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Interventional therapy of diabetes mellitus type 2 complicated with acute cerebral hemorrhage by using dexmedetomidine

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ABSTRACT

Objective: To study the effects of dexmedetomidine on cerebral injury, inflammation, oxidative stress and renal function of patients with diabetes mellitus type 2 complicated with acute cerebral hemorrhage.

Methods: A total of 98 cases who had been diagnosed with diabetes mellitus type 2 complicated with acute cerebral hemorrhage and treated with interventional therapy in Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine from September 2014 January 2016 were chosen to be our study subjects. Among them, 50 cases given dexmedetomidine treatment in the process of anesthesia were included in the dexmedetomidine group (Group A), while the other 48 cases treated with equal amount of normal saline were considered as the negative control group. The postoperative cerebral injury indexes and the serum biochemical indexes were detected after 24 h.

Results: The contents of serum S100β [(2.1 ± 0.2) μg/L] and neuron-specific enolase (NSE) [(14.2 ± 1.3) μg/mL] in Group A were all significantly lower than serum S100β [(2.9 ± 0.3) μg/L] and NSE [(16.6 ± 1.7) μg/mL] of patients in negative control group. The contents of cerebrospinal fluid S100β [(0.9 ± 0.1) μg/L] and NSE [(10.7 ± 1.3) μg/mL] in Group A were all significantly lower than cerebrospinal fluid S100β [(1.3 ± 0.2) μg/L] and NSE [(15.3 ± 1.7) μg/mL] of patients in negative control group. The contents of erythrocyte sedimentation rate [(11.7 ± 2.5) mm/h], c-reactive protein [(2.3 ± 0.4) mg/L], urea nitrogen [(10.7 ± 1.2) mmol/L] and serum creatinine [(151.6 ± 14.9)] μmol/L in Group A were all significantly lower than erythrocyte sedimentation rate [(23.6 ± 3.8) mm/h], c-reactive protein [(6.9 ± 1.1) mg/L], urea nitrogen [(16.7 ± 1.7) mmol/L] and serum creatinine [(192.5 ± 18.3)] μmol/L of patients in negative control group.

Conclusions: The application of dexmedetomidine in the interventional therapy of diabetes mellitus type 2 complicated with acute cerebral hemorrhage could protect brain and renal functions and reduce systemic inflammatory responses.

1. Introduction

Diabetes is a kind of common metabolic disorders characterized by a systemically chronic progressive increase of blood sugar level. Due to its long disease course, it can easily lead to metabolic disorders and affect systems of heart, renal, eye, nerve and so on. Cerebrovascular disease is one of the common complications of diabetes with an incidence rate of 20%–40%. The basic pathological of the disease is atherosclerosis[1–3]. In recent years, people have paid more and more attentions to the effect of dexmedetomidine on sedating, controlling the stress response and inhibiting the apoptosis of nerve cells in the perioperative period which has been used in the management and the protection of nerve function in the perioperative period of neurosurgical operation[4,5]. This study aimed to discuss the application and value of dexmedetomidine in patients with diabetes mellitus type 2 complicated with acute cerebral hemorrhage during the perioperative period.

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The study protocol was performed according to the Helsinki declaration and approved the Ethics Committee of Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine. Informed written consent was obtained from the selected patients and their families.

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2. Materials and methods

2.1. Clinical data

A total of 98 patients who had been diagnosed with diabetes mellitus type 2 complicated with acute cerebral hemorrhage, given interventional therapy in Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine from September 2014 to January 2016 and met the following inclusion criteria were selected to be the study subjects. The inclusion criteria required that the chosen patients should show the first-ever cerebral hemorrhage, have a history of diabetes and be treated with surgical intervention, while patients with severe hepatic and renal dysfunction, history of mental illnesses and long-term application of opioid drugs would be excluded. This study was confirmed and approved by the Ethics Committee of our hospital and consents from the selected patients and their families were obtained.

The endpoint of all the selected patients was conducted for 1 week after surgery. Patients given dexmedetomidine treatment in the process of anesthesia were included in the dexmedetomidine group (Group A), while patients treated with equal amount of normal saline were included in the negative control group (NC group).

2.2. Experimental methods

According to the process that whether patients were treated with dexmedetomidine during surgery or not, those 98 patients were divided into two groups. Patients given dexmedetomidine were regarded as Group A (n = 50), while patients without dexmedetomidine were considered as NC group (n = 48). All selected patients received routine anesthetic induction (midazolam, propofol, atracurium, etomidate, fentanyl); laryngeal masks were placed to manage their airways and 1%–2% sevoflurane was used to maintain anesthesia in the operation. At 5 min before the operation, dexmedetomidine (0.5 μg/kg/h) was infused intravenously in patients in Group A, which would stop at 20 min before the surgery was finished. Patients in NC group were given equal amount of normal saline by the same way. On 24 h after surgery, 5 mL peripheral venous blood and 2 mL cerebrospinal fluid samples of patients in the two groups were collected. Chemiluminescence immunoassay was used to test the contents of S100β and neuron-specific enolase (NSE). ELISA was used to determine the c-reactive protein (CRP) content; Westergren method was applied to examine erythrocyte sedimentation rate (ESR); fully automatic biochemistry analyzer was employed to detect blood urea nitrogen (BUN), serum creatinine (Cr), aspartate aminotransferase (AST) and alanine aminotransferase (ALT); and myocardial enzyme spectrum detection was used to detect the contents of creatine kinase (CK) and CK-MB.

