

## Dexmedetomidine as an Alternative for the Prevention of Delirium in Cardiac Surgery Patients

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### ABSTRACT

**Background:** Postoperative delirium is a serious complication in cardiac surgery patients, which leads to the development of long-term cognitive impairment, dementia, long-term hospitalization and this is becoming an important socio-economic problem in the modern world.

**Purpose of the study:** Evaluation of the effectiveness of using dexmedetomidine as part of multicomponent anesthesia for the prevention of postoperative delirium in cardiac surgery patients.

**Material and methods:** The study was conducted in the surgical clinic of the AMU. The study included 90 patients who underwent planned coronary artery bypass grafting at the age of 55-85 years with no history of mental disorders or dementia. The patients were divided into 2 groups: The main group (using dexmedetomidine) and the control group. During the work, the following examination methods were performed on all patients: A thorough study of the anamnesis; mean arterial pressure, heart rate; duration of anesthesia and surgery; the need for inotropic (dopamine) and vasopressor (norepinephrine) support; the presence of postoperative delirium, its duration and the number of points on the Nu-DESC scale; duration of mechanical ventilation; the length of patients' stay in the intensive care unit and in the hospital. The Nu-DESC scale was used to diagnose postoperative delirium. A result of  $\geq 2$  was considered positive.

**Results and discussion:** Postoperative delirium was detected in only 10 patients: 1 in the main group (with dexmedetomidine) and 9 in the control group. The incidence of postoperative delirium was 2.57%, compared to 28.5% in the control group.

**Conclusions:** Intraoperative dexmedetomidine infusion does not significantly increase the duration of prolonged mechanical ventilation in patients. Dexmedetomidine does not affect the length of the patient's stay in the intensive care unit or the length of hospitalization.

**Keywords:** Delirium; Dexmedetomidine; Cardiac surgery; Anesthesia

## INTRODUCTION

Delirium is an undesirable outcome in cardiac surgery patients in the intensive care unit, which contributes to the development of cognitive impairment in the postoperative period [1]. To reduce the incidence of postoperative delirium and its duration, both drug and non-drug preventive measures are used at four stages: Preoperative, intraoperative and postoperative. At the preoperative stage, risk factors should be assessed for each

individual patient. It is recommended to avoid routine use of benzodiazepines for premedication and anticholinergic agents. In recent years, dexmedetomidine has been included in delirium treatment and prevention protocols and has been used in patients at high risk of developing postoperative delirium. During the intraoperative period, it is necessary to monitor the depth of anesthesia, since too deep anesthesia provokes the development of postoperative delirium. In the postoperative period, both non-drug methods (orientation of the patient in

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time and space, ensuring adequate sleep, the minimum required number of catheters, early mobilization and nutrition) and drug use of dexmedetomidine are preferable for prevention [2].

## MATERIALS AND METHODS

The study was conducted in the surgical clinic of the AMU. The study included 90 patients who underwent planned coronary artery bypass grafting at the age of 55-85 years with no history of mental disorders or dementia. All operations were performed under multicomponent combined anesthesia with artificial ventilation of the lungs. The patients were divided into 2 groups: The main group (using dexmedetomidine) and the control group. Phenazepam 2 mg per os was used as premedication in the evening before the operation. Also, before admission to the operating room, midazolam was administered intravenously to patients at a rate of 0.1 mg/kg. After premedication in the operating room, additional peripheral venous access was provided by catheterization of the superficial veins of the forearm. During the entire time the patient was in the operating room, continuous monitoring of arterial pressure, five-lead electrocardiogram, pulse oximetry, central and peripheral temperature, hourly diuresis and capnometry were performed. Induction in patients of the control group was performed with propofol 2 mg/kg, fentanyl 8 mcg/kg and rocuronium bromide 0.6 mg/kg. After performing orotracheal intubation and connecting patients to automatic respirators, catheterization of the internal jugular vein and radial artery was performed. Patients of the main group (with dexmedetomidine) were given a loading dose of dexmedetomidine 1 mcg/kg within 10 minutes before induction of anesthesia. Then, 1 mg/kg propofol, 5 mcg/kg fentanyl, and 0.6 mg/kg rocuronium bromide were administered intravenously. Patients of the main group were given dexmedetomidine at a dose of 0.5 mcg/kg/h from the moment of installation of the central venous catheter, radial artery and until 2 hours after the end of the operation. Anesthesia was maintained in patients of both groups using sevoflurane, fentanyl and rocuronium bromide. In patients of

