

Gender Difference in Predisposing Factors of Overdose

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Abstract

Background Drug overdose is a one of common situations in emergency department (ED). We investigate gender difference and predisposing factors of overdose in emergency department (ED).

Materials and Methods We retrospectively analyzed overdose reports from January 2018 to August 2019. We selected study cases by the ICD-10 coding system which include T36 to T50. A total of 299 overdose reports were collected during this period. Data were collected including Glasgow coma scale and vital signs on arrival (including body temperature, heart rate, systolic blood pressure, and diastolic blood pressure, gender, age, marital status, arrival time, season on admission, previous suicide attempts, psychiatric history, related comorbidities, recent argues, categories of overdose with or without concurrent ethanol use, length of hospital stay and survival to discharge were analyzed.

Results The 196 enrolled patients ranged in age from 14 to 92 years (mean \pm standard deviation (S.D.): 39.2 ± 18.3). Of them, male intentional overdose patients were 8.1 years older than female ones (45.3 ± 19.5 vs. 37.2 ± 17.5 , respectively; $p < 0.05$)

Conclusion The most top three kinds of substance overdose are benzodiazepine (42.9%), mixed medications (32.1%) and acetaminophen (6.1%). Physicians should notify the centers of suicide prevention to pay concern about who are middle-aged male, facing conflicts, especially in the spring.

Introduction

Drug overdose is a one of common situations in emergency department (ED). In 2018, there were 67,367 drug overdose deaths in the United States and the age-adjusted rate of drug overdose deaths was 20.7 per 100,000 according to data from Centre for Disease Control and Prevention (CDC) in United States. Rates were higher for males than females. For males, the rate was 27.9 whereas the rate for females was 13.6 in 2018.

The incidence of overdose in Taiwan is about 0.16–0.22 per 1,000 population according to the Taiwan National Poison Centre [1]. Also, mortality rate of the poisoning is high which ranks fourth among unintentional injuries, of which the top three causes are automobile injuries, unintentional falls, and drowning [2]. Even though drug overdose deaths have great public attention, complications of nonfatal overdose including cognitive impairment, cardiac and muscular problems, renal failure, hearing loss and other injuries should be concerned [3,4]. The average hospital cost of overdosed patients who was treated and admitted is also notably tremendous [5].

Qin P *et al.* reported that although many studies have sought to interpret the gender gap in suicidal behavior where unemployment, retirement and being single, facing interpersonal conflicts were all significant risk factors for suicide in males, but no statistically significant risk factors other than mental

illness were reported in females [6, 7]. However, having a child less than 2 years old was significantly protective for women preventing suicide [7].

Therefore, recognizing the predisposing factors for drug overdose is an important issue and we investigated gender difference and predisposing factors of overdose in emergency department (ED).

Materials And Methods

Mackay Memorial hospital is one of tertiary care medical centers in northern Taiwan established in 1880 and has approximately 196,570 ED visits annually.

We retrospectively analyzed overdose reports from January 2018 to August 2019. This study was approved by the Institutional Review Board of Mackay Memorial Hospital (19MMHIS288e).

We selected study cases by the International Statistical Classification of Diseases and Related Health Problem 10th Revision (ICD-10) coding system which include poisoning by adverse effect of and underdosing of systemic antibiotics (T36), other systemic anti-infectives and antiparasitics (T37), hormones and their synthetic substitutes and antagonists (T38), nonopioid analgesics, antipyretics and antirheumatics (T39), narcotics and psychodysleptics [hallucinogens] (T40), anesthetics and therapeutic gases (T41), antiepileptic, sedative- hypnotic and antiparkinsonism drugs (T42), psychotropic drugs (T43), drugs primarily affecting the autonomic nervous system (T44), primarily systemic and hematological agents (T45), agents primarily affecting the cardiovascular system (T46), agents primarily affecting the gastrointestinal system (T47), agents primarily acting on smooth and skeletal muscles and the respiratory system (T48), topical agents primarily affecting skin and mucous membrane and by ophthalmological, otorhinolaryngological and dental drugs (T49), diuretics and other and unspecified drugs, medicaments and biological substances (T50).

