



อัตราการตายของภาวะขาดสุราหลังจาก ใช้แนวทางการรักษาของโรงพยาบาล ศรีนครินทร์

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บทคัดย่อ

วัตถุประสงค์ เพื่อศึกษาอัตราการตายจากภาวะขาดสุราและภาวะแทรกซ้อนที่สำคัญหลังจากใช้แนวทางการรักษาภาวะขาดสุราของโรงพยาบาลศรีนครินทร์ มหาวิทยาลัยขอนแก่น

วิธีการศึกษา ศึกษาแบบ prospective descriptive study ในกลุ่ม ผู้ป่วยอายุ 18-65 ปี ที่ได้รับการวินิจฉัยตามเกณฑ์ DSM IV-TR ว่ามีภาวะขาดสุราและเข้ารับการรักษานในหอผู้ป่วยจิตเวช ระหว่างวันที่ 18 พ.ค. 2556 ถึง 31 พ.ค. 2557 โดยได้รับการรักษาตามแนวทางการรักษาภาวะขาดสุราของโรงพยาบาลศรีนครินทร์ สถิติวิจัยใช้ร้อยละ ค่าเฉลี่ย ค่าเบี่ยงเบนมาตรฐาน และ survival analysis

ผลการศึกษา จากกลุ่มตัวอย่าง 43 ราย มี 35 รายที่ CIWA-Ar เพิ่ม 8 คะแนนขึ้นไป และมีเพียง 8 รายที่ CIWA-Ar น้อยกว่า 8 คะแนนตลอดการรักษา ผู้ป่วยเกือบทั้งหมดได้รับยา diazepam หรือ lorazepam รูปแบบ front-loading regimen พบอัตราการตายจากภาวะขาดสุราโดย CIWA-Ar ลดลงน้อยกว่า 8 คะแนน ติดต่อกัน 24 ชั่วโมงภายใน 3, 4 และ 5 วัน เป็นร้อยละ 82.9, 91.4 และ 100 ตามลำดับ จาก survival analysis พบว่าจำนวนผู้ป่วยร้อยละ 50 หายจากภาวะขาดสุราเมื่อเข้าสู่วันที่ 3 และทั้งหมดหายจากภาวะขาดสุราในวันที่ 5 ไม่พบภาวะแทรกซ้อนที่สำคัญ และไม่มีการเสียชีวิตตลอดการรักษา

สรุป แนวทางการรักษาภาวะขาดสุราของโรงพยาบาลศรีนครินทร์มีประสิทธิภาพในการรักษาตามสมมติฐาน กล่าวคือภาวะขาดสุราหายเร็วไม่เกิน 5 วัน และไม่พบภาวะแทรกซ้อนที่สำคัญ

คำสำคัญ อัตราการตาย ถอนแอลกอฮอล์ ขาดแอลกอฮอล์ แนวทาง การรักษา

วารสารสมาคมจิตแพทย์แห่งประเทศไทย 2558; 60(2): 139-148

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Remission rate of Alcohol Withdrawal Syndrome using the Srinagarind Hospital Clinical Practice Guideline

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ABSTRACT

Objective : To study the clinical outcomes of alcohol withdrawal syndrome in terms of the remission rate and major complications using the Srinagarind Hospital Clinical Practice Guideline.

Methods : This was a prospective descriptive study of patients between 18 and 65, diagnosed with alcohol withdrawal, alcohol withdrawal seizure or alcohol withdrawal delirium as per the DSM-IV-TR, hospitalized at the psychiatric unit between May 18, 2013, and May 31, 2014. All patients were treated according to the Srinagarind Hospital Clinical Practice Guideline. The data were analyzed using percentage, mean, standard deviation and survival analysis.

Results : The 43 patients were included in this study, 35 had CIWA-Ar scores of ≥ 8 and only 8 had a CIWA-Ar score < 8 throughout the hospitalization. The respective remission rate (CIWA-Ar score < 8) by day 3, 4 and 5 of treatment was 82.9%, 91.4% and 100%. The median time to remit from alcohol withdrawal syndrome was on the 3rd day of treatment. There were no major complications or mortality.

