereas such increased odds were not evident among hyponatremic men. Why might females be more likely to develop Ecstasy-associated hyponatremia and associated adverse outcomes? In females, the secretion of ADH by the posterior pituitary appears to be regulated in part by ovarian hormones, particularly estrogen. Estrogen increases ADH release in humans, although progesterone has no such effect (32). Tamoxifen, a selective estrogen receptor modulator (SERM) with competitive partial agonist inhibitor effects at the estrogen receptor, decreased plasma ADH levels in rats (33). Estrogen has also been shown to enhance ADH secretion by decreasing the osmotic ADH release threshold, or set point, in humans (34). In rats, estrogen has been shown to reduce the antidiuretic response to ADH (35), however, this effect has not been established in humans. In a study looking at factors associated with the development of encephalopathy in hyponatremic patients after surgery, menstruant females (those having regular menstrual periods) were shown to be 25 times more likely than adult males or postmenopausal females to die or have permanent brain damage after developing hyponatremic encephalopathy, although both males and females were equally likely to develop both hyponatremia and hyponatremic encephalopathy after surgery (36). Estrogen has been shown to inhibit the Na-K ATPase ion pump, which could theoretically impair resolution of cerebral edema by decreasing the ability to clear intracellular sodium as a

response (37). This mechanism may be involved in the increased odds of seizures or coma demonstrated among the hyponatremic females in our study. Estrogen levels are lowest at the time of the menstrual period and highest at ovulation - the extent to which the cyclical release of hormones throughout the menstrual cycle relates to the risk of Ecstasy-induced hyponatremia has yet to be determined.

Our study raises a number of questions for future work. The reasons for the decreased odds of tachycardia in all hyponatremic subjects in our study are unclear and represent an interesting area for future research. How to best increase public awareness of the risks of Ecstasy use is a challenge that needs to be addressed. Public sources of information most likely to reach the largest population of potential Ecstasy users should be updated with current, evidence-based recommendations for harm reduction. One such source, DanceSafe.org (a California-based harm reduction organization), while providing potentially useful education and even public testing of certain “designer drugs”, makes little mention of Ecstasy-associated hyponatremia and does not raise the possibility of a gender difference in the incidence of this condition (38). Continued educational efforts in this regard could help decrease the occurrence of Ecstasy-associated hyponatremia and other Ecstasy-related complications. Elucidation of the mechanisms underlying a possible predisposition of women to develop Ecstasy-associated hyponatremia and associated complications remains an interesting area for further study. In addition to potentially reducing Ecstasy-related morbidity and mortality, further research regarding the molecular mechanisms contributing to Ecstasy-associated hyponatremia may enhance our overall understanding of fundamental physiological processes involving hormonal, metabolic and homeostatic regulation in humans.

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Figure 1: Ecstasy-associated hyponatremia: Gender difference in California 2000 – 2005
Study Overview

