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A RANDOMIZED CONTROLLED STUDY OF ADDITIVE USE OF DEXMEDETOMIDINE TO BENZODIAZEPINES FOR PATIENTS WITH ALCOHOL WITHDRAWAL SYNDROME

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Dexmedetomidine has the ability of producing sedation and to inhibit the adrenergic system without respiratory depression, what makes it a promising agent in the management of alcohol withdrawal syndrome. So, the objective of this randomized controlled trial was to evaluate safety and efficacy of dexmedetomidine added to usual diazepam therapy compared to diazepam only. All eligible patients were randomly divided into two group: intervention (Group D; n=36) and control (Group C; n=36). In Group D dexmedetomidine infusion was started at a dose of 0.2–1.4 мg/kg/h and titrated up to achieving target sedation level (-2 to 0 on the Richmond Agitation Sedation Scale (RASS)) with symptom-triggered benzodiazepine (10mg bolus of diazepam) used as needed. Patients in control group received only diazepam boluses. Primary efficacy outcomes were: 24-hour diazepam consumption and cumulative diazepam dose through the period of ICU stay. Secondary outcomes were length of the ICU stay, sedation and communication quality and haloperidol requirements. Median 24-hour diazepam consumption was significantly lower in Group D, likewise the median cumulative diazepam dose. Patients in Group D had better median percentage of time in target sedation range ($p<0.001$). Also, DEX infusion was associated with better nurse-assessed patient communication ($p<0.001$) and fewer patients required haloperidol treatment. No severe adverse effects were registered in either group. All patients remained on spontaneous breathing. Bradycardia was more common adverse effect in Group D. Dexmedetomidine infusion was associated with higher amount of time in target sedation range, better nurse-patient communication and with reduced diazepam requirements and lower percent of patients who required haloperidol for severe agitation and hallucinations.

Keywords: *alcohol withdrawal syndrome; dexmedetomidine; benzodiazepines; sedation; randomized controlled trial.*

BACKGROUND

Alcohol withdrawal syndrome (AWS) is an often complication of the perioperative period or critical illnesses, and may increase the likelihood of admission to the intensive care unit (ICU) or the time, which patients spends in the ICU. Around 20% of hospitalized patients have alcohol dependence and 18% of them will develop AWS during their hospital stay [1]. The AWS symptoms are usually appearing 24–96 h after cessation of alcohol consumption and are characterized by sympathetic hyperactivity and metabolic and psychiatric disorders (e.g. agitation, hallucination and seizures). Benzodiazepines (BZDs) are commonly used to manage AWS and are effective for that purpose. Several studies have shown that BZDs reduce the incidences of seizures and delirium, and shorten the duration of AWS compared with placebo [2, 3]. However, BZD monotherapy may not be sufficient to control AWS symptoms [1] and large doses of BZD is associated with excessive sedation, respiratory failure, worsening of delirium, increased aspiration and intubation risks, increased length of hospitalization and increased hospital costs [3, 4]. Furthermore, chronic liver disease patients are at risk of oversedation and progression of hepatic encephalopathy while using BZDs [5].

At this moment, there is no alternative drugs with good efficacy and safety profiles for the management of AWS. [6]. Anticonvulsants, antipsychotics, ethanol, barbiturates and propofol have been used historically for this purpose [7, 8], but the evidence base for these agents is weak or absent [6]. There have also been several studies of clonidine as adjunct treatment for AWS in the ICU, which significantly decreases AWS symptoms [9] and BZD doses [10], but is associated with greater risk of adverse events such as bradycardia and hypotension [10,11]. Downsides of clonidine include that it produces only a mild sedative effect, its significant hemodynamic impact and long duration of action (up to 12–16 h) [7].

Dexmedetomidine (DEX) is a selective, central Q_2-receptor agonist which is approved for ICU sedation in mechanically ventilated patients and for procedural sedation for non-intubated patients [12]. When compared with clonidine, DEX offers more effective sedative and analgesic properties, a shorter half-life (2–3 h) and significantly lower rates of hemodynamic complication [12,13]. Moreover, DEX does not cause respiratory depression and decreases the duration of mechanical ventilation [12,13].