A total of 299 overdose reports were collected during this period. 196 intentional overdose patients were enrolled, and 103 patients excluded. Exclusion reasons are unintentional overdose, mis-swallowing, accidental adverse drug reaction (ADR), discharge from ED without complete treatment and unclear data (**Table.1**). Data were collected including Glasgow coma scale (GCS) and vital signs on arrival (including body temperature, heart rate, systolic blood pressure [SBP], and diastolic blood pressure [DBP]), gender, age, marital status, arrival time, season on admission, previous suicide attempts, psychiatric history, related comorbidities, recent argues, categories of overdose with or without concurrent ethanol use, length of hospital stay and survival to discharge were analyzed.

We used statistical software (IBM SPSS Statistics for Windows, Version 20.0; IBM Corp., Armonk, NY, USA) for the data analyses. Both Student's *t*-test and the Chi-square test were used in the statistical analyses, and the statistical significance was set at $p < 0.05$.

Results

The 196 enrolled patients ranged in age from 14 to 92 years (mean \pm standard deviation (S.D.): 39.2 ± 18.3) and male to female ratio was 1:3 (male, $n=49$; female, $n=147$). Of them, male intentional overdose patients were 8.1 years older than female ones (45.3 ± 19.5 vs. 37.2 ± 17.5 , respectively; $p<0.05$) (**Table 2**). About 32.1% patients (63/196) had previous intentional overdose history where 26.5% (13/49) and 34% (50/97) were male and female patients, respectively. In comparison with female patients, 6.1% (3/49) of male patients tended to have premeditated drug overdose after arguing with girlfriend which have significant difference ($p<0.05$). Moreover, more than half of overdose patients were single ($n=116$, 59.2%) which was considered as one of the risk factors in overdose.

In our research, 13.3% (26/196) of enrolled patients had repeated intentional overdose suicide attempts during our study period. Most intentional overdose cases occurred during the Spring season ($n=63$, 32.1%), especially in male patients ($n=28$, 57.1%; $p<0.001$). Majority of cases ($n=78$, 39.8%) sent to our ED in the evening (from 15:00 to 23: 00p.m). Estimated 31.6% (62/196) of argues with family would drive patient to commit premeditated drug suicide attempt. Benzodiazepines ($n=96$, 49%; $p<0.004$) were the most common drugs used in intentional overdose. In addition, approximately 8.2% of female patients (12/147) self-poisoned with acetaminophen (**Table.3**). A great number of intentional overdose patients had depression history ($n=96$, 49%) and insomnia problems ($n=79$, 40.3%). Concurrent ethanol consumptions were only about 27.6% of patients (54/196).

Body temperature (Celsius) was slightly higher in female than male patients (mean \pm S.D., 36.7 ± 0.6 vs. 36.5 ± 0.2 , respectively; $p<0.05$). Our study also revealed significantly higher levels of SBP and DBP in male than female patients. No significant differences were found in associated marriage status, comorbidities, and concurrent psychiatric diseases between the two gender groups. About 11.2% (22/196) and 2% (4/196) of total patients hospitalized to ward and intensive care units, respectively. Length of hospital stay is 2 ± 4.1 days and none of cases in our study was dead by intentional drug overdose.

Discussion

Gender difference in overdose by season

One of our interesting results indicated that spring is a peak season where intentional drug overdose cases most occurred. Many studies also revealed that suicide rates also peak during spring season [8]. It also has been suggested that the sudden increase in the duration and amount of sunlight is a conceivable reason for these phenomena. Hakko *et al.* found two peaks of suicide rates within the non-violent (*i.e.*, ingestion of poisons, drugs, gases, or vapors) subgroup approximately a 9% increase in spring and an 8% increase in fall [9]. This is compatible with our data that overdose rate rises in the spring, especially in all cases (32.1%) and male (57.1%) with statistical significance. A study in Iran also revealed that the peak and trough seasons were observed in taking medications and self-poisoning for spring and winter [10]. In our study, 57.1% of male patients tended to commit suicidal drug overdose during spring season. Rocchi *et al.* indicated that suicide cases had a seasonal peak distribution in both

males and females during spring^[11]. A study in Greece revealed that suicide attempts in males increased during spring and summer and significantly decreased in September^[12]. Previous research has shown that only a single spring peak is found in men, while two peaks in spring and fall have been reported in women