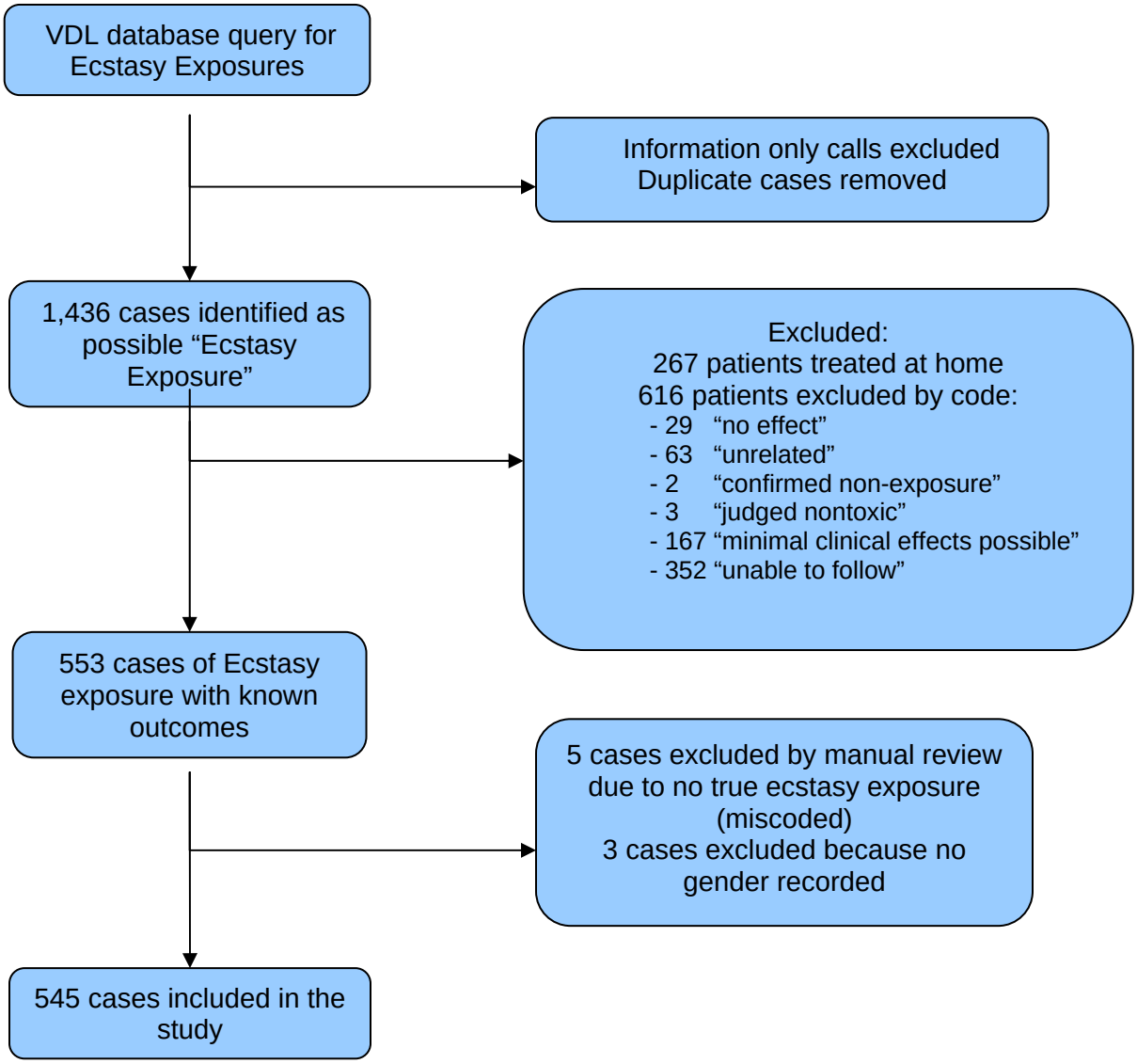

Figure 2. Documented serum sodium values, stratified by gender.