2.3. Statistical methods

The experimental data were typed and analyzed by SPSS 20.0.0. Measurement data were expressed by mean ± SD and analyzed by t-test and enumeration data were presented by frequency and analyzed by Chi-square test. Differences were statistically significant ($P < 0.05$).

3. Results

3.1. General data of the study subjects

Among those 98 cases, 50 of them were treated with dexmedetomidine. They were included in Group A. In Group A, 29 cases were males and 21 were females aging from (51 ± 6) years with a body mass index (BMI) of (24.2 ± 2.8) kg/m^2, preoperative blood glucose of 8–15 mmol/L [the average was (11.2 ± 0.8) mmol/L], disease courses of diabetes of 8–15 years [the average was (11.7 ± 1.5) years] and Glasgow coma scale (GCS) of 5–9 scores [the average was (6.8 ± 0.7) scores]. The other 48 cases were not treated with dexmedetomidine in the process of anesthesia. They were included in NC group. In NC group, 27 cases were males and 21 were females aging from (53 ± 5) years with a BMI of (24.6 ± 2.5) kg/m^2, preoperative blood glucose of 9–16 mmol/L [the average was (11.9 ± 1.2) mmol/L], disease courses of diabetes of 7–13 years [the average was (10.9 ± 1.7) years], GCS of 6–9 scores [the average was (6.7 ± 0.6) scores]. After statistically analyzing, it was found that the levels of genders, ages, BMI, blood glucose, disease courses, and GCS of the two groups showed no differences ($P > 0.05$).

3.2. Brain injury indexes

The serum indexes S100β of brain injury [(2.1 ± 0.2) μg/L] and NSE [(14.2 ± 1.3) μg/mL] of patients in the Group A were all significantly lower than those [(2.9 ± 0.3) μg/L and (16.6 ± 1.7) μg/mL, respectively] of patients in the NC group. Moreover, their cerebrospinal fluid indexes S100β of brain injury [(0.9 ± 0.1) μg/L] and NSE [(10.7 ± 1.3) μg/mL] of patients in the Group A were also distinctly lower than those [(1.3 ± 0.2) μg/L and (15.3 ± 1.7) μg/mL, respectively] in NC group ($P < 0.05$).

3.3. Serum biochemical index

On 24 h after surgery, ESR [(11.7 ± 2.5) mm/h], CRP [(2.3 ± 0.4) mg/L], BUN [(10.7 ± 1.2) mmol/L] and Cr [(151.6 ± 14.9) μmoL] in patients of Group A were all significantly lower than those [(23.6 ± 3.8) mm/h, (6.9 ± 1.1) mg/L, (16.7 ± 1.7) mmol/L and (192.5 ± 18.3) μmol/L, respectively] in patients of NC group. The differences of AST, ALT, CK and CK-MB between two groups showed no statistical significance (Table 1).

Table 1
Postoperative renal function indexes of patients in Group A and NC group.

Parameters	Group A (n = 50)	NC group (n = 48)	P
ESR (mm/h)	11.7 ± 2.5	23.6 ± 3.8	< 0.05
CRP (mg/L)	2.3 ± 0.4	6.9 ± 1.1	< 0.05
BUN (mmol/L)	10.7 ± 2.1	16.7 ± 2.8	< 0.05
Cr (μmol/L)	151.6 ± 30.4	192.5 ± 29.3	< 0.05
AST (IU/L)	12.3 ± 2.3	11.8 ± 2.5	> 0.05
ALT (IU/L)	15.8 ± 3.1	14.3 ± 2.7	> 0.05
CK (mmol/L)	214.3 ± 35.8	231.8 ± 40.7	> 0.05
CK-MB (mmol/L)	11.2 ± 2.5	10.9 ± 2.1	> 0.05

4. Discussion

Patients with diabetes complicated with cerebral hemorrhage are common in clinic. Interventional therapy has been proved to be an effective way to treat the disease. CT scan was used to determine the hematoma, and then a blunt needle core was placed in the hematoma slowly to suck and wash in order to eliminate the hematoma by haemostatic. During the interventional therapy of cerebral hemorrhage, situations such as cyclic drastic fluctuations, normal brain tissue injuries around the hemorrhage site and important organ dysfunctions may happen. Therefore, how to improve safety for patients during anesthesia and surgery has been the key point of clinical researches at present[6,7]. Dexmedetomidine is a kind of α2 receptor agonist of high selectivity. The receptor selectivity (α2:α1) is 1620:1. It has a role to play in sedation, analgesia, anti-anxiety and anti-sympathetic nerve activity, and it can also inhibit the increase of plasma catecholamine caused by surgical stimulation, which is conductive to the stability of haemodynamics in anesthesia[8,9]. Dexmedetomidine is applied successfully in many general surgery operations. It was explained elaborately in this study whether it works positively in treatments of neurosurgery such as cerebral hemorrhage operation.

