Original Article

JHSMR Journal of Health Science and Medical Research

Delirium Tremens in Psychiatric Ward at Songklanagarind Hospital

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Received 25 December 2017 ● Accepted 16 May 2018 ● Published online 20 August 2018

Abstract:

Objectives: To examine the epidemiology of delirium tremens patients in the psychiatric ward at Songklanagarind Hospital and to find factors associated with the disease.

Material and Methods: This was a cross-sectional study that collected data from alcohol dependent patients who were admitted in the psychiatric ward at Songklanagarind Hospital between January 2011 and December 2014. Descriptive statistics were used to analyze the data and logistic regression analysis used to analyze factors associated with the disease.

Results: The prevalence of delirium tremens in psychiatric ward was 28.0%. The study found that body temperature >37.8 °C (p-value=0.026), eosinophils >6.0% (p-value=0.046), hematocrit <40.0% (p-value<0.001), red blood cells <4.5x106/ul (p-value<0.001), MCV <83 or >97 g/dl (p-value<0.001), MCH <27 or >33 pg (p-value<0.001), platelets <150x10^3/ul (p-value<0.001), magnesium <16 mg/dl (p-value=0.043), zinc <0.7 mg/dl) (p-value=0.029), total bilirubin >1 mg/dl (p-value= 0.039) and direct bilirubin >0.2 mg/dl (p-value=0.036) were significant factors correlated with delirium tremens. Multiple logistic regression models found that only red blood cell count <4.5x10^6/ul (p-value<0.001) was a significant factor correlated with delirium tremens.

Conclusions: The prevalence of delirium tremens in this study was lower than in other Asian countries. Red blood cell count <4.5x10^6/ul (p-value<0.001) was correlated with delirium tremens.

Keywords: alcohol, delirium tremens, red blood cell, withdrawal syndrome

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J Health Sci Med Res 2018;36(3):205-214
DOI: http://dx.doi.org/10.31584/jhsmr.2018.36.3.17
www.jhsmr.org

Introduction

When an alcohol-dependent patient abruptly stops or decreases their alcohol consumption. Delirium tremens is cause by severe alcohol withdrawal symptoms that occurs 72-96 hours after the last drink.[1] The prevalence[2,7,8,10] of delirium tremens in alcohol dependence patients is 5-56 and these patients have an increased morbidity and mortality rate of 5.0-15.0%. In Thailand, the prevalence of delirium tremens in alcohol-dependent patients is 50.0-75.0%,[3,4] which is higher than in studies from other countries.

Ways have been found through which the physician can prevent severe withdrawal symptoms such as alcohol withdrawal seizure and delirium tremens.[5] A recent meta-analysis found that benzodiazepines showed a protective benefit against alcohol withdrawal symptoms, in particular seizures, when compared to placebo and other drugs.[6]

Many factors have been identified as increasing the risk for delirium tremens, including the number of days the patient has gone without alcohol, comorbid medical conditions or injury,[7] high blood urea nitrogen (BUN) and respiratory rate at the admission day, low albumin and systolic blood pressure,[8] history of delirium tremens,[9] pulse rate >100 bpm,[10] low platelet level,[11-13] low potassium level,[12,14] low zinc level,[15] and body temperature >38 °C.[16]

If the physician is aware of the predictive factors for delirium tremens, they can reduce the risk of this condition through various means, such as an alcohol detoxification regimen that can decrease mortality and morbidity in alcohol withdrawal patients.[1,4,5,7]

Objective

To find the prevalence and correlated factors of delirium tremens among alcohol-dependent patients in the Psychiatric Ward at Songklanagarind Hospital.

Material and Methods

This study was approved by the Faculty of Medicine, Prince of Songkhla University Ethics Committee in November 2014 (EC 57-258-03-4)

Population

Inclusion criteria

All 18-65 year-old patients diagnosed with alcohol dependence or delirium tremens by DSM-IV-TR and admitted to the Psychiatric Ward of Songklanagarind Hospital between January 2010 and December 2013.