There have been various reports of the successful use of DEX – usually as an adjunct to BZDs – in the management of AWS during the last 10 years. However, most publications have been limited to case reports [14], case series [15] and retrospective [1] and prospective observational studies [16]. Only one randomized controlled study has been published to date [17], in which the authors found that adjunct use of DEX was associated with DEX attenuation of AWS symptoms, with concomitant reductions in use of BZDs. The commonest side effects were hypotension and bradycardia.

The objective of this randomized controlled study was to evaluate whether addition of DEX to BZD therapy is effective and safe for AWS patients in the ICU. We hypothesized that DEX would reduce BZD consumption and the need for neuroleptics, as well as improving sedation quality.

METHODS

This randomized, single-center, controlled study was conducted in the adult mixed ICU at the private hospital 'Boris' in Kiev, Ukraine. The inclusion criteria were: age ≥ 18–75 years and AWS diagnosed by means of the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition criteria [18], plus the signed informed consent of either the patient or the patient's family or a legal representative. The exclusion criteria were age outside the specified range, history of use of other psychoactive substances or of withdrawal states, general anesthesia during the previous 24 h or other sedatives used, severe neurologic disorder (traumatic brain injury, acute stroke, severe dementia), pregnancy or lactation, severe comorbidities (severe heart failure, acute myocardial infarction, heart rate <50 beats/min, glomerular filtration rate <30 mL/min, liver failure Child-Pugh class C, acute respiratory failure) and known allergy to the study medication.

Typical reasons for ICU admission were severe agitation, hallucinations, Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar) score ≥ 15, history of seizures or previous delirium tremens (DT), coexisting medical problems (e.g. pancreatitis) or respiratory distress.

After the primary patient assessment, eligible participants were assigned in a 1:1 ratio to either the intervention (Group D) or control (Group C)

groups in blocks of four using randomization sequence, generated by the computer algorithm [19]. Randomization and data analysis were conducted by an independent blinded member of the research team.

In Group D, DEX infusion was started at a dose of 0.2–1.4 мg/kg/h and titrated up to achieving the target sedation level of –2 to 0 on the Richmond Agitation Sedation Scale (RASS) and CIWA-Ar score < 15. DEX loading doses were not used. Dosing and duration of DEX infusion was adjusted by the clinical management team based on sedation assessment. Duration of DEX infusion was no longer than 72 hours. In patients for whom increasing the DEX infusion rate to 1.4 мg/kg/h did not lead to achieving RASS –2 to 0 and/or a CIWA-Ar score of <15, diazepam (10 mg i.v.) was administered according to a symptom-triggered protocol. In Group C, the same symptom-triggered diazepam regimen protocol was used. In both groups diazepam was administered every 30 min as needed to control active withdrawal symptoms (CIWA-Ar score ≥ 15 or RASS score >+2), as prescribed by the clinical management team. Antipsychotics (i.m. haloperidol, 5mg boluses) were used as a rescue medication in both groups for severe agitation or hallucinations. Haloperidol was prescribed only if the QT interval (QT_c) was documented to be normal. No other sedatives or analgesics were allowed during the study period.

The primary efficacy outcomes were median 24-h diazepam consumption and median cumulative diazepam dose required over the course of the ICU stay.

Secondary efficacy outcomes included:

- length of ICU stay and intubation rates;
- sedation quality: time in the target sedation range [RASS score 0 to –2] as a proportion of total sedation time; the duration of insufficient sedation: time with RASS score ≥ +2 as a proportion of total sedation time; the duration of oversedation : time with RASS score ≤ –3] expressed as a proportion of total sedation time; and the number of rescue sedation boluses and sedation stops required over a 24-h period;
- the nurse-assessed communicability, such as an ability for asking for help or answering questions on comfort and pain, which was assessed during each shift (every 12 hours) on a scale from 0 to 10, where 0 = uncommunicative and 10 = patient communicates well;
- haloperidol requirements (number of patients who received haloperidol for severe agitation and hallucinations) and cumulative haloperidol dose.