Conclusion : The Srinagarind Hospital Clinical Practice Guideline is effective for treatment of alcohol withdrawal syndrome as alcohol withdrawal symptoms were relieved rapidly within 5 days of therapy without major complications or mortality.

Keywords : remission, alcohol withdrawal, treatment

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Introduction

In 2005, the WHO declared that excessive alcohol consumption was one of the most common substance abuse problems worldwide¹ as 2.5 million people died because of alcohol-related causes². One-third of the Thai population uses alcohol³. Since chronic heavy drinking results in alcohol dependence, decreasing consumption causes symptoms of withdrawal with potential for major morbidity (including delirium) and mortality⁴.

Pongtanya et al. studied pharmacotherapy among alcohol withdrawal inpatients and found that among 96.9% of alcohol dependent patients, 16.1% had severe withdrawal symptoms⁵. They also reported that 93.8% of clinical symptoms improved within 7 days of therapy⁵. Although there have been a few studies about remission rates after alcohol withdrawal treatment, there have been no studies of complications (including morbidity and mortality) after treatment, in Thailand.

In 2000, Srinagarind Hospital, Khon Kaen University developed a culturally and contextually relevant practice guideline (CPG) for alcohol withdrawal syndrome because of the wide variety of treatment and treatment outcome. In the first version, the guideline used CIWA-Ar to assess the severity of alcohol withdrawal state and give fixed dose regimen to patients in the mild and moderate groups and give front-loading regimen to patients in the severe group. In the second version, the problem of inter-rater inconsistency were solved by the training of nursing staffs. We can reduced the average length of stay in the hospital from

3 weeks to 2 weeks, but the patients with alcohol withdrawal delirium still have prolonged admission. In the third revision, the risk factors of alcohol withdrawal delirium were taken into account, patients who had at least one risk factor would received the front loading regimen. There were minor revision in fourth and fifth revision as changes of clinical indicator from length of stay in the hospital to the duration of the withdrawal syndrome and more flexible about the choice of benzodiazepine. The latest version, the fifth revision, determined the major factors influencing the severity of symptoms and their management.

The main difference from other CPGs is that patients with at least one risk factor for complicated withdrawal symptoms (having history of delirium tremens, severe withdrawal symptoms, drink all day and nights for more than 5 years, fever > 39 degree celsius, having serious medical illness or older than 60 years old) would get front-loading regimens, whether or not they had a low CIWA-Ar score⁶.

Patients with no risk factors were divided into 4 groups according to their CIWA-Ar score. Those with (1) mild symptoms having a CIWA-Ar score < 8 got symptom-triggered regimen; (2) moderate symptoms having a CIWA-Ar score between 8-14 got the standard oral fixed-dose regimen; (3) severe symptoms having a CIWA-Ar score between 15-19 got the oral front-loading regimen; and, (4) very severe symptoms having a CIWA-Ar score \geq 20 got the intravenous front-loading

regimen. The drug of choice was diazepam. Lorazepam was used for those with liver impairment.

In the current study, the authors aimed to evaluate the clinical outcomes of alcohol withdrawal syndrome using the CPG. The results will be of use for other hospitals implementing this CPG.

Objective

To study the clinical outcomes of alcohol withdrawal syndrome using the Srinagarind Hospital Clinical Practice Guideline in terms of the remission rate and major complications.

Methods

A prospective descriptive study was conducted for patients admitted to the psychiatric ward between May 18, 2013 and May 31, 2014. The study included patients between 18 and 65, diagnosed with alcohol withdrawal, alcohol withdrawal seizure, or alcohol withdrawal delirium as per the DSM IV-TR criteria. The study excluded those who could not follow the CPG. The remission of alcohol withdrawal syndrome was measured using (a) the CIWA-Ar questionnaire, and (b) remission means decreasing below a score of 8 for a full 24 hours within 3-7 days after a score ≥ 8 . The nurses who assess the CIWA-Ar were blinded about the group of the patients and were not in the statistical analysis team. Major complications of alcohol withdrawal syndrome included aspiration pneumonia and other morbidities or death. The primary outcome is remission rate, the

secondary outcome is major complication of alcohol withdrawal syndrome and the factors related to remission.