^[13]. Some studies suggested that seasonal variance in suicides depends on an underlying seasonal biological variance which affects the control of impulses. Explanation for such variance mostly related to serotonergic (5-HT) circuits since brain levels of serotonin are sensitive to climate change and a clear seasonal rhythm is evident in serotonergic functions. Abnormalities in number of serotonergic neurons, serotonin transportation, receptor binding and serotonin levels in key brain areas have all been linked with suicide^[14]. Functional imaging studies have demonstrated decreased serotonin transporter binding in attempted suicide^[15] Thus, low levels of serotonin are often associated with impulsive and aggressive behavior.

Gender difference in overdose by physiology

Body temperatures of self-poisoning females are slightly higher (0.2 degree) than male patients observed in our result. There are many factors leading to variation in normal body temperature including gender-based variation which indicated females have higher body temperature than males^[16]. Body temperature is also sensitive to hormone levels and females exhibit elevation in body temperature of about 0.9° Fahrenheit (F) at the time of ovulation^[17]. Contrary, the blood pressure of overdosed male patients was higher than females. A study reported that blood pressure is higher in men than in women at similar ages by using the technique of 24-hour ambulatory blood pressure monitoring^[18]. Increased body temperature and blood pressure mostly related to overdose from stimulants (*i.e.*, cocaine, amphetamine, methamphetamine). In our study, most patients were intentionally overdosed with benzodiazepines which would not significantly increase body temperature and blood pressure. Therefore, higher body temperature of females and blood pressure in male patients might be physiologically rather than relating to overdose.

Gender difference in overdose by incidence and age.

On the other hand, females had three times risk of premeditated drug overdose than males in our study. Y. Veisani *et al.* indicated that majority of non-violent suicide cases were females^[19]. Another study showed that poisoning was the most common non-violent suicidal method for women^[20]. In addition, WHO/EURO Multicenter study on Parasuicides indicated that the seasonal pattern of suicide attempts in women showed a peak in spring and nadir in winter^[21]. But no significant difference noted in incidence of self-poisoned female patients over four seasons in our study. It is worth noting that elder male patients had a greater tendency to self-poison than females ($p < 0.009$ for the pooled sample and males and females) despite females having a higher risk of intentional overdose. A study in Taiwan revealed the mean age of the suicidal victims was 49.4 (± 18.3) years and more than one half of non-violent (54.9%)

suicidal victims distributed between 35 to 64 years-old [22]. The mean age of male overdose cases is 8.1 years older than female ones with statistical significance in our study.

Gender difference in overdose by facing conflicts.

There was an obvious tendency to drive male patients to have premeditated drug overdose after arguing with their girlfriends. Although relationship breakdown is a known risk factor for suicide, but it may not equally be susceptible between men and women [23, 24]. Some studies noted that divorced men were more than eight times to commit suicide than divorced women [25]. A study in Korea indicated that interpersonal conflict was the most common precipitating event for the suicide attempt in adolescent whereas family conflict is one of main risk factors in older people [26]. People with unsettled conflicts are always accompanied with a higher level of suicidal ideation, hopelessness, and depression than those who could deal with their partner harmoniously [27]. Furthermore, men have been taught to lead independent lives and act decisively without approaching others in time of need [28]. Expression of a man's suicidal ideation may be deemed as a sign of weakness. Thus, men are particularly vulnerable and precludes help-seeking as hegemonic masculinity [29], whereas women are more likely to seek help [30]. Pollack (2006) implied that boys are imbued with hiding their emotions between the ages of 3 and 5 through a "boy code" that rewards toughness and enforces prohibition against emotional expression or vulnerability [31]. Although depression is a well-known risk factor for suicide [32], however, men don't realize when they are depressed because men are supposed to be in control all times for their masculinity ideas [33]. This explains in part how the dynamics of male suicide continue to be underestimated and poorly understood.