During the ICU stay, patients in both groups were evaluated by the nursing staff using the RASS and the CIWA-Ar scale (either every 2 h or prior to rescue therapy). The level of alertness was assessed using the Observer's Assessment of Alertness/Sedation (OAA/S) scale every 2 h.

Safety was assessed by monitoring vital signs, performing laboratory tests (partial oxygen pressure in arterial blood [PaO_2], partial carbon dioxide pressure in arterial blood [$PaCO_2$], oxygen saturation in arterial blood [SaO_2], blood glucose) and recording adverse events. Pulse, invasive blood pressure and electrocardiogram were monitored in all patients. QT_c was assessed for patients treated with haloperidol. Spontaneous breathing was assessed using continuous respiratory rate monitoring and pulse oximetry. Arterial blood gases were checked every 12 h or less if needed.

An adverse event was recorded if systolic blood pressure was <90 or >160 mmHg or if heart rate was <50 or >110 beats/min; desaturation was estimated as peripheral oxygen saturation (or SaO_2) <90%; hypoglycemia was defined as serum glucose <3.9 mmol/L and hyperglycemia as serum glucose >10 mmol/L. Interventions for hypertension and hypotension, bradycardia or tachycardia, included titration or interruption of study agent, or additional drug therapy.

Statistical analysis was performed using Statistica 8.0 and R software (StatSoft Inc., Tulsa, OK, USA). Categorical data are presented as proportions and continuous data as medians with 25–75% interquartile ranges (IQRs). Chi-square testing demonstrated that all of the study variables were discrete. To assess significance levels, a two-tailed Mann–Whitney U-test and Fisher's exact test were used. A p-value of <0.05 was considered significant.

This study was approved by the Bogomolets National Medical University ethics committee (approval code number 84).

RESULTS AND DISCUSSION

A total of 72 patients were randomized into two study groups (n=36 per group). The median time from hospital admission to the start of the study was 24 h (IQR 12–48 h) in Group D and

30 h (IQR 20–50 h) in Group C (p=0.9). There were no significant differences between the study groups referring to demographic characteristics, comorbidities, initial AWS severity and diazepam dose administered prior to study enrollment.

Baseline characteristics of the study population are presented in Table 1.

The median duration of DEX infusion was 36 h (IQR 24–42 h) with a median dose of 0.5 мg/kg/h (IQR 0.4–0.8 мg/kg/h). All patients survived to discharge.

The main outcomes of the study are presented in Table 2. As shown therein all the pre-specified dimensions of AWS symptomatology, BZD consumption, sedation quality, patient alertness and ability to communicate and use of rescue medications were favorably influenced by the use of DEX.

In this randomized controlled study, addition of DEX to BZD therapy significantly decreased 24-h diazepam consumption and cumulative diazepam dose during the ICU stay in AWS patients.

Sedation quality, as one of the secondary outcomes, differed significantly between the two groups. The median time in the target sedation range was significantly higher in Group D (D25%; p<0.001) and DEX infusion was associated with better patient communication (D3 points; p<0.001). The duration of excessive sedation, number of sedation stops, duration of insufficient sedation and number of rescue sedation boluses were all significantly higher in Group C (Table 2). CIWA-Ar psychometric values decreased in both groups with the course of AWS, with no significant differences in median values between the two groups.

The number of patients who received haloperidol as a rescue medication for severe agitation and hallucinations was lower in Group D (odds ratio 6.8, 95% confidence interval 1.4–33). Nevertheless, the cumulative dose of haloperidol during the ICU stay did not differ significantly between groups: median cumulative dose 50 mg (IQR 40–55 mg) in Group D and 60 mg (IQR 40–65 mg) in Group C (p=0.2). Other authors have reported about significant reduction in haloperidol use after addition of DEX [1], [20], although those studies were retrospective and had several design limitations. In the only controlled trial of DEX as adjunctive therapy for AWS reported to date,