The sample size was calculated from the previous remission rate of alcohol withdrawal syndrome of 0.9⁵ with a 95% confidence interval and acceptable error of 9%. According to the formula, $= \frac{(Z_{\alpha/2})^2 p(1-p)}{d^2}$, the sample size should be 43.

The Ethics Committee For Human Research, Khon Kaen University approved the study (HE561091).

Statistical analysis

STATA 5.0 was used to do the statistical analyses. The demographic data were analyzed for percentages, means, standard deviations and ranges. Survival analysis, 95% confidence interval and hazard ratio were used to analyze the relationship between the number of treated days and the remission from alcohol withdrawal syndrome.

Results

During the study period, 53 patients between 18 and 65 were admitted to the psychiatric ward diagnosed with alcohol withdrawal, alcohol withdrawal seizure or alcohol withdrawal delirium, as per the DSM IV-TR criteria. Eight patients could not follow the CPG. One case was discharged from the program and another was diagnosed with delirium due to multiple etiologies. Ultimately, a total of 43 patients were included in the study.

Demographic data

There were 41 males (95.3%) and 2 females (4.7%) with a mean age of 42.7 (SD 8.6; range, 23-65). The mean duration of alcohol dependence was 16.1 (SD=8.3) years. Most of the patients

(79.1%) had alcohol dependence for > 5 years.

The bimodal duration of alcohol dependence was 10-20 and 20-30 years (39.5% of patients for each duration). The demographic data are presented in Table 1.

Table 1 Demographic data

Demographic data	Percentage
Sex	
Male	95.3
Female	4.7
Marital status	
Married	58.1
Single	41.9
Occupation	
Unemployed	16.3
Student	2.3
Wage earner	25.6
Farmer	4.6
Business owner	23.3
Civil servant	27.9
Educational level	
Grade school (1-12)	67.5
Associate degree	9.3
Bachelor degree	20.9
Master degree	2.3
Income	
None	18.6
Below 9,000 baht	37.2
9,000-14,999 baht	9.3
15,000-29,999 baht	27.9
30,000 baht or more	7.0
Underlying disease	
Physical illness	55.8
Psychiatric illness	9.3
Both physical and psychiatric illnesses	2.3
History of alcohol withdrawal seizure	46.5
History of alcohol withdrawal delirium	58.1

Remission rate and major complications of alcohol withdrawal syndrome

The 43 patients were divided into 3 respective groups according to symptom severity. Group 1, 2 and 3 comprised 33 (76.7%), 2 (4.7%) and 8 (18.6%) patients with severe to very severe (CIWA-Ar ≥ 15), moderate (CIWA-Ar between 8-14) and mild (CIWA-Ar < 8) symptoms. Group 1 received diazepam or lorazepam with front-loading regimens. Group 2 had 1 case with risk factors for alcohol withdrawal delirium who received front-loading regimen and 1 without who received the standard oral fixed-dose regimen. Group 3 had 7 cases with risk factors who received front-loading

while the 1 other had no the risk factor and received a symptom-triggered regimen. Most of the cases (41 in 43) received a front-loading regimen.

According to the survival analysis of the 35 cases that had a CIWA-Ar score of > 8 , the median time for remission was at day 3 of treatment and the respective remission rate (CIWA-Ar score < 8) by day 3, 4 and 5 of treatment was 82.9%, 91.4% and 100%. Figure 1 shows the Kaplan-Meier survival estimate of the remission rate for alcohol withdrawal syndrome and there were neither (a) any significant factors associated with remission (Table 2) nor (b) any major complications or mortality throughout the hospitalization.