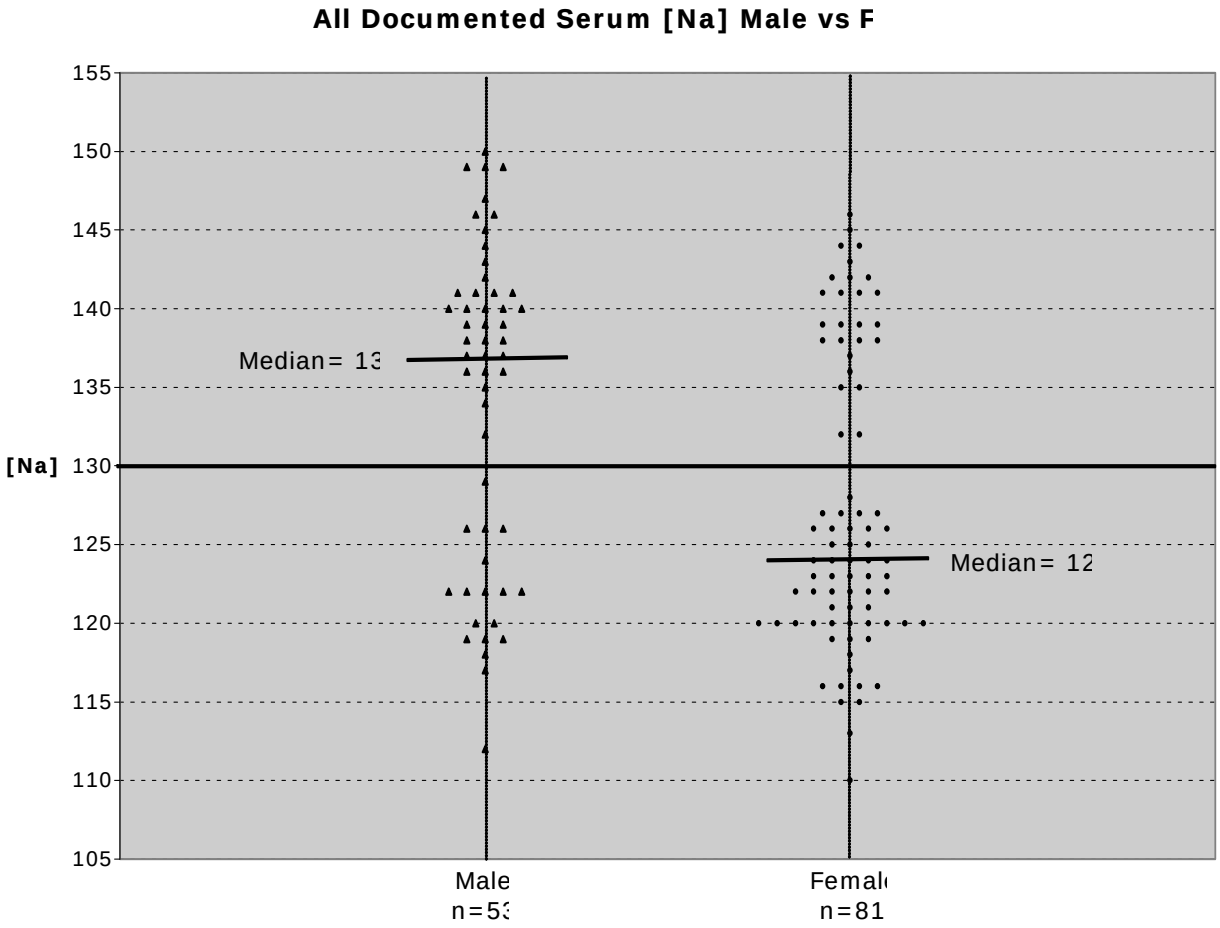

Table 1. Selected clinical characteristics among all study subjects with Ecstasy intoxication reported to CPCS* from 2000 - 2005.

	All (N = 545)	Female (N= 296)	Male (N=249)
	N (%)	N (%)	N (%)
Age	21.2 (SD = 6.8)	21.2 (SD = 6.76)	21.2 (SD = 6.76)
Clinical Findings			
Tachycardia	232 (42.6)	113 (38.2)	119 (47.8)
Agitation	174 (31.9)	91 (30.7)	83 (33.3)
Hyperthermia	40 (7.34)	16 (5.4)	24 (9.6)
Coma	54 (9.91)	33 (11.1)	21 (8.4)
Seizure	61 (11.2)	33 (11.1)	28 (11.2)
ICU Admission	153 (28.1)	77 (26.0)	74 (29.7)
Death	13 (2.4)	8 (2.7)	5 (2.0)
Documented Na	188 (34.5)	105 (35.3)	83 (33.3)

*CPCS: California Poison Control System

Table 2. Selected clinical characteristics among subjects with Ecstasy intoxication and a documented serum sodium stratified by gender.