Exclusion criteria

Patients diagnosed with alcohol-induced psychosis or alcohol-induced mood disorder or delirium from other causes such as hepatic encephalopathy, or with a history of other substance use disorders (except for nicotine) or severe head injury.

Study type: cross-sectional study

Tool

Questionnaire

1. General information: age, sex, occupation, education, religion, history of medical illnesses, history of psychiatric illnesses

2. Alcohol consumption data: type of alcohol, date stopped drinking, date of delirium tremens episode(s), history of delirium tremens, history of alcohol withdrawal seizures

3. Clinical data on date of admission: vital signs, complete blood count (CBC), liver function tests, serum electrolytes, calcium, magnesium, phosphate, zinc levels

Data collection

Researcher collected retrospective data from Songklanagarind Hospital's computer medical records in the Hospital Information System

Data analysis

This was a descriptive study. The data are presented percent, mean, standard deviation and used logistic regression analysis to find correlations between the factors and delirium tremens.

Results

1. Demographic data

The sample was 125 alcohol-dependent patients with a total of 190 addmission to the Psychiatric Inpatient Ward during the study period. Most were male (99.2%) and of the Thai nationality (97.6%). The mean age was 50.86±8.57 (range 28-65) years. Twenty-eight patients (22.4%) had a history of medical and/or psychiatric illness (Table 1).

One hundred and thirty-nine admissions (73.2%) from total of admitted times had been consuming liquor immediately before admission. One hundred and three admissions (54.2%) had a previous history of admission to a psychiatric ward for alcohol dependence, 40 admissions (21.1%) had a history of alcohol withdrawal seizure and 29 admissions (15.3%) had a history of delirium tremens.

Fifty-four patients (28.4%) were suffering from active delirium tremens at admission, and 41 patients (21.6%) from alcohol withdrawal seizure. The mean time the patients had not been drinking before admission was 1.02±1.63 days. The mean time to developing delirium tremens was 3.12±1.59 days (Table 2).

Table 1 Demographic data (n=125)

Demographic data	Number (%)
Age (years)	
Mean±S.D. (min-max)	50.86±8.57 (28-65)
Sex	
Male	122 (97.6)
Female	3 (2.4)
Marital status	
Single	14 (11.2)
Married	96 (76.8)
Divorced	15 (12.0)
Nationality	
Thai	124 (99.2)
Other	1 (0.8)
Religion	
Buddhist	121 (96.8)
Christian	1 (0.8)
Islam	3 (2.4)
Occupation	
None	18 (14.4)
Government officer	38 (30.4)
State enterprise employee	4 (3.2)
Employee	2 (1.6)
Farmer	23 (18.4)
Grocer	10 (8.0)
General laborer	23 (18.4)
Retired	7 (5.6)
Comorbid illness	
Medical and psychiatric illness	28 (22.4)
Psychiatric illness	12 (9.6)
Medical illness	58 (46.4)
None	27 (21.6)

S.D.=standard deviation

Table 2 Alcohol consumption data (n=190)

	Number (%)
Type	
Liquor	139 (73.2)
Spirits	26 (13.7)
Home-made liquor	23 (12.1)
Herbal liquor	17 (9.0)
Beer	56 (29.5)
Other	2 (1.0)
History of previous admission	
No	87 (45.8)
Yes	103 (54.2)
History of alcohol withdrawal seizure	
No	150 (78.9)
Yes	40 (21.1)
History of delirium tremens	
No	161 (84.7)
Yes	29 (15.3)
Delirium tremens	
No	136 (71.6)
Yes	54 (28.4)
Alcohol withdrawal seizure	
No	149 (78.4)
Yes	41 (21.6)
The number of days the patient has gone without alcohol (n=189)	
Mean±S.D. (min-max)	1.02±1.63 (0-14)
Median (IQR)	1 (0-1)
Time to delirium tremens (n=54)	
Mean±S.D. (min-max)	3.12±1.59 (0-8)