Secondary anoxia would often happen followed by cerebral hemorrhage in patients with diabetes mellitus type 2, which aggravated brain injury. After cerebral hemorrhage happened, due to pathologic change such as cerebrovascular injury and cerebral ischemia and anoxia, a large amount of free radicals were produced by *in vivo* xanthine oxidase system and arachidonic acid metabolism to strengthen lipid peroxidation and damage biological membrane[10]. Dexmedetomidine can protect the brain injury by decreasing its anti-sympathetic nerve activity, anti-inflammation, anti-oxidation and anti-apoptosis and improving the balance of cerebral oxygen supply and consumption during the period of ischemia. Traditional concepts claim that the nerve protection function is related to the inhibited locus coeruleus-eliminated methylepinephrine neuronal excitation, which worked by influencing the inset of action potential and releasing neurotransmitter[11,12]. The latest research states that α2 adrenaline receptor sub-types can protect the nerve. Intracerebral α2 adrenaline receptors gather in pons participating in the transmission of the sympathetic nerve signals from the main center to peripheral region. S100β proteins mainly distribute to the central nervous system and NSE specificity exists in neuron and neuroendocrine cells. After the neuron is damaged, S100β and NSE can be produced in abundance, which serves as a sensitive index for central nervous system injury[13–15]. It was found in the analysis of the contents of postoperative serum and cerebrospinal fluid related factors of patients with diabetes mellitus type 2 complicated with cerebral hemorrhage that on 24 h after surgery, the contents of S100β and NSE of patients treated with dexmedetomidine were decreased significantly. It could be concluded that dexmedetomidine played a protective role in treating cerebral hemorrhage during interventional therapy. It could reduce brain function injury for patients by decreasing neuron damage and increasing expressions of multiple growth factors[16,17].

CRP is the earliest inflammatory factor which appears in post-traumatic stress responses. Its great expression and release are closely related to the formation of encephaledema, destruction of blood-brain barrier and nerve degeneration[18]. The serum level of CRP can reflect the injury degree of brain tissues sensitively. The value of ESR was related to plasma viscosity, especially the cohesion between red blood cells. The stronger in the cohesion between red blood cells is, the higher the ESR is. All kinds of inflammations and tissue injury can accelerate ESR for patients. That is the inescapable consequence of the copious secretions of inflammatory factors including CRP, which can reflect the injury degree of cerebral hemorrhage operation indirectly[19]. After detecting the postoperative levels of ESR and CRP of patients in the two groups, it was found that the levels of postoperative ESR and CRP in patients of Group A were pretty low, which was related to the sedative and analgesic effects induced by dexmedetomidine through activating post-synaptic receptor. Dexmedetomidine could decrease sympathomimetic activity overall and inhibit the surgery-stimulated excitability of the sympathetic nervous system effectively[20–22].

When cerebral hemorrhage happens in patients with diabetes, it may cause concomitant injuries of important organ functions such as heart, liver and kidney, which might be related to the changes of multiple hormones levels in the body circulation. No significant differences have been found in the detection of the early postoperative myocardial enzymes indexes (CK and CK-MB) and liver function indexes (ALT and AST) of the two groups, which indicated that the application of dexmedetomidine in anesthesia could not influence the heart and liver functions distinctly[23]. Many domestic and abroad researches revealed that patients with acute cerebral hemorrhage may be accompanied with different degrees of decreased glomerular filtration rates, which has something to do with the renal ischemia injury. Renal ischemia injury is mainly caused by hypovolemia due to dehydration and limited liquid intake after cerebral hemorrhage interventional treatment. In interventional treatment of cerebral hemorrhage, mannitol, a commonly used dehydrating agent, could injury kidneys slightly[10]. When cerebral hemorrhage involved in hypothalamic-pituitary-adrenocortical system, which can increase diencephalon, rennin-angiotensin and thrombokinase and decrease glomerular filtration rate and neurons renal dysfunction may occur[24–26]. BUN and Cr are the commonest indexes reflecting renal function in clinic and they can embody the glomerular filtration effect. The latest study has shown that dexmedetomidine, to some degree, can protect renal functions. In this study, it was found in the detection of postoperative early renal function indexes in patients of the two groups that the values of serum BUN and Cr in patients treated with dexmedetomidine during operation are lower. It could be concluded that dexmedetomidine can protect renal function to some extend in interventional treatment of cerebral hemorrhage for patients with diabetes mellitus type 2. The renal function protection effect of dexmedetomidine may be related to its anti-sympathetic nerve activity, glomerular filtration rate improvement, reduction of the release of sympathetic-mediated renal presynaptic norepinephrine[27–29].

In conclusion, the application of dexmedetomidine in the interventional therapy in patients with diabetes mellitus type 2 complicated with acute cerebral hemorrhage could protect brain and renal functions and reduce systemic inflammatory responses.

Conflict of interest statement

The authors report no conflict of interest.

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