both groups who underwent surgery using a heart-lung machine, anesthesia was also maintained with propofol, fentanyl and rocuronium bromide during its operation [3]. Artificial ventilation of the lungs was performed using a semi-closed circuit with a fabius plus drager breathing apparatus in the IPPV mode under conditions of normoventilation (paCO<sub>2</sub> 32-35 mmHg) with an oxygen-air mixture with FiO<sub>2</sub> 0.4-0.5 and control of gas concentrations (O<sub>2</sub>, EtCO<sub>2</sub>, sevoflurane) during inhalation and exhalation. Monitoring of gas exchange parameters and respiratory mechanics was performed based on the analysis of blood gas composition. All patients received infusion therapy with crystalloid solutions. Infusion therapy was based on hemodynamic parameters, central venous pressure and diuresis rate. In the event of hypotension that was not corrected by infusion therapy, inotropic drugs (dopamine, norepinephrine) were used, the doses of which were selected individually depending on the patient's hemodynamic needs and were administered through perfusor Braun syringe infusion pumps. After the operation, all patients were transferred to intensive care units in a state of drug-induced sleep on artificial ventilation. In patients of the main group (group with dexmedetomidine), dexmedetomidine administration continued for 2 hours after the operation. And in patients of the control group, sedation was performed with propofol at a dose of 120-150 mg/kg. During the work, the following examination methods were performed on all patients: A thorough study of the anamnesis; mean arterial pressure, heart rate; duration of anesthesia and surgery; the need for inotropic (dopamine) and vasopressor (norepinephrine) support; the presence of postoperative delirium, its duration and the number of points on the Nu-DESC scale; duration of mechanical ventilation; the length of patients' stay in the intensive care unit and in the hospital. The Nu-DESC scale was used to diagnose postoperative delirium (Table 1). A result of  $\geq 2$  was considered positive [4].

**Table 1:** Nu-DESC delirium screening scale.

Disorientation	0	Awake, oriented in space, time and person
	1	Disoriented, but can easily be oriented
	2	Disoriented in 2-3 areas and cannot be oriented easily
Behavior	0	Calm and cooperative
	1	Concerned but cooperative
	2	Excited, trying to get out of bed, take off devices
Communication	0	Normal
	1	Unclear thinking or incoherent speech
	2	Incoherent, meaningless, unintelligible speech
Illusions /hallucinations	0	Not marked

1	Paranoia, fear
2	Hallucinations or distortion of visible objects

## RESULTS AND DISCUSSION

Postoperative delirium was detected in only 10 patients: 1 in the main group (with dexmedetomidine) and 9 in the control group. The incidence of postoperative delirium was 2.57%, compared to 28.5% in the control group. Our study results showed that even at low doses (0.5 mcg/kg/h), dexmedetomidine is effective in preventing delirium. By reducing the dose required to achieve the desired result, we reduced its costs per patient and thereby

increased the availability of this method for the prevention of delirium in the postoperative period. The diagnosis of postoperative delirium was carried out using the Nu-DESC scale. In 8 of the patients studied, the test result was positive, i.e., the number of points on this scale was  $\geq 2$ . And 24 patients scored 0 points during the assessment. The remaining 18 patients received a score of 1 point, which corresponds to a mild impairment of one of the mental functions studied (Table 2) [5].

**Table 2:** Nu-DESC scale scores by groups.

Nu-DESC scale scores	Main group (with dexmedetomidine)	Control group
0	18	9
1	6	9
$\geq 2$	1	7

In the main group (with dexmedetomidine), postoperative delirium developed in only one patient, lasted 8 hours and was stopped by intravenous administration of 1 ml of 0.5% haloperidol. In the control group, 7 cases of postoperative delirium development were noted, lasting from 16 to 48 hours.

Haloperidol was also used to stop the attack, and only in one case was aminazine 50 mg intramuscularly used. To assess the

effect of dexmedetomidine on hemodynamics, a comparison was made of the value of the mean arterial pressure and the frequency of mean contractions during the induction of anesthesia, 15 minutes after the beginning and at the end of it. The obtained data on the mean arterial pressure are shown in Tables 3 and 4.