Table 1. ***Demographic data and AWS severity at baseline***

	Group D (DEX)	Group C (Control)	P-value
Male	33/35 (94)	28/32 (88)	p=0.9
Age, median (IQR)	46,5 [43–50]	46 [42–50]	p=1.0
Comorbidities:			
Liver cirrhosis: Child-Pugh A, n (%)	1/35 (3)	1/32 (3)	p=1.0
Child-Pugh B, n (%)	2/35 (6)	1/32 (3)	p=0.9
Pneumonia, n (%)	1/35 (3)	0/32	p=1.0
Diabetes, n (%)	1/35 (3)	2/32 (6)	p=0.9
Congestive heart failure: NYHA class I, n (%)	1/35 (3)	1/32 (3)	p=1.0
NYHA class II, n (%)	1/35 (3)	1/32 (3)	p=1.0
Arterial hypertension n (%)	3/35 (9)	6/32 (19)	p=0.19
Other: leg fracture, n (%)	2/35 (6)	0/32	p=1.0
acute pancreatitis, n (%)	1/35 (3)	2/32 (6)	p=1.0
CIWA-Ar at ICU admission, median (IQR)	25 [18 to 29]	26 [17 to 28]	p=1.0
RASS at ICU admission, median (IQR)	+2 [+1 to +3]	+2 [+1 to +3]	p=1.0
Diazepam dose administered prior to study enrollment, mg, median (IQR)	30 [20 to 40]	30 [20 to 40]	p=1.0

CIWA-Ar - Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised; IQR - InterQuartile Range, NYHA - New York Heart Association Functional Classification .

Table 2. ***Efficacy outcomes in study groups***

	Group D (DEX)	Group C	P-value
Diazepam consumption in 24 h, mg	20 (20-30)	40 (40-50)	p<0.001
Cumulative diazepam consumption, mg	60 (50-60)	90 (80-100)	p<0.001
Time of target sedation, %	90 (90-95)	64.5 (60-72.5)	p<0.001
Time of insufficient sedation, %	7.75 (5-10)	15 (10-20)	p<0.001
Time of oversedation, %	2 (0-5)	15 (10-20)	p<0.001
Rescue sedation boluses, No. in 24h	1.25 (0-4)	4 (3-6)	p=0.004
Sedation stops, No. in 24h	0 (0-1)	2 (0-3)	p<0.001
Communication with patient	9 (7-10)	6 (5-6)	p<0.001
OAA/S scale	1 [0-2]	2 [1-4]	p=0.03
Haloperidol use, No. of patients (%)	2/32 (6)	10/32 (31)	p=0.02
Median cumulative haloperidol dose, mg	50 mg (IQR 40–55 mg)	60 mg (IQR 40–65 mg)	p=0.2

No – number; OAA/S - Observer's Assessment of Alertness/Sedation. Value expressed as medians (InterQuartile Ranges 25 to 75), unless otherwise specified.

haloperidol consumption and doses were not studied [17].

The median length of ICU stay was 50 h (IQR 46–65 h) in Group D and 70 h (IQR 65–90 h) in Group C (p=0.059). DT deve-loped in one patient in Group D and four in Group C (p=0.36). These patients were excluded from the analysis due owing to insufficient control of AWS symptoms with study medication (e.g. dexmedetomidine, diazepam, haloperidol) and other sedatives used (propofol), all of them were intubated for airway protection and respiratory support. To our knowledge, there is no clear evidence of benefit from DEX use in patients with DTs. One prospective trial reported some benefits with addition of DEX to BZD therapy in patients with DT [16]. However, that study had significant limitations: there was no comparison or control group and delirium was defined using the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU), with no clear distinction between delirium caused by AWS and other factors.

All patients remained on spontaneous breathing during the study period; desaturation was successfully treated with administration of extra oxygen and sedative drug titration. There were no statistically significant differences between Groups D and C regarding desaturation incidence (Table 3), respiratory rate and arterial PaO_2 or $PaCO_2$.

