

Delirium in Geriatric Patients with Hip Fracture

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Summary. *Introduction.* Delirium occurs in up to 87% of the intensive care unit (ICU) patients and is associated with numerous poor outcomes. The drug most commonly used to treat delirium is haloperidol, a centrally acting dopamine antagonist. Dexmedetomidine, a selective alpha2-adrenergic agonist, is another promising agent for the treatment of ICU-associated delirium. The aim of this study was to evaluate the frequency and risk factors of delirium and the treatment efficacy of dexmedetomidine vs. haloperidol in elderly patients treated in ICU for hip fracture.

Methods. The study included 207 geriatric patients hospitalized for hip fracture at the Institute of Traumatology and Orthopedics in Astana in 2017–2018 (data of 199 patients analyzed). The frequency and structure of delirium, as well as the efficacy of dexmedetomidine in the treatment of delirium compared with haloperidol, were evaluated. In the study, the patients were divided into 2 groups: a group of patients who developed delirium, and a control group. Subsequently, the patients with delirium were divided into two subgroups: subgroup D (dexmedetomidine subgroup) and subgroup H (haloperidol subgroup).

Results. The prevalence of delirium among geriatric patients of orthopedic and traumatological profile was 78%. On the first day after surgery, delirium developed in 48% of patients, of whom half were diagnosed with a hypoactive form of delirium. The first signs of delirium were most common on the second day with a mean duration of delirium of 2 days. The Barthel index was 44.3 ± 1.7 points in the delirium group and 70 ± 2.3 points in the control group ($p < 0.05$). The length of stay in the ICU in the dexmedetomidine subgroup was significantly shorter than in the haloperidol subgroup (1.9 ± 0.3 vs. 3.3 ± 0.2 days, respectively, $p = 0.001$). The duration of delirium was also shorter in the dexmedetomidine subgroup compared to the haloperidol subgroup (1.1 ± 0.2 vs. 2.3 ± 0.4 days, respectively, $p = 0.014$).

Conclusions. Delirium developed in 78% of geriatric patients treated in the ICU for hip fracture. Physical and cognitive dysfunction before surgery was associated with a higher incidence of delirium. Dexmedetomidine showed better efficacy compared to haloperidol in shortening the duration of both delirium and treatment in the ICU.

Keywords: delirium, geriatric patients, hip fracture, dexmedetomidine.

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INTRODUCTION

Delirium has been found to be the most prevalent psychiatric disorder in the hospital setting, especially in intensive care unit (ICU), with a prevalence of up to 87% in different ICU patient groups. Moreover, it is associated with increased mortality and morbidity [1]. Thus, delirium is a

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significant diagnostic and therapeutical challenge in the ICU, defined as an acute and fluctuating disturbance of consciousness and cognition [2]. Validated screening tools have improved the diagnosis and daily assessment of delirium and are now recommended as the standard for the delirium management [3].

Treatment of delirium includes non-pharmacologic (e.g., early physical therapy, reorientation, sleep hygiene) and pharmacologic (e.g., antipsychotics, sedatives, dexmedetomidine) strategies [4]. Haloperidol remains the most widely used agent for the treatment of agitation and/or delirium in ICU. However, dexmedetomidine, an alpha2-adrenergic receptors agonist, has shown its efficiency in the treatment of delirium in intubated and non-intubated patients [5]. Its use in the intensive care setting has grown over the years due to its favorable effect on reducing incidence and duration of delirium [6].

The proportion of gerontological patients hospitalized for hip fracture is steadily increasing [7]. Due to the presence of comorbidities and frailty, such patients are often admitted to the ICU. The development of delirium seriously complicates the recovery period after trauma and increases mortality in elderly patients with hip fractures. The frequency of postoperative delirium in this category of patients, according to different authors, ranges from 13 to 55.9% [8]. Various delirium prevention strategies such as minimal sedation during hip fracture repair have been carried out, regrettably with minimal effect [9]. Obviously, such a significant difference in performance is due to the lack of uniformity and clarity in identifying and documenting symptoms of delirium and, moreover, to different approaches to delirium management.

OBJECTIVE

The aim of this study was to evaluate the frequency and risk factors of delirium and the treatment efficacy of dexmedetomidine vs. haloperidol in elderly patients treated in the ICU for hip fracture.