Conclusion

Overdose is commonly seen in daily emergency practice. To prevent patients from intentional overdose, to know epidemiology and predisposing factors are all important. The most top three kinds of substance overdose are benzodiazepine (42.9%), mixed medications (32.1%) and acetaminophen (6.1%). In our study, 11.2% of overdose cases need hospitalization and 2% were admitted to intensive care unit. The length of stay is 2 ± 4.1 days. Physicians should notify the centers of suicide prevention to pay concern about who are middle-aged male, facing conflicts, especially in the spring.

Declarations

- **Ethics approval and consent to participate**

This study was approved by the Institutional Review Board of Mackay Memorial Hospital (19MMHIS288e).

- **Consent for publication**

Sheng-Teck Tan, Chih-Hung Lo, Chen-Hao Liao, Yu-Jang Su, all agree with publication.

• Availability of data and materials

Availability of data and materials by personal request is permeable.

• Competing interests

There is no competing interests.

• Funding

There is no finding in the article.

• Authors' contributions

Writing: Sheng-Teck Tan, Chih-Hung Lo, Chen-Hao Liao, Yu-Jang Su

Study design: Yu-Jang Su

Data collection: Sheng-Teck Tan, Chih-Hung Lo, Chen-Hao Liao, Yu-Jang Su

Statistical analysis: Yu-Jang Su

Revised and corresponded: Yu-Jang Su

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Tables

Non-intentional overdose cases	n (%)
Patient declared to deny overdose	27 (26.2)
Mis-swallowing	25 (24.3)
Cyproheptadine 3	
Mixed drug # 2	
Ibuprofen 2	
Fluoric 2	
Acetaminophen 2	
Warfarin 1	
Zolpidem 1	
Pyrethrin 1	
Pentoxifylline 1	
Nail Polish Remover 1	
Motilium 1	
Isoamyl acetate 1	
Detergent 1	
Decongestant 1	
Cetirizine 1	
Carvedilol 1	
Benzodiazepine 1	
Atenolol 1	
Amorolfine 1	
Against advised discharge	15 (14.6)
Adverse Drug Reaction	13 (12.6)
Benzodiazepine 6	
Oral hypoglycemic agent 2	
Digoxin 1	
Non-vitamin K oral anticoagulant 1	
Hypotensive 1	
Imipramine 1	
Cold tablet 1	
Data unclear or not available	9 (8.7)
Illicit drug abuser	8 (7.8)
Repeated record	4 (3.8)
Transfer from other hospital/ clinics	2 (2)
Total	103 (100)

one is Amlodipine 5mg, Valsartan 160mg, Imipramine 25mg, another is cold tablets.

Table. 1 List of 103 non-intentional overdose cases were excluded from our study.

