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Original Article

Anesthetic effect of butorphanol tartrate combined with dezocine in hysteroscopic surgery

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Abstract: Objective: Our aim was to investigate the sedative and analgesic effects of butorphanol tartrate combined with dezocine in hysteroscopic surgery. Methods: A total of 160 patients who voluntarily opted for hysteroscopic surgery in our hospital were randomized to fentanyl + propofol group with 40 cases (group A), butorphanol tartrate + propofol group with 40 cases (group B), dezocine + propofol group with 40 cases (group C), and butorphanol tartrate + dezocine + propofol group with 40 cases (group D). The fluctuation of mean arterial pressure (MAP), heart rate (HR), and respiratory (RR) were observed and recorded before the operation (T_0), after the induction (T_1), during the cervical dilatation (T_2), and after the operation (T_3). The number of patients with SpO_2<90% during the operation was recorded. The anesthetic effect during the surgery, the total dose of propofol, postoperative awake time, postoperative contraction pain score (VAS), and adverse reactions in the postoperative period such as nausea, vomiting, dizziness, excitement, and restlessness were all documented. Results: No distinctive difference was found in MAP, HR, and RR among these four groups at T_0 and T_3 (all P>0.05). Declines were observed in all groups at T_1 (all P<0.05) and a more pronounced decrease was seen in group A (P<0.05). At T_2, the MAP, HR, and RR of group B and group C were noticeably higher than those of group A and group D (P<0.05). The number of patients with SpO_2<90% in group A was markedly higher than that in group B, group C, and group D (P<0.05) while the number of patients with movement responses during the operation in group A and group D was much less than that in group B and group C (P<0.05). The total dose of propofol used in group A and group D was prominently less than that in group B and group C (P<0.05). There was no notable change in awake time in group B, group C, and group D but they were all apparently shorter than those in group A (all P<0.05). Postoperative VAS scores in group A and group D were markedly lower than those in group B and group C (P<0.05) and adverse reactions in the postoperative period such as nausea and vomiting in group D were apparently less than those in group A (P<0.05). Conclusion: The analgesic effect of butorphanol tartrate in combination with dezocine in hysteroscopic surgery is not only better than a single use of butorphanol tartrate or dezocine but also can achieve an equivalent sedative, analgesic, and anesthetic effect of fentanyl. Furthermore, respiratory depression, postoperative awake time, and adverse reactions in the postoperative period in patients show an outstanding benefit compared to those with fentanyl. Hence, it proves that butorphanol tartrate combined with dezocine can achieve potent anesthetic effects with less adverse reactions in hysteroscopic surgery.

Keywords: Butorphanol tartrate, hysteroscopy, dezocine

Introduction

Hysteroscopic surgery, a common gynecological examination or surgical treatment, is convenient and not time-consuming [1, 2] but the great amount of pain stimuli are virtually unbearable for patients under local anesthesia. Although anesthesia with propofol makes patients sedated, there is no analgesic effect [3, 4]. Postoperative patients tend to experience extreme contraction pains which propofol cannot alleviate. Thereby, analgesics are needed in the anesthesia of hysteroscopic surgery. Fentanyl, an opioid with a potent analgesic effect, has been commonly used as an analgesic in the past but it had obvious adverse reactions and greatly prolonged the awake time of patients. Therefore, finding new alternative medicines is of great importance in anesthesia of hysteroscopic surgery. Butorphanol tartrate (butorphanol tartrate injection) is a newly discovered mixed type opioid receptor agonist-inhibitor with prominent analgesic effects and less adverse reactions [5]. In comparison with butorphanol tartrate, dezocine is an opioid receptor agonist-antagonist with less potent

Table 1. Comparison of baseline characteristics in patients

Group	Age (years)	Body weight (kg)	ASA grade		The operation time (min)
			I	II	
Group A	48.5±5.72	62.7±7.54	22	18	30.8±5.35
Group B	46.7±6.45	64.8±6.23	23	17	32.4±4.43
Group C	50.2±4.35	60.3±8.23	19	21	28.9±6.28
Group D	47.6±5.42	63.6±4.98	21	19	29.5±7.21
P value	0.576	0.437	0.664	0.426	0.731
F value	11.76	10.89	12.82	10.73	14.25

Note: ASA, American Society of Anesthesiologists.

analgesic effects but less respiratory depression [6, 7]. In this paper, the analgesic effects and side effects of butorphanol tartrate in combination with dezocine and fentanyl, a traditional analgesic medicine, are compared to explore their clinical effects in hysteroscopic surgery.