METHODS

Approval of the Ethics Committee of Astana Medical University JSC (protocol No. 2 dated March 16, 2017) for the study was obtained. The study included 207 patients with hip fracture admitted on an emergency basis to the emergency room in the period 2017–2018 and hospitalized in the ICU postoperatively. In the study, the patients were divided into 2 groups: the main group included patients who developed delirium and the control group included patients without delirium. Subsequently, patients with delirium were divided into two subgroups depending on the treatment: subgroup D (sedation was performed with dexmedetomidine) and subgroup H (sedation was performed with haloperidol).

Inclusion criteria:

- Informed consent of patients or their caregivers to participate in the study
- Age of patients 60 years and more
- Traumatological profile of patients (hip fractures)
- The need for surgery followed by admission to the ICU

Exclusion criteria:

- Lack of voluntarily signed informed consent
- Long-term use of psychotropic drugs
- Severe and moderate dementia
- Traumatic brain injury
- Alcohol and drug abuse
- Any type of dialysis
- Aphasia and gross visual impairment

8 patients were excluded from the study (5 of them did not receive surgical treatment and 3 of them needed dialysis). Preoperative care was provided within 24 hours of admission to the hospital. The presence of comorbidities and medication were identified by talking with the patient himself or his relatives or from the data provided by the outpatient card. The diagnosis of delirium was established on the basis of daily examination and survey according to ICD-10 and DSM-V criteria and was confirmed using the CAM-ICU scale. Depending on the degree of sedation needed, the dose of sedative was selected. The choice of therapy was carried out by the doctor-intensivist. In subgroup D, the starting rate of dexmedetomidine infusion was 0.7 µg/kg/h and the maintenance dose was 0.2–1.4 µg/kg/h. Haloperidol was administered to the patients of subgroup H at a dose of 0.10–0.15 µg/kg intravenously. Titration of the dose was carried out in accordance with the Richmond Agitation Sedation Scale (RASS) level of sedation. If the patient's sedation according to the RASS was more than +1 score, it was necessary to decrease the sedative dose to achieve target level of sedation which was RASS score from –2 to +1. In the case of excessive sedation corresponding to RASS score from –3 to –5, the administration of the drug was interrupted until RASS score from –2 to 0 was reached and subsequently the patient's arousal and agitation was monitored. In the postoperative period, pain intensity was evaluated using the behavioral pain scale (BPS). Arterial and venous blood samples were taken to evaluate oxygenation in all groups on admission, on the 1st, 3rd, and 5th day after surgical intervention. Mortality was assessed within 30 days from admission to the ICU and two months after discharge from the hospital.

Proximal femoral nail (PFN) or gamma nail fixation (GNF) blocking osteosynthesis was performed for intertrochanteric hip fractures, while unipolar arthroplasty under spinal anesthesia with 0.5% bupivacaine at a dosage of 10–15 mg was performed for cervical hip fractures.

Statistical analysis was completed using SPSS 19 (USA, 2016). Comparison of the two groups by quantitative trait with a normal distribution of values was performed using Student's t-test for independent samples. Comparison of two independent groups on a quantitative basis with abnormal distribution was carried out using the

non-parametric Mann-Whitney U test. To compare two independent groups on a binary basis, four-field conjugacy tables were compiled using Pearson’s classical chi-square test (χ^2). In all tests, p value less than 0.05 was considered significant.

RESULTS

There was no statistically significant difference between the two groups with respect to gender and comorbidities (Table 1). The average age in the group with delirium was 80.7±0.9 years which was comparable to the control group 77.4±0.8 years (p=0.060). There were no significant differences in fracture characteristics and type of surgery (Table 2).

The average age in the dexmedetomidine (D) subgroup was 81.8±0.9, whereas in the haloperidol (H) subgroup, the average age was 79.7±0.7 (p=0.063). When comparing the subgroups by comorbidities, the nature of the injury, and the type of surgical treatment, there was no difference. Initially, all participants in the study had a low oxygen status: PaO₂=84.95±1.5 mm Hg, PvO₂=38.3±1.16 mm Hg, SaO₂=91.8±0.5%, SvO₂=48.2±1.6%; P/F remained within normal limits: 337.4±11.4 mm Hg. It was found that in the group with delirium the above parameters were lower than in the control group (Fig.).

Determination of the cognitive status of patients. On admission, the initial cognitive status of all patients was assessed using the Mini-Mental State Examination (MMSE) scale, which was 25.4±3.3 points. The proportion of distribution within this scale was as follows: 46.7% of the study participants had mild dementia (MMSE 20–23), 33.7% had mild cognitive impairment (MMSE 24–27), and only 19.6% had no significant cognitive impairment (MMSE 28–30) (Table 3).

