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Clinical Therapeutic Effect of Naloxone Combined with Hemodialysis on Acute Severe Alcoholism

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Background: The aim of this research was to investigate the treatment effect of naloxone combined with hemodialysis on acute severe alcoholism.

Material/Methods: We included 36 patients treated with naloxone combined with hemodialysis in Group I and 34 patients treated with naloxone without hemodialysis in Group II. The Glasgow coma scale (GCS) score, the consciousness recovery time, alanine amino transferase (ALT) level, and complications were analyzed.

Results: Mean GCS score in Group I was higher than that in Group II, with a significant difference ($P<0.05$). The consciousness recovery time in Groups I and II were 3.0±0.8 h and 6.9±2.1 h, respectively, with a significant difference ($P<0.05$). After naloxone treatment and hemodialysis, the ALT level in Group I was lower than that in Group II ($P<0.05$). Moreover, the incidence of hepatic and renal function damages in Group I was smaller than that in Group II ($P<0.05$). Only 1 patient in Group I developed pneumonia, which was fewer than that in Group II, with a significant difference ($P<0.05$).

Conclusions: Naloxone combined with hemodialysis effectively reduces the central inhibition of alcohol, shortens consciousness recovery time, improves respiratory and cardiovascular function, decreases hepatic and renal function damages, and reduces the incidence of complications.

MeSH Keywords: Acute Disease • Alcoholism • Glasgow Coma Scale • Hemodialysis Units, Hospital • Naloxone

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Background

Acute severe alcoholism (ASA) is a disease caused by the ingestion of large amounts of alcohol. It can cause a variety of clinical manifestations involving many organs, which can induce behavioral, cardiac, gastrointestinal, pulmonary, neurological, and metabolic dysfunctions [1]. ASA is also a medical emergency that can be life-threatening due to respiratory depression and inhalation of vomit [2]. Despite laws, policies, and health education efforts seeking to control daily alcohol intake levels, ASA remains common in China and around the world.

The opioid antagonist naloxone is a derivative of oxymorphone. There are many reports about naloxone in the treatment of ASA. It can reduce the level of β-endorphin in the brain and help patients regain consciousness. However, it may have a harmful effect on the cardiovascular system [3].

Recently, the mechanism of naloxone in ASA treatment has become increasingly clear [4]. Treatment with naloxone greatly helps in the recovery of patients by binding to reward-related regions of the brain [5]. Although it warrants further use in clinical therapy, naloxone is an antagonist of opioid receptors and plays a role in regulating cardiovascular and respiratory systems [6]. Naloxone does not produce secretions and it cannot effectively remove the metabolites of alcohol, leaving CO_2 and H^+ ions to be removed only by natural metabolism [7,8].

Hemodialysis is an important step of hemopurification, which removes metabolic waste through dialysate. Then, the purified blood is injected into the blood vessels [9]. It not only improve physiological and living qualities [10], but also effectively prevents death induced by circulatory and respiratory failures [11].

In the present study, patients in Group I received treatment with naloxone and hemodialysis, while patients in the control group (Group II) were only treated with naloxone. We compared these therapies to analyze the effect of hemodialysis on ASA and the effect of naloxone on ASA.

Material and Methods

Patients

We enrolled 70 ASA patients with an average age of 33.6±7.2 who were admitted to our hospital from January 2014 to December 2016. This research was approved by the Ethics Committee of Linyi City Yishui Central Hospital. All patients had ingested 400–700 ml of high-concentration alcohol. At an average of about 2 hours after the ingestion, they were admitted to our hospital.

Patients arrived in our hospital in unconscious state and many had vomited before becoming comatose. Physical examination demonstrated that all patients were in at least moderate-level coma, with Glasgow coma scale (GCS) score [12] lower than 8. Patients were breathing with snoring and apnea. They all had no reaction to painful stimuli, had slow pupillary light reflex, and lacked pathologic reflex. Alcohol concentration in the blood was more than 2500 mg/L and blood oxygen saturation was ≥90%. Most patients did not have a history of hypertension or cardiovascular, liver, or kidney diseases.

Treatment for patients

All patients were automatically treated with naloxone or naloxone combined with hemodialysis. There were 36 patients who received naloxone combined with hemodialysis treatment (Group I) and 34 patients received naloxone treatment without hemodialysis (Group II).