S.D.=standard deviation, IQR=interquartile range

The mean body temperature on admission was 36.97±0.49 °C, mean pulse rate 81.19±14.81 bpm, respiratory rate 21.77±1.93 bpm, mean systolic blood pressure 140.80±23.64 mmHg and mean diastolic blood pressure 84.89±13.58 mmHg. The mean white blood cell count (WBC) was $7.74x10^3$±8.18 /ul, mean red blood cell count (RBC) $4.34x10^6$+0.71/ul, mean platelet count $177x10^3$± 76.34/ul, mean serum potassium level 3.65±0.61 mmol/l, mean serum zinc level 0.59±0.16 g/dl and mean serum albumin level 4.31±0.45 g/dl (Table 3).

2. Factors associated to delirium tremens

During the study period, there were 190 admission of alcohol-dependent, whose data were patient used to calculate factors associated with delirium tremens. The variables which had a p-value from the univariate exploration lower than 0.2 were included as candidate variables (except for eosinophils and mean corpuscular hemoglobin (MCH) because of small sample size). The analysis indicated that body temperature >37.8 °C (p-value=0.026), eosinophil >6.0% (p-value=0.046), hematocrit <40.0% (p-value<0.001), red blood cell count <4.5x106/ul (p-value<0.001), MCV <83 or >97 g/dl (p-value<0.001), MCH <27 or >33 pg (p-value<0.001), platelet count $<150x10^3$/ul (p-value<0.001), magnesium <16 mg/dl (p-value=0.043), zinc <0.7 mg/dl) (p-value= 0.029), total bilirubin >1 mg/dl (p-value=0.039) and direct bilirubin >0.2 mg/dl (p-value=0.036) were all significantly correlated with delirium tremens (Table 4).

The associated factors were analyzed by multiple logistic regression using a backward-stepwise method, which indicated that only red blood cell count <4.5x106/uL (p-value<0.001) was significantly associated with delirium tremens (Table 5).

Table 3 Vital signs and laboratory data at the first admission (n=190)

Data	Mean±S.D.	Max–min
Vital signs		
Body temperature (°C)	37.0±0.5	36.0–39.0
Pulse rate (/min)	87.2±14.8	53.0–127.0
Respiratory rate (/min)	21.8±1.9	18.0–28.0
Systolic blood pressure (mmHg)	140.8±23.6	85.0–223.0
Diastolic blood pressure (mmHg)	84.9±13.6	50.0–126.0
CBC		
White blood cells ($x10^3$/ul)	7.7±8.2	1.9–86.7
Neutrophils (%)	61.5±15.6	6.6–98.6
Lymphocytes (%)	27.3±13.8	0.4–93.0
Eosinophils (%)	3.3±3.3	0.1–18.5
Hemoglobin (g/dl)	13.7±1.8	8.5–18.4
Hematocrit (%)	40.1±5.3	24.7–52.8
Red blood cells ($x10^6$/ul)	4.3±0.7	2.3–6.0
MCV (g/dl)	92.6±8.9	34.0–114.0
MCH (pg)	31.8±3.0	19.9–43.7
MCHC (g/dl)	34.2±1.1	30.1–38.1
RDW (%)	14.4±1.8	11.4–21.5
Platelets ($x10^3$/ul)	177.5±76.3	30.0–356.0
Electrolytes		
Sodium (mmol/l)	139.3±4.3	124.5–148.3
Potassium (mmol/l)	3.7±0.6	0.8–6.0
TCO_2 (mmol/l)	23.2±3.9	1.7–36.2
Magnesium (mg/dl)	14.5±3.4	7.8–26.7
Zinc (mg/dl)	0.6±0.2	0.3–1.3
Liver function test		
Total bilirubin (mg/dl)	1.0±0.9	0.2–5.5
Direct bilirubin (mg/dl)	0.5±0.6	0.0–3.6
SGOT (u/l)	129.4±117.4	14.0–834.0
SGPT (u/l)	57.1±47.3	6.0–361.0
ALP (u/l)	99.6±47.4	43.0–286.0
Total protein (g/dl)	7.4±0.7	4.9–9.0
Albumin (g/dl)	4.3±0.5	2.9–5.2

