Scientific Research Publishing

Advances in Bioscience and Biotechnology, 2022, 13, 454-459
https://www.scirp.org/journal/abb
ISSN Online: 2156-8502
ISSN Print: 2156-8456

Study on Analgesia and Sedation of Butorphanol Tartrate Combined with Dexmedetomidine in Severe Cerebral Hemorrhage for Patients with Mechanical Ventilation

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How to cite this paper: Yang, G., Yang, S.J. and Wang, C.B. (2022) Study on Analgesia and Sedation of Butorphanol Tartrate Combined with Dexmedetomidine in Severe Cerebral Hemorrhage for Patients with Mechanical Ventilation. *Advances in Bioscience and Biotechnology*, **13**, 454-459.
https://doi.org/10.4236/abb.2022.1310030

Received: April 31, 2022
Accepted: October 14, 2022
Published: October 17, 2022

Abstract

Objective: To analyze the effect and advantages in analgesia and sedation of butorphanol tartrate combined with dexmedetomidine in severe cerebral hemorrhage for patients with mechanical ventilation. **Methods:** 120 patients with severe cerebral hemorrhage requiring analgesia and sedation were randomly selected and divided into two groups: the control group (dexmedetomidine treatment group) and the test group (dexmedetomidine combined with butorphanol tartrate). Two groups of patients with different drugs were analyzed. **Results:** The average dose of dexmedetomidine (microgram) and the total adverse events (Times) in the test group were significantly lower than those in the control group within 48 hours ($P < 0.05$); The dose of Butorphanol in the test group was small, and the patients in the control group used other opioid analgesics to pump more significantly. **Conclusion:** Using butorphanol tartrate combined with dexmedetomidine can achieve the same sedative effect and enhance the analgesic effect as using dexmedetomidine alone with less dose of dexmedetomidine, and the clinical effect is significant. It also solves the problem that adverse reactions such as blood pressure change and bradycardia are easy to occur when using large dose of dexmedetomidine and the infusion speed is fast in clinical application, and significantly reduces the incidence of adverse reactions. It is worthy of clinical application.

Keywords

Butorphanol Tartrate, Dexmedetomidine, Severe Cerebral Hemorrhage,

Mechanical Ventilation, Analgesia and Sedation

1. Materials and Methods

1.1. General Information

From October 2020 to June 2022, 120 patients with severe intracerebral hemorrhage requiring analgesia and sedation were selected. All patients were ≥ 18 years old and had no contraindications for dexmedetomidine and butorphanol. Exclusion criteria: severe heart, lung, liver and kidney failure; allergic to dexmedetomidine and butorphanol; age ≥ 80 years. The patients were randomly divided into two groups: the control group was treated with dexmedetomidine, and the test group was treated with dexmedetomidine combined with butorphanol tartrate.

1.2. Methods

Patients in the control group were treated with 0.9% normal saline with dexmedetomidine (200 μg/2ml) to 50 ml and the first dose 1 μg/kg static push with 10 minutes, after loading dose, micro pump of 0.2 - 1 $\mu g \cdot kg^{-1} \cdot h^{-1}$ was continuously infused intravenously, and the Richmond agitation sedation scale (RASS) was evaluated at an interval of 2 h. If the RASS score was −2 - 1, it was unnecessary to adjust the dose and continue to maintain the pump for ≥ 48 h; If the score is more than 1, the pump dose will be increased according to the patient, up to 1.5 $\mu g \cdot kg^{-1} \cdot h^{-1}$; If the score is less than −2 points, it is 0.2 - 1 $\mu g \cdot kg^{-1} \cdot h^{-1}$, adjust the dose appropriately to make the RASS score between −2 and 1, and pump continuously for ≥ 48 h; If the (Critical care Pain Observation Tool, CPOT) score in the intensive care unit is more than 3 and the maximum dose of dexmedetomidine is reached, pump with other opioid analgesics.

The patients in the test group were given 200 mg/L butorphanol (10 mg plus 40 ml normal saline to make 50 ml) on the basis of the treatment scheme of the control group, and the dosage of butorphanol was 20 - 30 $\mu g \cdot kg^{-1} \cdot h^{-1}$ initial dose was pumped in. If (Critical care Pain Observation Tool, CPOT) score in the intensive care unit is ≤ 3, it is unnecessary to adjust the dose and continue to pump for ≥ 48 h; If the score is more than 3 points, increase the pump dose according to the patient; If the pumping dose reaches 30 $\mu g \cdot kg^{-1} \cdot h^{-1}$, CPOT score > 3, pump injection of other opioid analgesics may be considered.

The sedation effect of both groups reached RASS-2-1, and the analgesic effect reached CPOT score ≤ 3.

1.3. Efficacy Evaluation Criteria

The dosage of dexmedetomidine and the occurrence of adverse reactions were observed and the RASS and CPOT scores of the two groups were compared; compound other opioid analgesics pumping.

Adverse reactions during medication, including obvious heart rate lower than 50 beats/min, lasting for more than 10 minutes, and mean arterial pressure lower than 60 mmhg, lasting for more than 10 minutes.