All patients received basic treatment, including clean-out of vomitus, oxygen inhalation, warming, and fluid infusion. Patients in Group II were treated with 500 ml normal saline containing 0.2 mg naloxone and water-soluble vitamins and a 2000-ml glucose injection (5% glucose) by intravenous infusion and gastric mucosa-protective agents. In addition to these treatments, patients in Group I were also treated with hemodialysis. The initial velocity of the blood was 150 ml/min. If the vital signs of patients were improved 15 min later, the velocity was gradually increased to 500 ml/min for 3–4 h.

Clinical observation

Respiration, blood pressure, oxygen saturation, and heart rate were observed in real time during the treatment. After drug and hemodialysis treatments, consciousness recovery was observed and evaluated with GCS score, which helped us to estimate the treatment effects. The treatment was regarded as no effect at GCS <8 and significant treatment effect at GCS ≥12. The details are shown in Table 1.

We performed routine assessment of blood, urine, hepatic and renal functions, myocardial enzyme, arterial blood gas, and alanine amino transferase (ALT) before and after the treatments. Consciousness recovery time and complications after the treatments were also analyzed.

Statistical analysis

Statistical analysis was performed with SPSS 21.0. GCS scores, consciousness recovery time, and ALT level are shown as mean ± standard deviation and were analyzed using the *t* test. Complications of ASA patients after the treatments were analyzed by chi-square test. There was a significant difference at $P<0.05$.

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Table 1. GCS score and treatment effect.

Treatment effect	GCS	Symptom
No effect	<8	No pain reaction; slow pupillary light reflex; no pathologic reflex
Effect	8≤ GCS <12	Deep slumber or light coma; eyes could open under a strong stimulation; could point out the localization of pain
Significant effect	≥12	Sleepiness; could express with simple words

GCS – glasgow coma scale.

Table 2. Basic information of patients. The term "volume of alcohol" means the volume of alcohol absorbed by patients. The term "visiting time" means the time from alcoholism to visiting doctors.

Terms		Group I	Group II	P
Number		36	34	
Age		33.1±9.2	34.1±8.5	0.871
Gender	Male	25	26	0.515
	Female	11	8	
Weight (kg)		66.0±11.20	64.50±12.35	0.374
Volume of alcohol (ml)		342±59.2	334±61.0	0.905
Visiting time (h)		2.10±0.85	2.15±0.90	0.765

The T-test method was used for the comparison between two groups in age, gender, weight, volume of alcohol and visiting time. There is no difference between two groups in these terms.

Table 3. The GCS score and clinical treatment effect.

Groups	GCS (means)	Significant effect		Effect		No effect	
		Num.	Rate (%)	Num.	Rate (%)	Num.	Rate (%)
Group I	11.5±2.65	21	58.33	14	38.89	1	2.78
Group II	9.62±3.38	14	41.18	15	44.12	5	14.70
P				0.012			

The statistical analysis of GCS score were performed with T-test. P<0.05 indicates a statistically significant difference. GCS – glasgow coma scale.

Results

Basic information

Patients were divided into 2 groups and were given different treatments. In Group I, 36 patients were treated with naloxone combined with hemodialysis, and 34 patients treated with naloxone were in Group II. Results of statistical analysis showed that there were no significant differences in age, sex, volume of alcohol ingested, or the time from intoxication to admission at our hospital between the 2 groups ($P>0.05$) (Table 2).

GCS score and clinical treatment effect

After clinical treatment, the treatment effects in the 2 groups were estimated by GCS score. As shown in Table 3, mean GCS score in Group I was higher than that in Group II, with a significant difference ($P<0.05$). There were 21 patients with significant effect in Group I, which were more than in the control group (Group II). Moreover, the higher efficacy rate in Group I demonstrated that hemodialysis had a significant treatment effect (Table 3).

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Table 4. The consciousness recovery and ALT level of two groups.

Group	Consciousness recovery (h)	ALT (U/L)	
		Before treatment	After treatment
Group I	3.0±0.8	163.59±40.50	60.1±36.76
Group II	6.9±2.1	158.41±52.87	186.36±45.12
P	1.10×10^{-17}	0.35	1.28×10^{-19}

The statistical analysis of consciousness recovery time and ALT level were performed with T-test. P<0.05 indicates a statistically significant difference. ALT – alanine amino transferase.

Table 5. Complications of ASA patients in two groups.

Terms	Group I	Group II	P
Myocardial injury	3	2	0.69
Hepatic and renal function damage	2	10	8.1×10^{-3}
Pneumonia	1	6	0.038

The statistical analysis of complications was performed with Chi-square test. P<0.05 indicates a statistically significant difference.

