Effects of different doses of dexmedetomidine on analgesic efficacy and inflammatory cytokines in patients undergoing laparoscopic surgery

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Abstract. The effects of different doses of dexmedetomidine on analgesic efficacy and inflammatory cytokines in patients with laparoscopic surgery were investigated. A total of 179 laparoscopic patients from March 2015 to May 2017 were enrolled and randomly divided into the control group (group A) and three experimental groups with different doses of dexmedetomidine (group B: 0.25; group C: 0.5 and group D: 1 μg/kg). Results showed that there was no significant difference between the four groups in the operation time, the amount of surgical bleeding and intraoperative fluid infusion. The VAS score of group A was significantly higher than the other three groups. In addition, the VAS score of group D at each time-point was the lowest. There was no significant difference regarding the agitation score and sedation score between group A and group B. Furthermore, the restlessness score and sedation score in group C were significantly lower than those in group A and group B. Next we found that CRP and TNF-α in group A and group B were significantly higher than those in groups C and D. In addition, IL-10 in group D was significantly higher than that in group C. Moreover, patients in group C had the least adverse reaction effects. In conclusion, medium dosage of dexmedetomidine cannot only effectively relieve the pain of laparoscopic patients but also regulate the secretion of inflammatory cytokines.

Introduction

Patients receiving hysteroscopic and laparoscopic surgery commonly experience severe pain during surgery. In addition, there is a relatively great impact on the nervous system at the same time (1,2). As an anesthetic adjuvant drug, dexmedetomidine has a good sedative effect in surgery. Also, dexmedetomidine is an adrenergic receptor agonist with good efficacy on sedation, anti-anxiety and neuroprotection (3-5).

In this study, patients receiving hysteroscopic and laparoscopic surgery in our hospital were selected and given different doses of dexmedetomidine, respectively, to explore the anesthetic effects of the drug in the process of surgery and determine the optimal dose for achieving the best efficacy.

Patients and methods

Objects of study. A total of 179 patients who received laparoscopic surgery in The First People's Hospital of Wujiang District (Suzhou, China) from March 2015 to May 2017 were selected and randomly divided into the control group and three groups with different doses of dexmedetomidine. Among them, the control group (group A) included 42 patients aged 23-43 years, with an average age of 34.4±7.3 years; the low-dose group (group B) included 47 patients, aged 22-44 years, with a mean age of 35.4±6.8 years; the middle-dose group (group C) had 45 patients, aged 22-45 years, with a mean age of 34.9±6.4 years; and the high-dose group (group D) had 45 patients, aged 23-44 years, with a mean age of 36.9±6.8 years. There were no significant differences in age and pathogenetic condition of the patients among the four groups ($p>0.05$), and the data were comparable. All patients were aware of the clinical protocol before the study and signed the informed consent. This study was approved by the Ethics Committee of The First People's Hospital of Wujiang District (Suzhou, China). Inclusion criteria were: female patients aged 20-45 years and rated as class 1 based on the America society of Anesthesiologist (ASA) classification. Exclusion criteria were: patients with mental disease or with injury in the heart, liver, kidney and other vital organs.

Methods. The four groups of patients received anesthesia induction, in which, the medication dosages were 0.6 mg·kg^{-1}, 2 mg·kg^{-1} and 2 μg·kg^{-1} for rocuronium bromide, propofol and fentanyl, respectively, and tracheal intubation was also performed. Patients in groups B, C and D were given 0.25, 0.5 and 1 μg/kg dexmedetomidine, respectively, while those in group A were administered with the same dose of 0.9% NaCl solution. Patients in each group received intravenous infusion

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Table I. Surgical situations of patients in four groups (mean ± SD).

Group	n	Operation duration (min)	Intraoperative bleeding volume (ml)	Intraoperative transfusion volume (ml)
A	42	181.2±4.5[a]	109.3±5.2[a]	2,299±102.3[a]
B	47	179.5±6.4	110.2±6.3	2,208±130.4
C	45	180.9±7.3	108.9±4.8	2,219±128.6
D	45	180.1±6.9	109.4±5.8	2,297±185.8

[a]Compared with those in the other three groups, p>0.05.

Table II. VAS scores of patients in four groups after operation (mean ± SD).