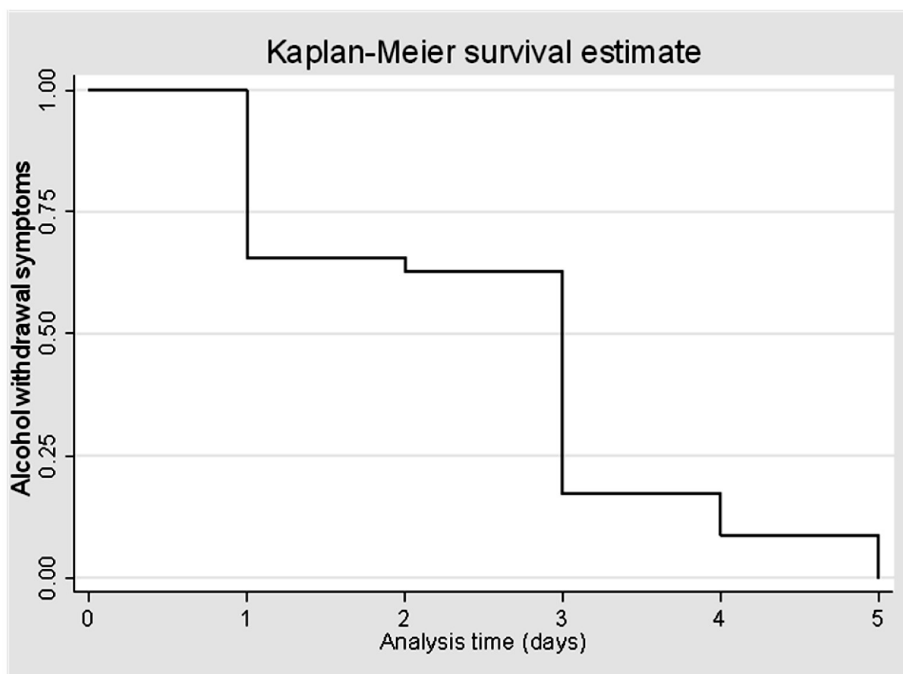


Figure 1 Kaplan-Meier survival estimate of remission rate for alcohol withdrawal syndrome

Table 2 Factors associated with remission rate

Factors	Hazard ratio	95%CI	P-value
Age			
<43 years	1		
≥43 years	0.990	0.95-1.03	0.63
Duration of alcohol dependence			
<16 years	1		
≥16 years	0.999	0.96-1.04	0.98
History of alcohol withdrawal seizure			
None	1		
Presence	1.013	0.52-1.98	0.97
History of alcohol withdrawal delirium			
None	1		
Presence	1.001	0.50-1.99	1.00
Both physical and psychiatric illnesses			
No	1		
Yes	1.106	0.56-2.18	0.77
Physical illness			
None	1		
Presence	0.960	0.49-1.87	0.91
Psychiatric illness			
None	1		
Presence	1.434	0.50-4.12	0.50

Discussion

In this study, the respective remission rate (CIWA-Ar score < 8) by day 3, 4 and 5 of treatment was 82.9%, 91.4% and 100%. There were neither major complications nor mortality. These findings demonstrate that use of the Srinagarind Hospital Clinical Practice Guideline (CPG) helped to relieve alcohol withdrawal symptoms to reach remission. By comparison, Surachet et al. found that 93.8% of patients showed clinical improvement or remission within 7 days of treatment⁵. The authors found a higher remission rate within 7 days (100% vs.

93.8%) and remission was faster (5 days vs. >7 days) than the previous study, suggesting that use of the Srinagarind CPG helps patients with severe alcohol withdrawal syndrome in early remission better than standard treatment. The results might be influenced by the natural course of alcohol withdrawal syndrome which usually improves within 7 days of developing symptoms^{4,7}; except that in our study, 82.9% of the patients remitted within 3 days and all of the cases remitted within 5 days of therapy.

Most patients (93%) received a front-loading regimen because they had severe or very severe

symptoms or had risk factors of complicated withdrawal symptoms. The overall remission rate within 3 days was 82.4%, and 69.8% of these patients had either a history of alcohol withdrawal seizure or delirium. The majority of the patients (79.1%) had alcohol dependence for > 5 years and 62.8% had either physical or psychiatric illness. These factors might increase the severity of symptoms and duration of treatment^{4,7-14}. Although almost all of the patients had at least one risk factor for alcohol withdrawal delirium and had severe or very severe symptoms, the treatment outcomes were satisfactory. In most of the patients, the CIWA-Ar decreased to below 8 within 3 days, all patients remit within 5 days. Although high-dose benzodiazepines can worsen symptoms or cause delirium or accidents^{6,16}, 41 of the patients who received high-dose benzodiazepines did not experience any of those conditions. The authors concluded that high-dose benzodiazepines are safe and suitable for use in patients at potential risk of developing alcohol withdrawal delirium. This CPG supports the hypothesis regarding risk factors for developing alcohol withdrawal delirium and was thus beneficial for identification of patients with alcohol dependence. When these patients suddenly stop drinking and come to hospital with mild symptoms of alcohol withdrawal, clinicians can aggressively treat with diazepam or lorazepam in a front-loading regimen in order to prevent the occurrence of alcohol withdrawal delirium.

