DEXMEDETOMIDINE USED IN THE PREVENTION AND TREATMENT OF INTENSIVE CARE UNIT DELIRIUM

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Abstract: *A 41-year-old patient, victim of a car accident developed ICU delirium after several days of intensive care stay being treated with dexmedetomidine. Objectives. The purpose of this presentation is to show the importance of using dexmedetomidine for the prevention and treatment of ICU delirium, a frequent ICU-related pathology with narrow therapeutic options. Material and method. The patient was admitted to our ICU, following a car accident, with respiratory failure due to multiple rib fractures, without neurological lesions, no parenchymal organ damage. Results. On the fifth day of ICU, the patient underwent orthopedic surgery under general anesthesia with endotracheal intubation (American Society of Anesthesiology score III. In the immediate postoperative period, the patient was continuously sedated with opioid (fentanyl) and benzodiazepine (midazolam). On the second postoperative day and the eighth day of intensive care stay, the continuous sedation was gradually withdrawn and the patient was extubated. The patient was hemodynamically stable, but he developed restlessness, increased quantity of motor activity and showed a positive confusion assessment method for the ICU score, with poor psychomotor reflexes. Treatment with haloperidol was initiated for two days with no response. On the tenth day of hospitalization, dexmedetomidine was administered (0.2 mcg/kg/h). Treatment with dexmedetomidine was continued for the next 10 days. The patient had a positive treatment-response to dexmedetomidine and was released from ICU on day 27. Conclusion. Dexmedetomidine, an important drug in intensive care but lacking in Romania, would be of great benefit for the patients who develop ICU-delirium. It also decreases the requirements for opioid-analgesics due to its alpha-2 receptor agonist.*

INTRODUCTION

Dexmedetomidine is an alpha 2 receptor agonist that has sedative, analgesic effects and does not depress ventilation. Dexmedetomidine lowers sympathetic tone, with attenuation of the neuroendocrine and hemodynamic responses to anesthesia and surgery; it reduces anesthetic and opioid requirements, and causes sedation and analgesia. It allows psychomotoric function to be preserved while letting the patient rest comfortably. Dexmedetomidine has adverse effects like hypotension, bradycardia, and sympathetic rebound. In general, presynaptic activation of the $\alpha_2$adrenoceptor inhibits the release of norepinephrine, terminating the propagation of pain signals. Postsynaptic activation of α_2 adrenoceptors in the central nervous system (CNS) inhibits sympathetic activity and thus, it can decrease blood pressure and heart rate. Combined, these effects can produce analgesia, sedation, and anxiolysis. Dexmedetomidine combines all these effects, thus avoiding some of the side effects of multiagent therapies.

ICU delirium is an acute confusional state with attention deficit, disordered thinking, and a fluctuating course. Up to 80% of mechanically ventilated ICU patients develop delirium and it is associated with many negative outcomes such as increased lengths of ICU stay, decreased survival and increased cognitive dysfunction.(2) Physiologically, delirium is characterized by a derangement of cerebral metabolism with cerebral dysfunction and it is usually caused by a general medical illness, intoxication, or substance withdrawal.(4,5)

There are three subtypes of delirium, hyperactive (often called ICU psychosis), hypoactive (also called quiet delirium), and mixed (fluctuation between hypo and hyper).(1) The two most common types of delirium in the ICU are mixed and hypoactive. Hypoactive delirium is more frequently in older patients compared with other types of delirium and has a worse prognosis.(6)

Numerous studies have found ICU delirium to be associated with many negative outcomes, such as: increased ventilation days, longer ICU and hospital lengths of stay, increased costs, higher mortality, long term cognitive dysfunction.(3) When copmared with other sedatives, like benzodiazepines, dexmedetomidine is associated with fewer episodes of delirium.(3) Patients trated with dexmedetomidine spent less time on the ventilator, experienced less delirium, and developed less tachycardia and hypertenssion, and the most notable adeverse effect of dexmedetomidine was bardycardia.(7)

CASE REPORT

A 41-year-old man, weight 105 kg, height 172 cm was admitted to the ICU following a car accident with multiple lesions, mainly fractures (multiple ribs fractures and hip fracture, without neurological lesions, without parenchymal organ damage, fracture of nasal pyramid, fracture of the left maxillary sinus wall, fracture of the left orbit, left zygomatic arch fracture.

After appropriate care in the emergency department

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the patient was admitted to our ICU. Upon arrival, the patient was conscious, Glasgow Coma Score-GCS-of 15 points, with cold extremities, with decreased bread sounds on the lower left pulmonary lobe, hemodynamically stable with a blood pressure of 146/ 80 mmHg and a heart rate of -120 b/min, with normal urine outpit.

Our ICU, treatment plan included pain management with analgesics (metamizol, tramadol, cyclooxygenase 2 -COX-2 inhibitors), antibiotics (3^{rd} generation cephalosporin and a fluoroquinolone), stress ulcer prophylaxis (with proton pomp inhibitor), hepatoprotective, prophylactic anticoagulation for DVP-deep venous thrombosis with a low molecular weight heparin.

The patient had a favourable outcome under this treatment. On day 5 of intensive care, the patient was transported to the orthopedics operating theatre, where general anesthesia with endotracheal intubation was preformed for acetabular fixation with plate and screw through left olecranon. The surgery was uneventful.

After the surgery, the patient was taken to intensive care without reversal of anesthesia, intubated, mechanically ventilated in an assisted mode, hemodynamically stable.

The treatment plan initiated on admission was resumed with the addition of a benzodiazepine and an opioid (midazolam, 50 mcg/kg/h and fentanyl 1microg/kg/h). The patient was sedated until the 8^{th} ICU day. On the 9^{th} day, the patient was extubated, but immediately became agitated. We initiated haloperidol at 2,5 mg iv for a total of 3 doses. The use of haloperidol was ineffective during the 9^{th} day. On the 10^{th} day, dexmedetomidine was initiated in a dose of 0.2 mcg/kgc/h. The treatment with dexmedetomidine was continued for ten days. The patient had a positive treatment response to dexmedetomidine and the patient was discharged from intensive care on day twenty seven.

DISCUSSIONS

Our patient developed a hyperactive type of delirium; this type is the most frequent form of ICU delirium with bad outcomes.

The treatment with haloperidol was not effective in this case, although haloperidol is the first choice for the pharmacological treatment of delirious patients, and so, we used dexmedetomidine, stopping the opioid and benzodiazepine therapy. Dexmedetomidine is, in many countries, the first line of therapy for sedation and analgesia in ICU, and the study showed that this drug decreases the incidence of ICU delirium.

The time of treatment with dexmedetomidine was over the recommendation of guidelines because of the pressure exercised by de provider and by the need of the patient who became almost euphoric and refused other analgesic medications, raising the suspicion of a possible addictive effect of dexmedetomidine.

This is the first case when dexmedetomidine was used in the treatment of ICU delirium in our hospital.

CONCLUSIONS

Dexmedetomidine, an important drug in intensive care but lacking in Romania, would be of great benefit for the patients who develop ICU-delirium. It also decreases the requirements for opioid-analgesics due to its alpha-2 receptor agonist.

Dexmedetomidine significantly shortened the time to extubation and decreased ICU length of stay.

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