	Time (h)			
Group	2	4	12	24
A	4.2±0.9[a]	2.9±0.3[a]	2.4±0.3[a]	1.4±0.2[a]
B	2.9±0.4	2.1±0.2	1.7±0.2	0.9±0.1
C	2.7±0.3	2.0±0.2	1.6±0.1	0.7±0.1
D	2.4±0.2	1.9±0.1	1.3±0.2	0.6±0.1

[a]Compared with those in groups B, C and D, p<0.05.

for 10 min. After incubation, mechanical ventilation was carried out with tidal volume set at 8 ml/kg and respiratory rate at 8 breaths per minute. During surgery, doses of propofol and fentanyl were adjusted according to the patient's condition. When the endoscope was withdrawn, medication was stopped immediately.

Observation indicators and efficacy evaluation. The operation duration, intraoperative bleeding volume and intraoperative transfusion volume of each patient were recorded. Serum inflammatory cytokines [C-reactive protein (CRP), tumor necrosis factor-α (TNF-α) and interleukin-10 (IL-10)] of patients were detected. Visual analogue scale (VAS) scoring. Agitation scoring and Sedation scoring were also recorded for each patient (6-10).

Statistical analysis. SPSS 19.0 software (IBM, Armonk, NY, USA) was used for statistical analysis. All quantitative data were expressed as mean ± standard deviation (SD). Comparison between groups was done using one-way ANOVA test followed by post hoc test (Least Significant Difference). P-values <0.05 were considered statistically significant.

Results

Surgical situations of patients in four groups. The operation duration, intraoperative bleeding volume and intraoperative transfusion volume of the four groups of patients showed no differences (p>0.05) (Table I).

Postoperative VAS scores of patients in four groups. It was found that the VAS scores at all time-points in the control group were significantly higher than those in the other three treatment groups after operation, and the scores in group D were the lowest (Table II).

Comparison of agitation score and sedation score in patients among four groups. In comparison with group A, group C had obviously decreased agitation score and sedation score (p<0.05); there were no evident differences in agitation score and sedation score between groups A and B; sedation score in group D was clearly higher than that in group C (Table III).

Comparison of serum inflammatory cytokines in patients among the four groups. The levels of CRP, TNF-α and IL-10 in groups A, B and C were significantly increased at T2, T3 and T4, while the levels of IL-10 at T2, T3 and T4 in group D were overtly higher than that at T1 (p<0.05), while the levels

Table III. Comparison of agitation score and sedation score in patients among four groups (mean ± SD).

Group	Agitation score	Sedation score
A	2.7±0.2	1.1±0.1
B	2.2±0.2	1.1±0.1
C	1.2±0.1[a]	1.9±0.2[a]
D	2.2±0.1	5.5±0.2[a,b]

[a]Compared with group A, p<0.05. [b]Compared with group C, p<0.05.

Table IV. Comparison of serum inflammatory cytokines in patients among four groups (mean ± SD).

Group	Time	CRP (mg/l)	TNF-α (ng/l)	IL-10 (ng/l)
A	T1	11.45±2.12[a]	19.25±3.32	12.57±1.78
	T2	36.71±6.32	32.45±6.43	16.79±1.98
	T3	64.98±4.75	56.39±6.43	18.69±2.09
	T4	44.62±4.53	46.21±6.78	19.79±2.34
B	T1	11.50±1.64[a]	18.29±3.45	12.10±2.12
	T2	34.26±7.43	31.20±6.43	12.21±1.97
	T3	64.98±7.54	53.96±4.77	16.92±2.32
	T4	43.21±6.78	44.05±4.56	19.41±1.98
C	T1	11.27±2.43[a]	18.56±2.43	12.31±1.02
	T2	24.07±3.43[b]	24.15±3.45[b]	21.09±2.98
	T3	43.52±4.32[b]	36.21±3.75[b]	24.69±2.0[b]
	T4	33.21±3.86[b]	28.42±4.32[b]	25.76±2.21[b]
D	T1	11.72±2.43	18.26±4.21	12.09±1.09[a]
	T2	16.21±4.54[b]	19.45±2.11[b]	23.21±2.02
	T3	18.21±4.52[b]	22.45±2.31[b]	25.76±2.01[b]
	T4	16.52±3.87[b]	21.69±2.67[b]	24.5±62.78[b]

[a]Compared with those at T2, T3 and T4, p<0.05. [b]Compared with those in groups A and B, p<0.05.