Table 3. ***Complications and adverse events rates in both groups***

	Group D (DEX)	Group C	Odds ratio (CI 95%)	P-value
Adverse events: Hypotension, n (%)	8/35 (23)	4/32 (13)	2 (0.48 to 11)	p=0.34
Hypertension, n (%)	0/35	4/32 (16)	11 (0.6 to 190)	p=0.05
Tachycardia, n (%)	0/35	5/32 (16)	14 (0.9 to 283)	p=0.02
Bradycardia, n (%)	10/35 (31)	2/32 (6)	6 (1.3 to 73)	p=0.03
Desaturation, n (%)	1/35 (3)	5/32 (15)	5.3 (0.6 to 280)	p=0.2
Hypoglycemia, n (%)	2/35 (6)	1/32 (3)	2 (0 to 114)	p=1.0
Hyperglycemia, n (%)	5/35 (14)	9/32 (28)	2 (0.7 to 9)	p=0.2
Complications: Hospital pneumonia, n (%)	1/35 (3)	2/32 (6)	2 (0.1 to 125)	p=0.6

No severe adverse events were identified (Table 3). The commonest adverse events observed were hypotension, hypertension and desaturation, with similar incidence in study groups; bradycardia, which was observed significantly more often in Group D (p=0.01); and tachycardia, which was observed significantly more often in Group C (p=0.02). Hospital-acquired pneumonia was diagnosed in one patient in Group D and two patients in Group C. No seizures were observed during the study.

After discharge from ICU, patients continued treatment in the general department ward with oral diazepam. The median duration of hospitalization was 9 days (IQR 8–10 days) in Group D and 11 days (IQR 10–13 days) in Group C (p=0.034).

DEX is an attractive drug for AWS management because of its ability to produce arousable sedation and to inhibit the adrenergic system without respiratory depression [12]. The benefits of DEX in AWS management have been shown in several retrospective series [1], [13–15]. Rayner et al. [1] published a retrospective review of 20 AWS patients admitted to the ICU, with DEX being used in addition to BZDs. The mean dose of DEX was 0.53 μg/kg/h and the mean duration of therapy was 49.1 h. Adjunctive DEX decreased severity score, haloperidol use and diazepam dose within 4 h. Dailey et al. [21] published a retrospective chart review of 10 patients with AWS who were treated with DEX. The mean dose was 0.7 μg/kg/h and the mean infusion time was 50 h. The authors reported a significant diazepam dose reduction from 13 mg/h prior to DEX infusion to 3 mg/h in the 24 h after treatment. All patients in the study had normal spontaneous breathing. Other studies have reported similar results, although the majority of them were observational or retrospective [14–16].

To date only a few prospective controlled studies of use of DEX in AWS patients have been published [16], [17]. The authors of that research concluded that DEX shows promise as an adjunct to BZDs but concluded that further studies are needed to fully profile the clinical impact of DEX in AWS. Our study is a modest addition to the dataset of prospectively-derived data and is supportive of earlier conclusions but it is still necessary to conduct larger randomized trials of DEX in AWS.

The limitations of this study include the partially blinded design with absence of placebo control and the small sample size (n=72), which make it difficult to draw definitive conclusions. The exclusion of all patients who developed DT precludes any conclusions of the effectiveness of DEX in that situation but the indications are that it adds little to the treatment options for that aspect of AWS.

Nevertheless, this trial supports adjunctive DEX use for many AWS patients in the ICU and provides efficacy and safety outcomes. In the authors' opinion, we now have enough data to consider DEX as a effective adjunct to BZD therapy for AWS patients in the ICU. However, more data and new large studies is necessary to formulate definite medical conclusions and for evaluation of cost-effectiveness.

CONCLUSIONS

Addition of DEX to BZD therapy is effective and safe for AWS patients in the ICU. DEX significantly reduces diazepam requirements as well as improving both sedation quality and patient communication. Addition of DEX to diazepam decreased the number of patients who required haloperidol for severe agitation. Monitoring for bradycardia is necessary during DEX infusion.