Clinical Findings in patients with a documented serum Na	Female (N= 105)	Male (N= 83)
	N (%)	N (%)
Hyponatremia*	55 (52.4)	18 (21.7)
Tachycardia	30 (28.6)	42 (50.6)
Agitation	30 (28.6)	24 (28.2)
Hyperthermia	10 (9.5)	12 (14.5)
Coma	18 (17.1)	11 (13.3)
Seizure	33 (31.4)	18 (21.7)
Coma or Seizure	44 (41.9)	25 (30.1)
Death	5 (4.8)	3 (3.6)

*OR = 3.97 (95% CI 2.08 – 7.59)

Table 3. Hyponatremia and adverse outcomes among subjects with Ecstasy intoxication, stratified by gender.

Outcomes	Hyponatremia in Females (55/105)	Hyponatremia in Males (18/83)
	OR (95% CI)	OR (95% CI)
Tachycardia	0.33 (0.14 – 0.81)	0.13 (0.04 – 0.51)
Agitation	0.41 (0.17 -0.98)	1.3 (0.43 – 4.00)
Hyperthermia	0.58 (0.15 – 2.17)	0.29 (0.04 – 2.40)
Coma	3.93 (1.20 -12.9)	0.78 (0.15 – 3.97)
Seizure	4.38 (1.74 – 11.0)	2.21 (0.69- 7.07)
Death	1.39 (0.22 – 8.65)	1.85 (0.16 -21.7)

Appendix A: CPCS Ecstasy-Associated Fatalities 2000 – 2005

Case	Gender	Age	Serum Na	Description	Toxicology data
1	M	22	147	Found down by EMS in cardiac arrest after ingestion of Soma, Xanax, Trazadone and Ecstasy. Brain death leading to withdrawal of support.	Benzodiazepines, THC
2	F	29	136	Presented agitated and thrashing after reported ingestion of Ecstasy. Developed sudden onset of severe headache, vomiting and decreased level of consciousness. Patient had large intracranial hemmorhage.	Amphetamines
3	F	16	NR	Found unresponsive, pupils fixed and dilated after reported ingestion of Ecstasy at a party. Declared brain dead.	Amphetamines, THC
4	F	18	NR	Found in jail cell in ventricular fibrillation after reported ingestion of Ecstasy and GHB. Patient developed hyperthermia (38.8 C). Died of anoxic brain injury.	Not recorded
5	M	18	NR	Brought to Emergency Department from Rave party with core temperature of 44 C, comatose, tachycardic and hypertensive. Patient died from complications of hyperthermia.	Cocaine, Amphetamines, THC
6	F	14	NR	Brought in by ambulance in asystolic cardiac arrest after reported Ecstasy ingestion. Unable to resuscitate.	Not recorded
7	F	16	NR	Presented with obtundation and vomiting after found down by friends, brought in by ambulance in asystolic cardiac arrest. Unable to resuscitate.	MDMA
8	M	29	141	Presented with seizures, agitation, hyperthermia (41.6 C). Patient developed status epilepticus and died of complications related to hyperthermia.	Amphetamines, Benzodiazepines, Opiates
9	F	29	NR	Brought in by ambulance in cardiac arrest after reported Ecstasy ingestion. Patient developed massive subarachnoid bleed.	Negative for Amphetamines
10	F	16	123	Presented with seizures, hypotension, coma. Diffuse cerebral edema on CT, pulmonary edema on CXR.	Amphetamines
11	F	20	119	Presented with hypotension, respiratory depression, hypothermia (34.4 C). Developed acidosis, cardiac arrest.	Amphetamines, THC
12	F	20	124	Presented comatose, with profound hypotension, cerebral edema on CT.	Amphetamines
13	19	M	122	Presented comatose, hypotensive. Cerebral edema on CT. Pronounced brain dead. Multiple failed attempts at intubation secondary to “tightly clenched jaw”.	Amphetamines (MDMA)

NR = Not reported