**Table 3:** Change in mean arterial pressure in the study groups.

Mean arterial pressure	Main group (min-max) mmHg	Control group (min-max) mmHg
During induction of anesthesia	66,0 (60,0-89,0)	60,6 (52,0-87,8)
15 minutes after the start of the operation	65,0 (51,0-83,9)	63,5 (53,5-71,5)
At the end of the operation	65,9 (52,0-74,0)	63,5 (56,2-82,2)

**Table 4:** Changes in heart rate in the study groups.

Heart rate	Main group (min-max)	Control group (min-max)
During induction of anesthesia	50,0 (42,0-68,0)	51,0 (43,0-62,0)
15 minutes after the start of the operation	49,0 (37,0-75,0)	52,0 (45,0-67,0)
At the end of the operation	67,0 (59,0-98,0)	64,5 (49,2-75,2)

During coronary artery bypass grafting, inotropic and vasopressor agents were required to correct hypotension. To assess the effect of dexmedetomidine on hemodynamic

parameters, changes in the dose of dopamine and norepinephrine were also compared in different groups, which are presented in Table 5.

**Table 5:** Comparison of drug responses between main and control groups.

Drug	Main group	Control group
Dopamine	28	22
Norepinephrine	10	14
Total	29	28

Suppression of the patient's hemodynamics negatively affects blood circulation in the vessels of the brain, which is extremely sensitive to hypoxia and therefore, among other things, leads to an increased risk of developing neurological complications. Therefore, hypotension and bradycardia, the most common side effects of dexmedetomidine due to its effect on central  $\alpha$ -adrenergic receptors, are of particular concern when using it. These complications are noted in different studies, Tosun et al. and Sheikh et al. [6]. Thus, Tosun et al. note that after the administration of dexmedetomidine, systolic blood pressure significantly decreases (106 versus 124) in the control group, although 2 hours after the end of the infusion, the indicators of both groups equalize. In patients receiving dexmedetomidine in the study by Sheikh et al., mean arterial pressure was lower than in the control group (receiving propofol) from induction to anesthesia and until the end of surgery. However, in this study, the patient groups did not differ in either mean arterial pressure or heart rate. These discrepancies may be explained by the fact that these studies used a different dexmedetomidine administration scheme: A loading dose of 0.5-1.0 mcg/kg/h for 10 minutes, then administration of the drug at a rate of 0.2-0.6 mcg/kg/h until the end of the operation. Consequently, it is the loading dose that contributes to hemodynamic depression, and its refusal to use it increases the safety of the drug, while preserving its preventive properties in relation to postoperative delirium. According to the data obtained, dexmedetomidine also does not require an increase in the doses of inotropic and vasopressor drugs, which indirectly confirms the hypothesis of the absence of hemodynamic depression when it is used. Similar results were obtained in 2018 by Sheikh et al.

Numerous studies have shown that the development of delirium in the postoperative period leads to an extension of the time spent in intensive care and hospitalization, and therefore to an increase in the cost of treatment. Since dexmedetomidine reduces the incidence of postoperative delirium, does not suppress hemodynamics and does not prolong the duration of artificial ventilation in the patient, it could be assumed that due to these properties, when it is used, the duration of hospitalization will decrease, as well as the number of days spent by patients in the intensive care unit [7].

However, our data show that dexmedetomidine has no effect on either the length of hospitalization or the length of stay in the intensive care unit. These findings are consistent with the world literature.

Thus, it can be concluded that perioperative dexmedetomidine infusion reduces the risk of postoperative delirium in cardiac surgery patients. The use of dexmedetomidine in low doses (0.5 mcg/kg/h), without the use of a loading dose, is beneficial for intraoperative hemodynamics, does not cause the most common complications for this drug bradycardia and hypotension, does

not require additional inotropic and vasopressor support. Due to its minimal effect on respiration, dexmedetomidine does not prolong artificial ventilation of the patient's lungs and therefore the time of his stay in the intensive care unit. However, the hypothesis that the use of dexmedetomidine can reduce the duration of the patient's stay in the intensive care unit and in the hospital has not been confirmed. Thus, dexmedetomidine can be used in anesthesia care during aortocoronary bypass in patients with a high risk of developing postoperative delirium as a means of preventing its occurrence [8].

## CONCLUSIONS

- Perioperative use of dexmedetomidine reduces the incidence of delirium after coronary artery bypass grafting from 28.5% to 2.57%.
- When using dexmedetomidine at a dosage of 0.5 mcg/kg/h without a loading dose, the drug does not have a significant effect on hemodynamics and does not require an increase in inotropic or vasopressor support.
- Intraoperative dexmedetomidine infusion does not significantly increase the duration of prolonged mechanical ventilation in patients.
- Dexmedetomidine does not affect the length of the patient's stay in the intensive care unit or the length of hospitalization.

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