Symptoms improvement

After clinical treatment, all symptoms disappeared several hours later. However, there were also some differences between the 2 groups. The consciousness recovery time in Groups I and II were 3.0±0.8 h and 6.9±2.1 h, respectively, with a significant difference ($P<0.05$). After treatment, ALT level was remarkably changed, but there was no difference between the 2 groups before treatment ($P=0.35$). Nevertheless, ALT level in Group I after the treatment with naloxone and hemodialysis was lower than that in the control group after the treatment with naloxone, with a significant difference ($P<0.05$). This demonstrates that naloxone combined with hemodialysis can decrease ALT level and promote recovery of consciousness (Table 4).

Complications after treatment

Common complications of ASA were myocardial injury, hepatic and renal function damages, and pneumonia [13]. In this research, there was no difference in myocardial injury between the 2 groups ($P=0.69$). The incidence of hepatic and renal function damages in Group I was lower than that in the control group, with a significant difference ($P<0.05$). In addition, 1 patient suffered from pneumonia in Group I, which was fewer than that in the control group, with a significant difference ($P<0.05$) (Table 5).

Discussion

In the 19th century, alcoholism started being regarded as a disease in the broader sense, as a physical and mental disorder [14]. The metabolic effects of alcohol include decreased synthesis of albumin, in addition to decreased serum concentration of magnesium, calcium, and phosphate [15]. Due to the direct or indirect toxic action of alcohol, it decreases the absorption of folic acid and the production of red blood cells [16,17]. Metabolites of alcohol can act on opioid receptors in the cerebrum and regulate the brain condition from excitation to inhibition. Subsequently, the subcortical center, cerebellum, and vasoconstriction and respiratory center in the medulla oblongata are gradually damaged [18,19]. Thus, removing of metabolites of alcohol is very important in ASA treatment. Naloxone can play a major role in improving a patient's condition [20], but it has a limited ability to remove alcohol metabolites, which can be addressed with the use of hemodialysis.

In this research, patients in Group I were given hemodialysis treatment. Compared to the control group, GCS scores in Group I were significantly higher ($P<0.05$), which demonstrates that the treatment effect in Group I was better than that in the control group. Significant treatment effects were observed in 21 patients (58.33%) in Group I and 14 patients (41.18%) in Group II. Although there was no noticeable effect in 1 patient in Group I, he quickly recovered consciousness. Consciousness recovery time in Group I was 3.0±0.8 h, which was much shorter than in the control group. This might be related to the removing of alcohol metabolites. Hemodialysis can transfer alcohol metabolites to dialysate by ion-exchange, which can directly or indirectly influence the dopamine system and play a positive role in regulating the biological consequences of alcoholism [21].

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Moreover, ALT level in Group I after treatment was remarkably lower than that in Group II ($P<0.05$), and the complications, including pneumonia ($P<0.05$) and hepatic and renal function damages ($P<0.05$), in Group I were significantly lower than in Group II. Thus, the synergistic effect of naloxone combined with hemodialysis was fully demonstrated. The main function of hemodialysis was to remove ethanol and alcohol metabolites and correct the acid-base balance to stabilize the environment. Naloxone is a specific antagonist of endogenous opioid substances, which can play a role in the combination of β-endorphin and intracranial opioid receptors and reduce the level of β-endorphin [22]. The combination of naloxone and hemodialysis can effectively shorten the ethanol removal time and overturn the central inhibitory effect of ethanol to improve respiratory function and circulation, as well as speeding the recovery of consciousness and reducing the occurrence of complications [23].

Conclusions

Our results show the significant therapeutic effect of naloxone combined with hemodialysis. Hemodialysis can remove alcohol metabolites and regulate water and electrolyte disturbances [24], and naloxone can interrupt β-endorphin binding to opioid receptors [25]. The combination of naloxone and hemodialysis can effectively reduce central inhibition induced by alcohol, shorten the consciousness recovery time, improve respiratory and cardiovascular functions, decrease hepatic and renal function damages, and reduce the incidence of complications. Therefore, hemodialysis as an adjuvant therapy should be broadly applied in ASA treatment.

Conflict of interest

None.