The subjects of the main group were divided into subgroups. When conducting a comparative analysis, it was found that in the control group, normal cognitive status was significantly more often (36.4%) than in delirium subgroups (D=17.4% vs. H=12.8%, p<0.05).

Assessment of the level of physical activity in geriatric patients with hip injury. It was revealed that 13.1% of the study participants were completely inactive and 51.3% had a low level of activities of daily living. An average level of activity was observed in 33.1% of cases and only 2.5% of patients showed gross activity. On admission, the functional state of patients according to the Barthel index in the delirium group was lower than in the control group. In the group with delirium, the Barthel index corresponded to 44.3±1.7 points compared to 70±2.3 points (p<0.05) in the control group without delirium. A comparative analysis of the functional state in everyday life was conducted between subgroups and

Table 1. Patient gender and comorbidities in study groups

	Delirium (n=155)	Control (n=44)	p value
Gender			
Female	81.3% (126)	72.7% (32)	0.304
Male	18.7% (29)	27.3% (12)	
Comorbidities			
Diabetes	6.2% (11)	16% (7)	0.133
Arterial hypertension	65.2% (101)	72.7% (32)	0.448
Atherosclerotic cardiovascular disease	64.5% (100)	47.7% (21)	0.066
Chronic cardiac failure	35.5% (55)	31.8% (14)	0.786
Chronic renal insufficiency	6.4% (10)	11.3% (5)	0.444
Chronic obstructive pulmonary disease	15.4% (24)	9% (4)	0.406
Brain vascular disease	33.0% (51)	16% (7)	0.045

Table 2. Characteristics of fractures and surgery in study groups

	Delirium (n=155)	Control (n=44)	p value
Fracture characteristics			
Intertrochanteric fracture	63.2% (98)	63.6% (28)	0.899
Cervical hip fracture	36.8% (57)	36.4% (16)	
Type of surgery			
Proximal femoral nail	56.8% (88)	54.5% (24)	0.928
Gamma nail fixation	7.1% (11)	9.1% (4)	0.906
Unipolar prosthetics	36.1% (56)	36.4% (16)	0.881

Table 3. Cognitive assessment in study groups

MMSE points	Delirium (n=155)	Control (n=44)	p value
28–30	14.8% (23)	36.4% (16)	0.003
24–27	33.5% (52)	34.1% (15)	0.910
20–23	51.7% (80)	29.5% (13)	0.016

MMSE – mini-mental state examination

controls. In subgroup D, the Barthel index was 42.3±2.2 points, in subgroup H – 46.16±2.5 points, whereas in the control group – 70±2.3 points.

Dynamics of oxygenation. On admission, all patients had poor blood oxygenation (Table 4).

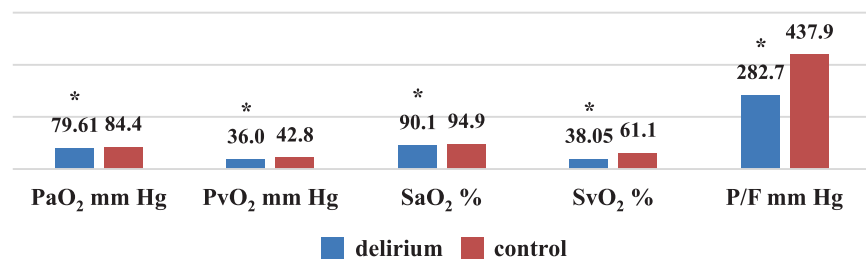


Fig. Data of arterial and venous blood gas samples in the patients
Note: *p<0.05 between the group with delirium and the control group

Table 4. Comparative analysis of the oxygen status in the delirium subgroups and control group