CBC=complete blood count, MCV=mean corpuscular volume, MCH=mean corpuscular hemoglobin, MCHC=mean corpuscular hemoglobin concentration, RDW=red blood cell distribution width, TCO_2=total carbon dioxide, SGOT=serum glutamic oxaloacetic transaminase, SGPT=serum glutamic pyruvate transferase, ALP=alkaline phosphatase

Table 4 Crude association between vital signs and laboratory data and delirium tremens (the result from univariate analysis)

Data	Delirium tremens Number (%)		Chi-square P-value
	Yes (n=54)	No (n=136)	
Body temperature (°C)			
>37.8	8 (14.8)	6 (4.4)	0.026[a]
≤37.8	46 (85.2)	130 (95.6)	
CBC			
Neutrophils (%)			
>70	19 (35.2)	37 (27.4)	0.14
40-70	34 (63.0)	85 (63.0)	
<40	1 (1.9)	13 (9.6)	
Lymphocytes (%)			
Others	23 (42.6)	41 (30.4)	0.152
20-50	31 (57.4)	94 (69.6)	
Eosinophils (%)			
>6	1 (2.4)	17 (15.9)	0.046
0-6	41 (97.6)	90 (84.1)	
Hemoglobin (g/dl)			
<13	22 (40.7)	37 (27.4)	0.107
13-18	32 (59.3)	98 (72.6)	
Hematocrit (%)			
<40	38 (70.4)	50 (37.0)	<0.001
40-54	16 (29.6)	85 (63.0)	
Red blood cells (/ul)			
$<4.5x10^6$	48 (88.9)	62 (45.9)	<0.001
$4.5-6.3x10^6$	6 (11.1)	73 (54.1)	
MCV (g/dl)			
<83	1 (1.9)	14 (10.4)	<0.001
83-97	25 (46.3)	95 (70.4)	
>97	28 (51.9)	26 (19.3)	
MCH (pg)			
<27	1 (1.9)	4 (3.0)	<0.001[a]
27-33	24 (44.4)	101 (74.8)	
>33	29 (53.7)	30 (22.2)	
Platelets (/ul)			
$<150x10^3$	32 (60.4)	41 (31.3)	<0.001
$150-450x10^3$	21 (39.6)	90 (68.7)	

Table 4 (continued)

Data	Delirium tremens Number (%)		Chi-square P-value
	Yes (n=54)	No (n=136)	
Electrolytes			
Sodium (mmol/l)			
<136	16 (30.2)	25 (18.7)	0.128
136-146	37 (69.8)	109 (81.3)	
Magnesium (mg/dl)			
<16	43 (84.3)	87 (68.0)	0.043
16-26	8 (15.7)	41 (32.0)	
Zinc (mg/dl)			
<0.7	43 (89.6)	90 (72.6)	0.029
0.7-1.5	5 (10.4)	34 (27.4)	
Liver function test			
Total bilirubin (mg/dl)			
>1	26 (51.0)	43 (33.1)	0.039
0.2-1	25 (49.0)	87 (66.9)	
Direct bilirubin (mg/dl)			
>0.2	44 (86.3)	90 (69.8)	0.036
0-0.2	7 (13.7)	39 (30.2)	
SGOT (u/l)			
>37	47 (90.4)	107 (81.1)	0.187
0-37	5 (9.6)	25 (18.9)	
Albumin (g/dl)			
<4.2	21 (40.4)	34 (25.8)	0.076
4.2-5.3	31 (59.6)	98 (74.2)	

[a]p-value from Fisher's exact test

CBC=complete blood count, MCV=mean corpuscular volume, MCH=mean corpuscular hemoglobin, MCHC=mean corpuscular hemoglobin concentration, RDW=red blood cell distribution width, TCO_2=total carbon dioxide, SGOT=serum glutamic oxaloacetic transaminase, ALP=alkaline phosphatase