REFERENCES

1. *Rayner SG, Weinert CR, Peng H, Jepsen S, Broccard AF. Dexmedetomidine as adjunct treatment for severe alcohol withdrawal in the ICU. Ann Intensive Care 2012; 2(1):12.*
2. *Amato L, Minozzi S, Vecchi S, Davoli M. Benzodiazepines for alcohol withdrawal. Cochrane Database Syst Rev. 2010;(3):CD005063.*
3. *Mayo-Smith MF, Beecher LH, Fischer TL et al. Management of alcohol withdrawal delirium. An evidence-based practice guideline. Arch Intern Med. 2004; 164(13):1405-1412.*
4. *Al-Sanouri I, Dikin M, Soubani AO. Critical care aspects of alcohol abuse. South Med J. 2005; 98(3): 372-381.*
5. *Peppers MP. Benzodiazepines for alcohol withdrawal in the elderly and in patients with liver disease. Pharmacotherapy. 1996; 16(1): 49-57.*
6. *Barr J, Fraser GL, Puntillo K et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the Intensive Care Unit: executive summary. Am J Health Syst Pharm. 2013; 70(1):53-58.*
7. *Sarff M, Gold JA. Alcohol withdrawal syndromes in the intensive care unit. Crit Care Med. 2010; 38(9 Suppl): 494-S501.*
8. *Awissi DK, Lebrun G, Coursin DB, Riker RR, Skrobik Y. Alcohol withdrawal and delirium tremens in the critically ill: a systematic review and commentary. Intensive Care Med. 2013; 39(1):16-30.*
9. *Baumgartner GR, Rowen RC. Transdermal clonidine versus chlordiazepoxide in alcohol withdrawal: a randomized, controlled clinical trial. South Med J. 1991; 84(3):312-321.*
10. *Adinoff B. Double-blind study of alprazolam, diazepam, clonidine, and placebo in the alcohol withdrawal syndrome: preliminary findings. Alcohol Clin Exp Res. 1994; 18(4):873-878.*

11. Spies CD, Dubisz N, Neumann T et al. Therapy of alcohol withdrawal syndrome in intensive care unit patients following trauma: results of a prospective, randomized trial. Crit Care Med. 1996; 24(3):414-422.
12. Gerlach AT, Murphy CV, Dasta JF. An updated focused review of dexmedetomidine in adults. Ann Pharmacother. 2009; 43(12):2064-2074.
13. Muzyk AJ, Fowler JA, Norwood DK, Chilipko A. Role of alpha2-agonists in the treatment of acute alcohol withdrawal. Ann Pharmacother. 2011; 45(5):649-657.
14. Rovasalo A, Tohmo H, Aantaa R, Kettunen E, Palojoki R. Dexmedetomidine as an adjuvant in the treatment of alcohol withdrawal delirium: a case report. Gen Hosp Psychiatry. 2006; 28(4):362-363.
15. DeMuro JP, Botros DG, Wirkowski E, Hanna AF. Use of dexmedetomidine for the treatment of alcohol withdrawal syndrome in critically ill patients: a retrospective case series. J Anesth. 2012; 26:601-605.
16. Tolonen J, Rossinen J, Alho H, Harjola VP. Dexmedetomidine in addition to benzodiazepine-based sedation in patients with alcohol withdrawal delirium. Eur J Emerg Med. 2013; 20:425-7.
17. Mueller SW, Preslaski CR, Kiser TH, Fish DN, Lavelle JC, Malkowski SP, et al. A randomized, double-blind, placebo-controlled dose range study of dexmedetomidine as adjunctive therapy for alcohol withdrawal. Crit Care Med. 2014;42:1131-9.
18. Moss HB, Chen CM, Yi HY. DSM-IV criteria endorsement patterns in alcohol dependence: relationship to severity. Alcohol Clin Exp Res. 2008;32:306-13.
19. Random.org: True Random Number service. http://www.random.org. Accessed 15 Jan 2013.
20. Lizotte RJ, Kappes JA, Bartel BJ, Hayes KM, Lesselyoung VL. Evaluating the effects of dexmedetomidine compared to propofol as adjunctive therapy in patients with alcohol withdrawal. Clin Pharmacol 2014;6:171-7.
21. Dailey RW, Leatherman JW, Sprenkle MD. Dexmedetomidine in the management of alcohol withdrawal and alcohol withdrawal delirium. Am J Respir Crit Care Med. 2011;183: A3164.