Materials and methods

General data

This study was approved by the Hospital Ethics Committee. A total of 160 patients who voluntarily opted for hysteroscopic surgery in our hospital from July 2016 to July 2017 were recruited.

Inclusion criteria: (1) Patients who were in American Society of Anesthesiologists (ASA) grade I-II, aging from 18 to 65 years old, weighed between 40 and 80 kg were chosen. (2) Patients without a history of narcotic or analgesic drug tolerance, allergy, or addiction were recruited. (3) Patients that did not take any analgesics within 24 hours before surgery were selected. (4) Patients without functional impairment of vital organs such as heart, lung, brain, liver, and kidney were enrolled. (5) All patients voluntarily opted for anesthesia and informed consent was obtained, through which the possible risks of treatment were made known.

Study subject

A hundred and sixty patients were randomly assigned into four equal groups including 40 patients in fentanyl + propofol group (group A), 40 patients in butorphanol tartrate + propofol group (group B), 40 patients in dezocine + propofol group (group C), and 40 patients in butorphanol tartrate + dezocine + propofol group (group D).

Anesthesia treatment

All patients were fasted and water deprived for eight hours before the operation and venous accesses were placed. Blood pressure (BP), mean arterial pressure (MAP), heart rate (HR), respiration (RR), and oxygen saturation (SpO_2) were monitored and inhalation of 5 L/min O_2 by a facemask was given sufficiently before anesthesia. Patients in group A, group B, and group C were administered fentanyl 2 μg/kg, butorphanol tartrate 20 μg/kg and dezocine 5 mg by intravenous drip, respectively, while patients in group D received an intravenous infusion of dezocine 5 mg followed by butorphanol tartrate 20 μg/kg. Five minutes after being given the analgesics, the four groups of patients were injected with propofol 2 mg/kg within 30 seconds and the operations were not performed until the patients were unconscious. During the operation, propofol was administered according to patient movement response, blood pressure, heart rate, etc. Patients remained on 3 L/min oxygen inhalation by a facemask during the operation and assisted ventilations were given by supporting the mandible when SpO_2 in patients was less than 90%.

Observation index

(1) The fluctuation of MAP, HR, and RR was observed and recorded before the operation (T_0), after the induction (T_1), during the cervical dilatation (T_2), and after the operation (T_3); the number of patients with SpO_2<90% during the operation was documented as well. (2) The total dose of propofol used in patients was recorded. (3) Postoperative awake time of patients was documented. (4) After the patient was completely awake, Visual Analogue Scale (VAS) score of contraction pain in the lower abdomen was recorded: a 10 cm horizontal line on a piece of paper with 0 on one end and 10 on the other was drawn; patients were asked to mark the level of their pain on this line based on their perceptions. The higher the score, the more severe the pain would be. (5) The number of patients with postoperative anesthesia responses such as nausea, vomiting, dizziness, headache, excitement, and restlessness in the four groups of patients was recorded.