Groups	On admission	Study time (day)		
		1	3	5
PaO ₂ (mm Hg)				
D	79.1±2.5	84.1±2.9	79.7±2.4	76.3±1.8**
H	77.1±2.9	78.0±1.7*	70.6±1.9**	75.2±2.2**
C	84.4±1.5	89.5±3.7	87.3±2.9	90.1±4.1
PvO ₂ (mm Hg)				
D	36.1±1.9*	39.3±2.5	40.7±2.2	41.1±2.5
H	35.9±1.8*	33.5±1.6*	32.4±1.3**	36.7±1.4**
C	36.7±2.0	41.1±1.8	44.0±1.8	46.6±1.8
SaO ₂ (%)				
D	90.9±0.7**	90.5±0.8**	89.7±0.9**	90.5±0.7**
H	89.3±0.9**	88.5±1.0**	89.0±1.1**	89.2±1.0**
C	94.9±0.6	94.4±0.6	94.2±0.7	94.0±0.6
SvO ₂ (%)				
D	38.5±2.0**	39.5±2.5**	40.4±2.7**	40.5±2.5**
H	37.6±1.9**	37.8±2.4**	38.5±2.5**	40.2±2.7**
C	61.1±2.0	68.3±2.2	70.3±1.8	70.1±2.0
P/F (mm Hg)				
D	298.3±10.4**	269.5±12.0**	245.1±12.2**	279.9±11.3**
H	267.1±11.4**	268.0±12.4**	244.2±12.9**	264.2±10.8**
C	437.9±22.8	430.7±23.0	455.7±20.7	409.0±15.6

Note: *p<0.05 between the subgroup and the control group, **p 0.001 between the subgroup and the control group. D - dexmedetomidine subgroup, H - haloperidol subgroup, C - control group.

Table 5. Length of stay in ICU (days)

Indicator	Subgroup D (n=69)	Subgroup H (n=86)	p value
Length of stay of the patients in the ICU	1.9±0.3	3.3±0.2	0.001

ICU - intensive care unit, D - dexmedetomidine subgroup, H - haloperidol subgroup

Prevalence and structure of delirium. Delirium developed in 78% of geriatric patients treated in the ICU for hip fracture. The prevalence of delirium was 17.2% on admission, 48.7% one day after surgery, and 34.1% on the 3rd postoperative day. The hypoactive form was found in 52.4% of the study participants, hyperactive - in 35.3%, and mixed - in 12.3%. The leading clinical symptoms of the hypoactive delirium were psychomotor retardation and apathy while hyperactive delirium, on the contrary, was characterized by agitation, psychomotor agitation, or even aggression. The mixed form showed signs of both. Delirium started at 2.0±1.4 days of admission with an average duration of 2.2±1.2 days.

Comparative evaluation of the efficacy of dexmedetomidine and haloperidol for sedation of geriatric patients with hip fractures. With the development of delirium, either dexmedetomidine or haloperidol was adminis-

tered. The choice of the drug was made by the ICU doctor. In subgroup D, the starting rate of dexmedetomidine infusion was 0.7 µg/kg/h, while the maintenance rate was 0.2-1.4 µg/kg/h. Haloperidol was administered to the patients of subgroup H at a dose of 0.10-0.15 µg/kg intravenously. The duration of delirium in the subgroup D was 1.1±0.2 days compared with the subgroup H where the duration of delirium was 2.3±0.4 days (p=0.014). Length of stay in the ICU department in subgroup D was shorter than in subgroup H (Table 5).

The average consumption of narcotic analgesics in the subgroup with dexmedetomidine was twice lower than in the subgroup with haloperidol. Thus, the average consumption of trimeperidine hydrochloride in patients of subgroup D was 6.9 mg vs. 14.1 mg in subgroup H (p=0.004). Mortality in the group with delirium was 3.2% two months after discharge from the hospital compared with the control group where the number of deaths was zero.

DISCUSSION

Delirium occurs in approximately 20% of older people after hip fracture repair [10]. According to our study about half of our patients developed delirium on the first day after surgery. It should be noted that half of them had a hypoactive form of delirium which often goes unnoticed.

Risk factors for developing delirium in ICU in general and in the elderly group of patients with hip fracture were investigated in several studies and meta-analyses. The latest systematic review showed strong evidence that older age, dementia, hypertension, pre-ICU emergency surgery or trauma, higher Acute Physiology and Chronic Health Evaluation II score, mechanical ventilation, metabolic acidosis, delirium on the prior day, and coma are risk factors for delirium in the ICU [11]. A meta-analysis of 24 studies involving a total of 5,364 patients with hip fractures showed that elderly patients with preoperative cognitive impairment, advanced age, heart failure, total hip arthroplasty, multiple comorbidities, morphine use, and institutional living were more likely to develop delirium after hip surgery [10]. However, in our study, neither gender, comorbidities, fracture site, nor type of surgery affected the incidence of delirium, but a higher risk of developing delirium was associated with pre-existing physical and cognitive dysfunction.