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ВИКОРИСТАННЯ ДЕКСМЕДЕТОМІДИНУ ЯК АДЬЮВАНТА ДО БЕНЗОДІАЗЕПІНІВ ДЛЯ СЕДАЦІЇ ПАЦІЄНТІВ ЗІ СТАНОМ ВІДМІНИ АЛКОГОЛЮ: РАНДОМІЗОВАНЕ КОНТРОЛЬОВАНЕ ДОСЛІДЖЕННЯ

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Дексмедетомідін має ефект контрольованої седації та пригнічує адренергічну систему без впливу на дихання, що робить його перспективним агентом для контрольованої седації пацієнтів зі станом відміни алкоголю (СВА). Метою даного рандомізованого контрольованого дослідження було оцінити безпечність та ефективність додавання дексмедетомідину до стандартної терапії діазепамом у пацієнтів зі СВА. Всі пацієнти були рандомізовані до двух груп: дексмедетомідину (група D; n = 36) і контролю (група C; n = 36). У групі D інфузію розпочинали зі швидкістю 0,2–1,4 мкг/кг/год і титрували до досягнення цільового рівня седації (-2 до 0 за шкалою Річмонда) з додаванням бензодіазепінів за симптом-залежним протоколом (10 мг діазепаму болюс). Пацієнти в контрольній групі отримували тільки болюси діазепаму за симптом-залежним протоколом. За результатами дослідження пацієнти в групі D мали достовірно кращу якість седації та комунікації з медичним персоналом (p <0,001), дотовірно менша кількість пацієнтів, потребували призначення галоперидолу. Всі пацієнти залишалися на спонтанному диханні. Брадикардія була більш частим побічним ефектом в Групі D. Таким чином, інфузія дексмедетомідіну підвищувала якість контрольованої седації, комунікації з пацієнтом та зменшувала споживання діазепаму і потребу у призначенні галоперидолу.

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ИСПОЛЬЗОВАНИЕ ДЕКСМЕДЕТОМИДИНА КАК АДЬЮВАНТА БЕНЗОДИАЗЕПИНОВ ДЛЯ СЕДАЦИИ ПАЦИЕНТОВ С СИНДРОМОМ ОТМЕНЫ АЛКОГОЛЯ: РАНДОМИЗИРОВАННОЕ КОНТРОЛИРУЕМОЕ ИССЛЕДОВАНИЕ

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Дексмедетомидин имеет седативный эффект и подавляет адренергическую систему без влияния на дыхание, что делает его перспективным препаратом для контролируемой седации пациентов с синдромом отмены алкоголя (СОА). Целью данного рандомизированного контролируемого исследования было оценить безопасность и эффективность применения дексмедетомидина как адьюванта к стандартной терапии диазепамом у пациентов с СОА. Все пациенты были рандомизированы на две группы: дексмедетомидина (группа D; n = 36) и контроля (группа C; n = 36). В группе D инфузию дексмедетомидина начинали со скоростью 0,2-1,4 мкг/кг/ч и титровали до достижения целевого уровня седации (-2 до 0 по шкале Ричмонда) с добавлением бензодиазепинов по симптом-зависимому протоколу (болюс диазепама 10 мг). Пациенты в контрольной группе получали только болюсы диазепама по симптом-зависимому протоколу. По результатам исследования пациенты в группе D имели достоверно лучшее качество седации и коммуникации с медицинским персоналом (p <0,001), достоверно меньшее количество пациентов нуждались в назначении галоперидола. Брадикардия была более частым побочным эффектом в группе D. Таким образом, инфузия дексмедетомидина повышала качество контролируемой седации, коммуникации с пациентом и уменьшала потребление диазепама и потребность в назначении галоперидола.