Table 2. Changes of MAP, HR, and RR at each time point in each group

Group	Time point			
	T_0	T_1	T_2	T_3
Group A				
MAP (mmHg)	92.73±9.684	71.53±7.15***	82.8±4.847	87.33±6.831
HR (times/min)	82.2±8.351	63.93±4.935**	70.47±6.424	75.2±8.205
RR (times/min)	15.73±3.515	9.87±2.2**	12.8±1.859	12.6±2.165
Group B				
MAP (mmHg)	94.13±8.903	83±5.057$^{**,\Delta\Delta\Delta}$	102.07±8.73★★★,☆☆☆	90.4±6.4
HR (times/min)	85.27±8.311	76.33±5.839$^{*,\Delta\Delta}$	91.87±4.969★★★,☆☆☆	80.8±6.085
RR (times/min)	16.67±2.059	12.4±1.882$^{*,\Delta}$	18.87±2.031★★,☆☆	13.93±2.712
Group C				
MAP (mmHg)	93.07±7.507	81.87±5.579$^{**,\Delta\Delta\Delta}$	103.07±10.33★★★,☆☆☆	90.4±6.4
HR (times/min)	84.93±9.743	75.67±8.372$^{*,\Delta\Delta}$	92.27±8.623★★★,☆☆☆	85.33±7.979
RR (times/min)	16.27±2.604	12.53±1.846$^{*,\Delta}$	18.07±2.865★★,☆☆	14.2±3.299
Group D				
MAP (mmHg)	92.27±11.09	81.93±6.181$^{**,\Delta\Delta\Delta}$	83.47±6.198	88.13±9.768
HR (times/min)	82.33±8.974	73.93±5.75$^{*,\Delta\Delta}$	73.87±5.78	79.33±7.138
RR (times/min)	16.53±2.232	12.8±2.242$^{*,\Delta}$	13.73±2.789	14.07±2.84

Note: MAP, mean arterial pressure. HR, heart rate; RR, respiratory. In comparison with T_0, *P<0.05; compared with T_0, **P<0.01; compared with T_0, ***P<0.001. In comparison with group A, $^{\Delta}$P<0.05; compared with group A, $^{\Delta\Delta}$P<0.01; compared with group A, $^{\Delta\Delta\Delta}$P<0.001. In comparison with T_1, ★★P<0.01; compared with T_1, ★★★P<0.001. In comparison with group A and group D, ☆☆P<0.01; compared with group A and group D, ☆☆☆P<0.001.

Safety assessment

If poor anesthetic effect and vigorous response to pain presented, addition of remifentanil was administered and this case was assigned as an invalid case.

Statistical analysis

Experimental data were analyzed and plotted by SPSS19 and GraphPad Prism5 software. The measurement data are expressed as mean ± standard deviation ($\bar{x}$ ± sd). Repeated measurements of variance analyses were used at various time intervals among the groups. Post-hoc Bonferroni test was adopted to compare the differences of measurement data at each time point between every two groups while the quantitative data are expressed in terms of rate. Chi-square test was used for comparisons among the groups. *P* values were judged as significant if they were less than 0.05.

Results

Patient baseline characteristics

There was no apparent difference in age, weight, ASA grade, and operation time among these four groups (P>0.05). See **Table 1**.

Changes of MAP, HR, RR, and SpO_2 at different times in four groups of patients

There was no pronounced difference in each index among these four groups before the operation (T_0) and after the operation (T_3) (all P>0.05). Each index of patients in the four groups was decreased after induction (T_1) (all P<0.05); more marked decreases were noted in group A (P<0.05) and there was no evident difference among the other three groups (P> 0.05). During cervical dilatation (T_2), no notable change was observed in each index of group A and group D while indexes of group B and group C were noticeably increased. The differences were statistically significant (all P<0.05). The number of patients with SpO_2<90% during the surgery was obviously increased in group A (P<0.05) while the other three groups showed no remarkable difference (all P>0.05). See **Tables 2** and **3**.

Comparisons of total dose of propofol, awake time, and postoperative VAS score in four groups of patients

The total dose of propofol used in group B and group C was evidently higher than that in group A and group D (all P<0.05) and there was no apparent difference between group A and

Table 3. Number of patients with SpO_2<90% during operation in the four groups

Group	Group A	Group B	Group C	Group D
SpO_2<90%	28	15*	13*	14*

Note: SpO_2, oxygen saturation. In comparison with group A, *P<0.05.