Intentional overdose	all	Male	Female	P value, 2-tailed
n (%)	196 (100)	49 (25)	147 (75)	
Age (years old)	39.2±18.3	45.3±19.5	37.2±17.5	0.009*
Times of overdose	1.2±0.7	1.1±0.3	1.2±0.8	0.339
Seasons (n, %)				0.000*
Spring	63 (32.1)	28 (57.1)	35 (23.8)	
Summer	43 (21.9)	5 (10.2)	38 (25.9)	
Autumn	45 (23.0)	6 (12.2)	39 (26.5)	
Winter	45 (23.0)	10 (20.5)	35 (23.8)	
Arrival time				0.127
Day	55 (28.1)	16 (32.7)	39 (26.5)	
Evening	78 (39.8)	23 (46.9)	55 (37.4)	
Night	63 (32.1)	10 (20.4)	53 (36.5)	
History of Ever overdose	63 (32.1)	13 (26.5)	50 (34)	0.331
<i>Marriage status</i>				
Single	117 (59.2)	27 (55.1)	90 (61.2)	0.507
Marriage	60 (30.6)	19 (38.8)	41 (27.9)	0.157
Divorced	19 (9.7)	3 (6.1)	16 (10.9)	0.329
Alcohol-drinking				
Body temperature (Celsius)	36.6±0.6	36.5±0.5	36.7±0.6	0.026*
Heart rate (beats per minute)	88.9±19.9	89.1±16.9	88.9±20.9	0.583
Systolic blood pressure (mmHg)	116.9±21.2	123.1±20.1	114.9±21.3	0.014*
Diastolic blood pressure (mmHg)	68.7±14.4	75.1±15.6	66.6±13.4	0.001*
Glasgow coma scale	12.9±3.6	13.1±3.4	12.8±3.7	0.676
Hypertension	21 (10.7)	6 (12.2)	15 (10.2)	0.689
Diabetes mellitus	14 (7.1)	5 (10.2)	9 (6.1)	0.337
uremia	3 (1.5)	1 (2)	2 (1.4)	0.737
Depression	96 (50)	23 (46.9)	73 (49.7)	0.741
Personality disorder	75 (38.3)	23 (46.9)	52 (35.4)	0.149
Bipolar affective disorder	25 (12.8)	4 (8.2)	21 (14.3)	0.266
Schizophrenia	10 (5.1)	1 (2)	9 (6.1)	0.261
Argue with Family members	62 (31.6)	17 (34.7)	45 (30.6)	0.595
Argue with Father	10 (5.1)	4 (8.2)	6 (4.1)	0.261
Argue with Mother	13 (6.6)	1 (2.0)	12 (8.2)	0.136
Argue with Friends	43 (21.9)	8 (16.3)	35 (23.8)	0.273
Argue with Boy Friends	4 (2.0)	0 (0)	4 (2.7)	0.243
Argue with Girl Friends	3 (1.5)	3 (6.1)	0 (0)	0.003*
Conflict with Company	10 (5.1)	4 (8.2)	6 (4.1)	0.454
Suffering from insomnia	79 (40.3)	20 (40.8)	59 (40.1)	0.933
Hospitalization to ward	22 (11.2)	4 (8.2)	18 (12.2)	0.433
Intensive care unit admission	4 (2)	1 (2)	3 (2)	1.000
Length of stay (days).	2.0±4.1	2.1±4.2	2.0±4.1	0.183

Table. 2 Gender difference in 196 cases of intentional overdose from January 2018 to August 2019. * indicates reaching statistical difference ($p < .05$).

Substance of overdose n, (%)	All 196, (100)	Male 49 (25)	Female 147 (75)
Benzodiazepine	62 (31.6)	20 (41.0)	42 (28.5)
Flunitrazepam	10 (5.1)	3 (6.2)	7 (4.7)
Estazolam	7 (3.6)	2 (4)	5 (3.4)
Alprazolam	4 (2.1)	1 (2)	3 (2)
Lorazepam	3 (1.6)	2 (4)	1 (0.7)
Bromazepam	1 (0.5)	0 (0)	1 (0.7)
Clonazepam	1 (0.5)	1 (2)	0 (0)
Mixed medications	63 (32.1)	9 (18.8)	54 (36.6)
Acetaminophen	12 (6.1)	0 (0)	12 (8.2)
Non-benzodiazepine hypnotics	6 (3.1)	2 (4)	4 (2.7)
Zolpidem	5 (2.6)	0 (0)	5 (3.4)
Stilnox	4 (2.1)	2 (4)	2 (1.4)
Anti-depressants	2 (1)	0 (0)	2 (1.4)
Diphenhydramine	2 (1)	0 (0)	2 (1.4)
Amphetamine	2 (1)	2 (4)	0 (0)
Baclofen	1 (0.5)	0 (0)	1 (0.7)
Bromadiolone	1 (0.5)	0 (0)	1 (0.7)
Bupropion	1 (0.5)	0 (0)	1 (0.7)
Gasoline	1 (0.5)	1 (2)	0 (0)
Humalog Mix (Insulin)	1 (0.5)	1 (2)	0 (0)
Iron	1 (0.5)	1 (2)	0 (0)
Ketamine	1 (0.5)	0 (0)	1 (0.7)
Norvasc	1 (0.5)	0 (0)	1 (0.7)
Quetiapine (Anti-psychotics)	1 (0.5)	1 (2)	0 (0)
Sertraline	1 (0.5)	0 (0)	1 (0.7)
Valsartan	1 (0.5)	0 (0)	1 (0.7)
Zolpiclone	1 (0.5)	1 (2)	0 (0)
Total	196	49	147

Table. 3 Substance of intentional overdose. Chi-squared test in gender to substance overdose analysis reaches a p value of 0.004<.05