Hypoxic events in 48 hours after multiple injuries without intracranial hemorrhage do not directly correlate with ICU delirium or long-term cognitive impairment [12]. However, we found that elderly patients with lower saturation on admission had greater risk to develop delirium. According to other studies, neither anemia, uremia, nor bilirubin were associated with a higher risk of delirium, and only metabolic disturbances can precipitate delirium. We did not analyze the impact of acid base balance on the delirium, however, we can speculate that lower oxygen delivery to the cell may lead to some metabolic changes.

Haloperidol remains the most widely used agent for the treatment of agitation and/or delirium in ICU however,

dexmedetomidine, an alpha2-adrenergic receptor agonist, has shown its efficiency in treating delirium in intubated and non-intubated patients. Several studies have found that dexmedetomidine is a promising treatment for ICU-associated delirium and may be useful as a rescue drug for delirium in patients in whom haloperidol has failed [13, 14]. In our study, we also found that dexmedetomidine is superior to haloperidol for elderly patients with hip fracture. Dexmedetomidine was associated with a shorter duration of delirium and stay in ICU compared to haloperidol.

CONCLUSIONS

Delirium developed in 78% of geriatric patients treated in the ICU for hip fracture. Physical and cognitive dysfunction before surgery was associated with a higher incidence of delirium. Dexmedetomidine showed superior efficacy compared to haloperidol resulting in a shorter duration of both delirium and ICU stays.

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SENŲVO AMŽIAUS PACIENTŲ, PATYRUSIŲ ŠLAUNIKAULIO PROKSIMALINĖS DALIES LŪŽI, DELYRAS

Santrauka

Įvadas. Delyras pasireiškia iki 87 % reanimacijos ir intensyvio- sios terapijos skyriaus (RITS) pacientų ir yra susijęs su daugeliu rizikos veiksnių. Dažniausiai delyru gydyti vartojamas haloperidolis, centrinio veikimo dopamino antagonistas. Tačiau deksmedetomidinas, selektyvus alfa 2 adrenerginis agonistas, yra perspektyvus vaistas gydant delyrą RITS. Šio tyrimo tikslas yra įvertinti pagyvenusių pacientų, gydytų RITS dėl šlaunikaulio lūžio, delyro dažnį, rizikos veiksnius ir gydymo veiksmingumą, skiriant deksmedetomidiną arba haloperidolį.

Tiriamieji ir tyrimo metodas. Į tyrimą įtraukti 207 geriatriniai pacientai, hospitalizuoti dėl šlaunikaulio lūžių į Astanos traumatologijos ir ortopedijos institutą 2017–2018 m. (analizuoti 199 pacientų duomenys). Įvertintas delyro dažnis, delyro pobūdis, rizikos faktoriai ir palygintas deksmedetomidino ir haloperidolio veiksmingumas, jį gydant. Tyrimo metu pacientai buvo suskirstyti į 2 grupes: pacientų, kuriems išsivystė delyras, grupę ir kontrolinę grupę. Pacientai su delyru buvo suskirstyti į du pogrupius: D pogrupio pacientams buvo skirtas deksmedetomidinas, H pogrupio – haloperidolis.

Rezultatai. Delyro dažnis tarp traumatologinio profilio geriatrinų ligonių siekė 78 %. Pirmą parą po operacijos delyras išsivystė 48 % pacientų, iš jų hipoaktyvi delyro forma buvo diagnozuota pusėi atvejų. Dažniausiai delyras pasireiškė antrą parą, o vidutinė trukmė buvo 2 dienos. Delyrą turinčioje grupėje Barthelio indeksas atvykus buvo 44,3 ± 1,7 balo, kontrolinėje grupėje – 70 ± 2,3 balo, p < 0,05. Deksmmedetomidino grupėje gulėjimo RITS trukmė buvo daug trumpesnė – 1,9 ± 0,3 dienos, lyginant su haloperidolio grupe – 3,3 ± 0,2 dienos, p = 0,001. Deksmmedetomidino grupėje delyro trukmė taip pat buvo trumpesnė – 1,1 ± 0,2 dienos, lyginant su haloperidolio grupe – 2,3 ± 0,4 dienos, p = 0,014.

Išvados. Delyras išsivystė 78 % geriatrinų pacientų, gydytų RITS dėl šlaunikaulio lūžio. Fizinė ir kognityvinė disfunkcija prieš operaciją buvo susijusi su didesniu delyro dažniu. Deksmmedetomidinas parodė geresnį veiksmingumą, lyginant su haloperidoliu, nes sutrumpino tiek delyro, tiek gydymo RITS trukmę.

Raktažodžiai: delyras, senyvi pacientai, šlaunikaulio lūžis, deksmedetomidinas.

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