Based on the literature review, the major factors affecting the severity of symptoms were

(a) duration of alcohol dependence¹⁰, (b) history of alcohol withdrawal seizure or delirium¹¹⁻¹³, and (c) physical and psychiatric illnesses^{4,8,13-15}. The authors did not, however, find any major association between age, duration of alcohol dependence, history of alcohol withdrawal seizure or delirium, physical or psychiatric illnesses and the number of days to remission (decreasing CIWA-Ar to < 8). Our sample size might have been too small to determine such a major association, however, the analyzed hazard ratio and 95% confidence interval trended to show that the group without risk factors for alcohol withdrawal delirium remitted earlier than the group who did.

Pongtanya et al. also studied pharmacotherapy among alcohol withdrawal inpatients, their sample have a narrower range of age (22-54) than current study (23-65), shorter time of alcohol dependent (16.1 versus 21.6), less patients that have severe alcohol withdrawal symptoms (16.1% versus 76.6%). There were not much difference in co-morbid physical illness and mental illness in both population, they have the 43.5 % of patients with physical illness compares to 55.8% in this study and they have 12.5% of mental illness compare to 9.3% in current study⁵. Most common physical illness in both studies were liver disease, diabetes and hypertension and most common mental illness is depressive disorder. In this study, we have more patients with severe withdrawal symptoms and longer duration of alcohol dependent but more remission rate with this CPG. Compare to their study, we have better outcome with this CPG

as all sample in this study reached remission within 5 days while 93.8% of clinical symptoms in their sample improved within 7 days⁵.

There were no major complications or mortality throughout the hospitalization; consistent with a previous study by Pongtanya et al. who found no mortality and that none of their patients needed to be referred because of the use of medication⁵. In general, the mortality rate of severe alcohol withdrawal or alcohol withdrawal delirium is between 5-25% in untreated groups and 1-2% in treated groups^{7,12,17}. Although some cases did not die from any injuries, they had complications such as Wernicke's syndrome, Korsakoff's syndrome and aspiration pneumonia, in untreated or inadequately treated cases^{4,12}. We found that there were no such major complications; thereby affirming the effectiveness of the Srinagarind Hospital CPG.

Strengths and limitations: (1) This study enrolled patients with non-severe medical illnesses so the study lacks information regarding severe medical illness. (2) The sample size was too small to detect the relationship between factors associated with remission.

Suggestions for further research: In follow-on research, the authors recommend a study of the CPG for alcohol withdrawal syndrome with regard to common severe physical conditions.

What is already known on this topic: (a) The natural course of alcohol withdrawal syndrome usually improves within 7 days of developing symptoms^{4, 6}; (b) Treating alcohol withdrawal

syndrome with high-dose benzodiazepine can worsen the symptoms or cause and worsen delirium^{6,16}.

What this study adds: (a) Alcohol withdrawal syndrome with adequate treatment can remit within 3 days; (b) Even though they do not have severe symptoms on the first day of treatment, patients with at least one risk factor for alcohol withdrawal delirium may benefit from a front-loading regimen; and, (c) High-dose benzodiazepine helps to improve the symptoms of alcohol withdrawal syndrome in patients with risk factors for alcohol withdrawal delirium, and symptoms do not worsen.

Conclusion

The Srinagarind Hospital Clinical Practice Guideline is effective for alcohol withdrawal syndrome. The respective remission rate by day 3, 4 and 5 of treatment were 82.9%, 91.4% and 100% and there were neither any major complications nor mortality.

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Potential conflicts of interests: None.

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