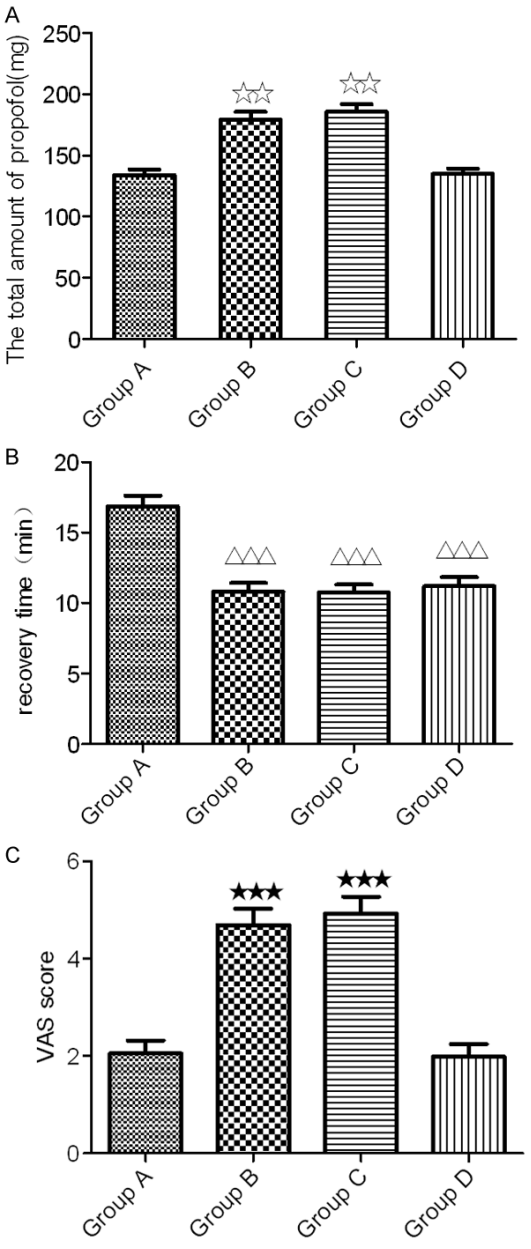

Figure 1. Comparison of total dose of propofol, awake time, and VAS score in the four groups of patients. VAS, Visual Analogue Scale; A. The total dose of intraoperative propofol used in four groups of patients: compared with group A and group D, ☆☆P<0.01; B. The postoperative awake time in four groups of patients: compared with group A, △△△P<0.001; C. The postoperative VAS scores in four groups of patients: compared with group A and group D, ★★★P<0.001.

group D (both P>0.05). The awake time of patients in group A was distinctively longer than that in the other three groups (P<0.05) and no marked difference was noted among the other three groups (all P>0.05). The VAS scores in group B and group C were prominently higher than those in group A and group D (P<0.05) and no outstanding difference was observed between group A and group D (both P>0.05). See **Figure 1**.

Comparisons of the number of patients with movement responses during the operation and with postoperative adverse reactions in the four groups

During the operation, the number of patients with movement responses in group B and group C was much more than that in group A and group D and there was no difference between group A and group D. The number of patients with adverse reactions in group A was outstandingly higher than that in group B, group C, and group D (P<0.05). No remarkable difference was found among group B, group C, and group D (all P>0.05). See **Table 4**.

Discussion

Hysteroscopy, an outpatient procedure, is often extremely painful and virtually unbearable [8, 9]. But with the discovery of propofol and the development of painless techniques in recent years, more and more clinical examinations and surgeries can be carried out under general anesthesia such as painless gastrointestinal endoscopy, painless abortion, etc. [10, 11]. Analgesics with a rapid onset of action, a wide safety margin, potent analgesic effects, and minimal side effects are expected in outpatient clinics whereas the commonly used drugs in recent years are fentanyl or sufentanil, which have a powerful analgesic effect but can easily cause respiratory depression, addiction, and severe adverse reactions [12-15]. Butorphanol tartrate and dezocine, which are highly selective for activating κ receptors, have potent analgesic effects and provide sedation of some degree [16, 17]. Butorphanol tartrate is a partial agonist at α receptors while dezocine has almost no effect on α receptors [18-19]. Thus, adverse reactions such as dysphoria seldom occur with these two medicines. In addition, with less respiratory depression, nausea, vomiting, and drug dependence, butorphanol tartrate and dezocine can partially antagonize μ

Table 4. Number of patients with movement responses during operation and postoperative adverse reactions in the four groups

Group	Movement response in operation	Nausea and vomiting	Dysphoria	Dizziness
Group A	8	13	5	9
Group B	24***	5☆☆	2	3★
Group C	25***	3☆☆	3	1★
Group D	12	6☆☆	3	4★

Note: In comparison with group A and group D, ***P<0.001; compared with group A, ☆☆P<0.01; compared with group A, ★P<0.05.

receptors as well [20-22]. Therefore, less potent analgesic effects but less adverse reactions are expected in treatment of butorphanol tartrate and dezocine in comparison with the pure opioid receptor agonist. In this paper, compared with the traditional analgesic fentanyl, butorphanol tartrate and dezocine were chosen in order to study their analgesic effects in hysteroscopic surgery, providing a clinical basis for analgesic use of butorphanol tartrate and dezocine.