Table 5 Factors associated with delirium tremens by multiple logistic regression (n=161)

Factors	Delirium tremens		P-value LR-test
	Crude OR (95% CI)	Adjusted OR (95% CI)	
Red blood cells			
4.5-6.3x10^6/ul	1	1	<0.001
<4.5x10^6/ul	30.2 (6.97-130.71)	23.9 (5.43-105.83)	
Platelets			
150-450x10^3/ul	1	1	
<150x10^3/ul	4.04 (1.95-8.37)	2.07 (0.92-4.69)	0.078

OR=odds ratio, CI=confidence interval, LR=likelihood ratio

Discussion

The prevalence of delirium tremens in this study was 28.0% of all alcohol dependence patient, although when compared to other studies this was lower than in other Asian countries such as India[2] (2013 42.0%) and Korea (2003 42.0%).[10] But the prevalence was higher than in European countries, such as Sweden[8] (2008 3.0%) and Germany[11] (2011 6.0%). The cause of these differences in prevalence of delirium tremens between this study and other studies may be from different genetics and cultures between Thai and European countries, and the different regimens of treatment between Songklanagarind Hospital and other countries that use a fixed dose and symptom-triggered benzodiazepine regimen together to prevent delirium tremens.

Other studies found the risk factors of delirium tremens to be number of days the patients has gone without alcohol, comorbid medical conditions or injury,[8] high BUN and respiratory rate, low albumin and systolic blood pressure,[7] history of delirium tremens,[10] pulse rate>100 bpm,[10] low platelet level,[11-13] low potassium level,[12,14] low zinc level,[15] and body temperature >38 °C.[16] The present study probably did not find these risk factors because some patients in this study were admitted on the day that the delirium tremens occurred.

Many studies found a low platelet level[11-13] to be a risk factor for delirium tremens. A meta-analysis from Sweden in 2009 found that a lower initial platelet count was predictive of an occurrence of delirium tremens.[17] Another study from India found that the platelet counts at baseline and all 4 days of collection were significantly lower in their delirium tremens group than the no delirium tremens group. Platelet counts increased gradually from baseline until the 10th day of alcohol withdrawal.[18] In this study, we didn't find a correlation between low platelet level and delirium tremens, perhaps because of our smaller sample size than these other studies.

It is known that there are RBC changes in heavy drinkers. A previous study found that RBC exposed to ethanol exhibited cell abnormalities[19] and altered morphology with decreased resistance to osmotic hemolysis.[20] This study found that low RBC counts were correlated with delirium

tremens. Although it is not clear how a low RBC count correlates with delirium tremens, it may be related to the chronic alcohol use of patients in the delirium tremens group causing RBC abnormalities and decreased RBC count.

The strength of this study was that we had complete data on all patients because of our hospital's Hospital Information System medical records.

There were some limitations of this study. First, this was cross-sectional study and we could not analyze causation. A prospective cohort study should be done to explore this factor. Second, the sample from this study was from the psychiatric Ward of Songklanagarind Hospital, which is a tertiary and referral hospital serving all of southern Thailand, thus the result cannot be generalized to other populations. So alcohol dependent patients from other wards should be included in further studies.

Conclusion

The prevalence of delirium tremens in this study was lower than the prevalence from other Asian countries. A red blood cell count <4.5x106/ul (p-value<0.001) was correlated with delirium tremens, which was different from many previous studies that found a low platelet count was a correlated factor. Based on this finding, it would be useful for the physician to assess their patient's CBC to reduce the risk of morbidity and mortality from delirium tremens by providing an adequate dose of benzodiazepine where indicated.

Acknowledgements

The authors wish to thank the following for substantial help with this project, Mrs. Nisan Werachattawan, Mrs. Areena Aubdullous, Ms. Kreuwan Jongborvornwiwat.

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