1.4. Statistic Analysis

SPSS 19.0 statistical software was used to process the data. The measurement data were expressed as mean ± standard deviation (x ± s), and t-test was used. The counting data were χ^2 test, $P < 0.05$, the difference was statistically significant.

2. Results

The average dose of dexmedetomidine (microgram) and the total adverse events (Times) in the test group were significantly lower than those in the control group within 48 hours ($P < 0.05$); The dose of butorphanol in the test group was small, and the patients in the control group used other opioid analgesics to pump more significantly. (Table 1)

3. Discussion

Neurosurgery patients need safe and reasonable sedation and analgesia to treat, eliminate or reduce the pain and discomfort of patients, reducing stress reaction so as to facilitate medical care operation, maintaining the stability of vital signs, and more importantly, brain protection improves prognosis [1] [2] [3]. There is an urgent need for safe and effective analgesia and sedation programs in clinical work.

Dexmedetomidine hydrochloride and butorphanol tartrate injection are two promising drugs with different pharmacological characteristics in severe neurological diseases; Dexmedetomidine hydrochloride is a novel and highly selective G-protein coupling agent *α*2 adrenergic receptor agonist, an imidazole derivative, which produces sedation, analgesia, hypnosis, anti-anxiety and other effects by acting in the locus coeruleus nucleus of the brain stem *α*2A receptor, and maintains natural non eye movement sleep. It is characterized by maintaining

Table 1. Comparison between two groups after treatment.

Groups	cases	Average use of dexmedetomidine (microgram) within 48 hours	Average use of butorphanol within 48 hours (mg)	Total occurrence of adverse events (Times)	Compound use of other opioid analgesics (Times)
control group	60	3550	/	56	12
test group	60	2460	14.6	19	0

the patient's consciousness while sedating, and has no obvious respiratory inhibition. It can be safely used in Neurosurgery ICU patients [4] [5] [6].

When butorphanol tartrate injection has no opioid in vivo μ Receptor agonists, it is mainly dose-dependent and has a ceiling effect κ Receptor analgesia. In Patients with receptor agonists exert antagonism μ Receptors, alleviating or eliminating μ Side effects such as respiratory inhibition of receptors and agitation κ Analgesic effect of receptors.

Butorphanol tartrate injection has an effect on κ Receptors, the effect on δ receptor is not obvious, and μ receptor has the dual effects of agonism and antagonism, and has the intensity effect on κ, δ, μ was 25:4:1. Due to this unique effect of butorphanol tartrate injection on opioid receptors, it has the following clinical application characteristics: 1) it has good analgesic effect of opioid drugs and little clinically significant respiratory inhibition; 2) it rarely causes decrease of gastrointestinal activity and spasm of smooth muscle; 3) rarely cause skin itching; 4) rarely causing urinary retention; 5) somatic dependence is extremely low [7] [8] [9] [10] [11]. Butorphanol tartrate injection has been widely used in analgesia treatment such as postoperative pain in China, and it is commonly administered by intravenous, intramuscular injection and nasal spray.

There has been a consensus at home and abroad that dexmedetomidine should be used for analgesia and sedation of surgical patients. However, in clinical, it is found that dexmedetomidine is easy to cause adverse reactions such as blood pressure change and bradycardia when it is applied at a large dose and the infusion speed is fast, and the analgesic effect of dexmedetomidine alone is not good. Our previous clinical shows that dexmedetomidine hydrochloride combined with butorphanol tartrate has the advantages of rapid sedation and analgesia in neurosurgical patients, easy wake-up, stable hemodynamics, mild respiratory inhibition, low incidence of delirium and other adverse reactions [12] [13].

Dexmedetomidine combined with butorphanol for sedation for patients with mechanical ventilation after severe intracerebral hemorrhage is rarely reported at home and abroad. This study finds the effective analgesia and sedation for patients with mechanical ventilation after severe intracerebral hemorrhage and guide clinical medication.

Through the comparative study of two groups of patients, it was found that under the condition of no significant difference in RASS and CPOT scores between the two groups, the dosage of dexmedetomidine and the incidence of adverse reactions in the test group were significantly lower than those in the control group. The dosage of butorphanol in the test group was small, and the patients in the control group used other opioid analgesics for pumping.

Dexmedetomidine combined with butorphanol has a synergistic effect in sedation and sedation treatment of mechanical ventilation patients after severe intracerebral hemorrhage, which can significantly reduce the dosage of dexmedetomidine and reduce the occurrence of serious adverse reactions.

4. Conclusion

Using butorphanol tartrate combined with dexmedetomidine can achieve the same sedative effect and enhance the analgesic effect as using dexmedetomidine alone with less dose of dexmedetomidine, and the clinical effect is significant. It also solves the problem that adverse reactions such as blood pressure change and bradycardia are easy to occur when using large dose of dexmedetomidine and the infusion speed is fast in clinical application, and significantly reduces the incidence of adverse reactions. It is worthy of clinical application.

Fund-Supported Projects

"Xingchen" Scientific Research Fund project.

Zhejiang Health Development Foundation 2019ZA127, 2019ZD059.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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