The results demonstrate that after induction of anesthesia, patients with fentanyl had pronouncedly lower MAP, HR, and RR than those with butorphanol tartrate or dezocine, indicating that the patient's hemodynamics produces greater fluctuation due to the induction of fentanyl. Regardless of treatment with butorphanol tartrate, dezocine, or a combination, the effect on hemodynamics is less than that with fentanyl, illustrating that an induction of butorphanol tartrate or dezocine is more stable in comparison with fentanyl. During cervical dilatation, pain is often intense in patients undergoing hysteroscopy. This study concludes that MAP, HR, and RR are all noticeably increased in patients with a single use of butorphanol tartrate or dezocine during cervical dilatation whereas those with fentanyl or butorphanol tartrate in combination with dezocine show a negligible rise. This confirms that the analgesic effect of butorphanol tartrate or dezocine alone is not yet perfect as the patient is still sensitive to painful stimuli. Nevertheless, fentanyl and butorphanol tartrate combined with dezocine can achieve comparable analgesic effects, suggesting a synergistic effect between butorphanol tartrate and dezocine exists and a combination of the two can enhance the analgesic effect of each other. Butorphanol tartrate in combination with dezocine can not only achieve an equivalent analgesic effect of fentanyl during the operation but also the similar effect of fentanyl in pain inhibition of uterine contractions in the postoperative period. This study shows that postoperative VAS scores in patients with butorphanol tartrate or dezocine alone are higher than those with fentanyl or butorphanol tartrate combined with dezocine and no distinctive difference is observed in the latter two, further confirming that butorphanol tartrate and dezocine do have a synergistic effect.

Butorphanol tartrate in combination with dezocine can not only achieve powerful analgesic effects but also shorten the awake time of patients and reduce postoperative adverse reactions such as nausea, vomiting, dizziness, and irritability. There was no marked difference in the total dose of propofol between the fentanyl group and butorphanol tartrate in combination with dezocine group but the awake time of patients was outstandingly shortened and the number of patients with SpO_2<90% during the operation was decreased notably in the butorphanol tartrate combined with dezocine group. Furthermore, there was a reduction in the number of patients with postoperative adverse reactions such as nausea, vomiting, and dizziness whereas no prominent increase in patients with intraoperative movement responses was noted. This illustrates that in comparison with fentanyl, butorphanol tartrate in combination with dezocine can achieve the equivalent effect but with mild adverse reactions such as respiratory depression. In addition, compared with a single use of butorphanol tartrate or dezocine, patients with SpO_2<90% and postoperative adverse reactions showed no evident increase in number and the awake time of patients did not prolong as well in co-treatment group, indicating that the combination of butorphanol tartrate and dezocine does not augment the effects of adverse events.

Taken together, butorphanol tartrate combined with dezocine displays a potent analgesic effect in hysteroscopic surgery with shorter postoperative awake time, beneficial analgesia effects in the postoperative period, mild respiratory depression, and less adverse reactions like

nausea and vomiting. This proves that butorphanol tartrate in combination with dezocine is an excellent analgesic medication for outpatient surgery.

A reservation about our study should be addressed. In this paper, only patients with fairly good general conditions, those in ASA grade I-II, and aged 65 years or younger were recruited. We have not yet been able to identify whether the combination of butorphanol tartrate and dezocine will still show a satisfactory analgesic effect with mild adverse reactions in patients having at least ASA grade II. Further studies are needed to answer this question. The risk of anesthesia in elderly patients with poor general health undergoing hysteroscopic surgery can be reduced if we can prove that butorphanol tartrate combined with dezocine shows a beneficial effect in hysteroscopic surgery with slight circulation inhibition and mild respiratory depression.

Disclosure of conflict of interest

None.

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