References:

1. Vonghia L, Leggio L, Ferrulli A et al: Acute alcohol intoxication. Eur J Intern Med, 2008; 19: 561–67
2. Devi G: Management of drug and alcohol withdrawal. N Engl J Med, 2003; 349: 405–7; author reply 405–7
3. Xuan HL: Clinical observation of naloxone combined with xingnaojing injection in the treatment of 87 cases of acute severe alcoholism. Contemporary Medine, 2010; 10: 145–47
4. Tong W, Wenli L: Refreshing static joint curative effect observation of treatment of acute alcohol intoxication of naloxone. Medicine & People, 2014; 3: 045
5. Laukkanen V, Karkkainen O, Kautiainen H et al: Decreased [3H] naloxone binding in the dentate gyrus of cloninger type 1 anxiety-prone alcoholics: A postmortem whole-hemisphere autoradiography study. Alcohol Clin Exp Res, 2015; 39: 1352–59
6. Dwyer K, Walley AY, Sorensen-Alawad A et al: Opioid education and nasal naloxone rescue kits in the emergency department. West J Emerg Med, 2013; 16: 381–84
7. Salman S, Buttigieg J, Zhang M, Nurse CA: Chronic exposure of neonatal rat adrenomedullary chromaffin cells to opioids *in vitro* blunts both hypoxia and hypercapnia chemosensitivity. J Physiol, 2013; 591: 515–29
8. Salman S, Buttigieg J, Nurse CA: Ontogeny of O2 and CO2//H+ chemosensitivity in adrenal chromaffin cells: role of innervation. J Exp Biol, 2014; 217: 673–81
9. Mori Y, Toyoda M: Hemodialysis apparatus and method for hemodialysis. U.S. Patent, 2013
10. Suri RS, Larive B, Sherer S et al: Risk of vascular access complications with frequent hemodialysis. J Am Soc Nephrol, 2013; 24: 498–505
11. Koo JR, Kim JC, Yoon JW et al: Failure of continuous venovenous hemofiltration to prevent death in paraquat poisoning. Am J Kidney Dis, 2002; 39: 55–59
12. Hansen B, Quick J, Sinkovits E, Smith JC: Glasgow coma scale: How to improve and enhance documentation. J Trauma Nurs, 2014; 21: 122–24; quiz 125–26
13. Kasztelan-Szczerbinska B, Surdacka A, Slomka M et al: Association of serum adiponectin, leptin, and resistin concentrations with the severity of liver dysfunction and the disease complications in alcoholic liver disease. Mediators Inflamm, 2013; 2013: 148526
14. Sabino KR, Petroianu A, Alberti LR: Influence of the acute alcoholism on the phagocytic function of the mononuclear phagocytic system. J Med Life, 2011; 4: 421–23
15. Money SR, Petroianu A, Kimura K, Jaffe BM: Acute hypocalcemic effect of ethanol in dogs. Alcohol Clin Exp Res, 1989; 13: 453–56
16. Bjorneboe GE, Bjorneboe A, Johnsen J et al: Calcium status and calcium-regulating hormones in alcoholics. Alcohol Clin Exp Res, 1988; 12: 229–32
17. Miljanovic B, Dana R, Sullivan DA, Schaumberg DA: Impact of dry eye syndrome on vision-related quality of life. Am J Ophthalmol, 2007; 143: 409–15
18. Bart G, Kreek MJ, Ott J et al: Increased attributable risk related to a functional mu-opioid receptor gene polymorphism in association with alcohol dependence in central Sweden. Neuropsychopharmacology, 2005; 30: 417–22
19. Dai LF: Observation of the clinical effect of naloxone joint Xingnaojing injection on treating acute severe alcoholism. Practical Journal of Cardiac Cerebral Pneumal and Vascular Disease, 2013; 21: 128–29
20. Jeffcoate WJ, Herbert M, Cullen MH et al: Prevention of effects of alcohol intoxication by naloxone. Lancet, 1979; 2: 1157–59
21. Deehan GA Jr., Hauser SR, Wilden JA et al: Elucidating the biological basis for the reinforcing actions of alcohol in the mesolimbic dopamine system: The role of active metabolites of alcohol. Front Behav Neurosci, 2015; 7: 104
22. Shi BQ, Zhu H, Liu CJ: [Naloxone clinical application.] Hebei Medicine, 2003; 25: 702 [in Chinese]
23. Yang M: [Nursing care of acute alcoholism induced by naloxone in promoting awakening.] Chinese Journal of Misdiagnostics, 2007; 7: 381 [in Chinese]
24. Ryu J, Lim KH, Ryu DR et al: Two cases of methyl alcohol intoxication by subchronic inhalation and dermal exposure during aluminum CNC cutting in a small-sized subcontracted factory. Ann Occup Environ Med, 2016; 28: 65
25. Gaveriaux-Ruff C: Opiate-induced analgesia: contributions from mu, delta and kappa opioid receptors mouse mutants. Curr Pharm Des, 2013; 19: 7373–81

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