Table V. Comparisons of adverse reactions in patients among four groups (n).

Adverse reaction	A	B	C	D
Tachycardia	9	7	0[a]	0
Bradycardia	7	7	0[a]	5
Hypertension	7	2	1[a]	2
Hypotension	2	0	1	4
Nausea and vomiting	0	1	0	0
Respiratory depression	1	1	0	0
Delayed recovery	1	0	0	1

[a]Compared with those in groups A and B, $p<0.05$.

of inflammatory cytokines in groups A and B had no significant differences. In addition, the levels of CRP and TNF-α in patients in groups A and B were clearly higher than those in groups C and D, while the increases in levels of IL-10 in groups C and D were significantly higher than those in the first two groups ($p<0.05$) (Table IV).

Comparison of adverse reactions in patients among four groups. Adverse reactions of patients in the four groups were compared, and it was found that group C had significantly fewer cases in tachycardia, bradycardia and hypertension compared with those in groups A and B. Finally, patients in group D had symptoms of bradycardia and hypotension, and sometimes hypertension and delayed recovery (Table V).

Discussion

With the development of medical devices, hysteroscope combined with laparoscope has been applied in a variety of gynecological diseases, such as uterine fibroids and uterus septum, and the use can improve the accuracy of diagnosis and cure rate, with an easy operation (11). However, during the operation, the patient may have pain and have adverse reaction effects on inflammation and nerves at the same time. Therefore, the application of an effective anesthetic method is especially important. The use of an appropriate dose of anesthetic in the operation can relieve the pain of the patient, and is also able to reduce the damage to the patient tissue (12,13).

Among anesthetics, dexmedetomidine is an adrenergic receptor agonist, which is widely used in anesthesiology. It suppresses the central and sympathetic nerves so as to reduce the tension on the sympathetic nerve and increase the activity of vagas nerve, thereby lowering the release of noradrenaline in the body and achieving the sedation effect on the patient (14,15).

Important factors for the assessment of inflammation are CRP, TNF-α and IL-10. A stress response in the body can stimulate the secretion of CRP (an acute phase protein). A trauma or an infection of the body is sure to result in a sharp increase in TNF-α, and hypersecretion of this factor can trigger an inflammatory response (16). However, IL-10 inhibits TNF-α in the body. Therefore, its increased secretion will relieve the inflammatory condition when inflammation occurs (17-20).

In this study, it was found that the cellular inflammatory cytokines CRP and TNF-α in dexmedetomidine groups were significantly lower than those in the control group, and IL-10 in groups C and D were overtly higher than those in the other two groups, indicating that the use of dexmedetomidine is able to relieve the body's inflammation and protect it from invasion of pathogens. The agitation, sedation and VAS scoring carried out on patients revealed that the control group had increased agitation and VAS scores in comparison with dexmedetomidine groups, and reduced sedation score compared with those in groups C and D. Among the three dexmedetomidine groups, the situation of agitation and sedation of patients were the best in group C, so the dose of 0.5 μg/kg was the optimal dose. It was also found that the number of patients with adverse reactions was the minimum in group C and significantly lower than those in groups A and B, and there was a greater number of cases with symptoms of bradycardia and hypotension in group D, which also well proved that the dose of 0.5 μg/kg was the best choice. This study found that the patients in the three dexmedetomidine groups had few effects on T-lymphocyte subsets, which could ensure stable T-lymphocyte subsets in patients.

In conclusion, the use of dexmedetomidine in patients undergoing hysteroscopic surgery can relieve the patient's pain, decrease the release of inflammatory cytokines *in vivo* and protect cellular immunity. Dexmedetomidine has a high clinical therapeutic value, which is worth promoting and applying in clinical practice.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

ZW and JW designed the study. HC and LW collected the patient data. ZW and JW analyzed the patient data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of The First People's Hospital of Wujiang District (Suzhou, China). All patients were aware of the clinical protocol before the study and signed the informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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