Comparison of bolus remifentanil-propofol versus bolus fentanyl-propofol for dilatation and sharp curettage

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Summary

Background and Objective: The study was conducted to determine whether bolus administrations of remifentanil-propofol could provide adequate analgesia and similar patient comfort with a faster recovery profile compared with bolus administrations of fentanyl-propofol during dilatation and sharp curettage. *Methods:* The patients were randomized to a remifentanil group (n = 36) or fentanyl group (n = 36). The remifentanil group received an IV bolus dose of 1 μg kg^{-1} remifentanil. The fentanyl group received an IV bolus dose of fentanyl 0.5 μg kg^{-1}. The Verbal Pain Scale (VPS), modified Aldrete scores, blood pressure, heart rate, peripheric oxygen saturation, recovery time from anesthesia and adverse events during or after surgery were evaluated. *Results:* The groups were found to be similar in duration of the surgical procedure, anesthesia time and hemodynamic variables and VPS scores. Patients in the remifentanil group recovered from anesthesia earlier. Modified Aldrete scores were higher in the remifentanil group at 5 and 10 min postoperatively. The frequency of perioperative adverse events did not differ significantly between the groups. *Conclusions:* Bolus injections of remifentanil appear to be a safe and effective alternative to fentanyl, producing faster recovery in providing analgesia during dilatation and sharp curettage procedures.

Key words: : Remifentanil; Fentanyl; Dilatation and Curettage; Propofol.

Introduction

Attaining a faster recovery time from anesthesia is extremely important for brief outpatient surgical procedures such as dilatation and sharp curettage. Dilatation and sharp curettage, a short-lasting procedure, is one of the most frequently performed gynecological surgical procedures. This procedure is performed for the diagnosis and treatment of endometrial and intrauterine disorders. Patients are day-case patients who are usually discharged and able to return to their routine daily activities after a brief hospital rest. Despite its shortness, the procedure generally causes considerable pain due to cervical dilatation that is usually performed by Hegar dilators and tissue extraction. The procedure therefore necessitates rapid-acting intense analgesia [1, 2].

Opioids are generally used during the dilatation and sharp curettage procedure [3, 4]. Fentanyl has generally been used as the first choice to provide analgesia [5, 6]. Remifentanil, which has recently gained popularity, may be a good alternative to fentanyl for dilatation and sharp curettage since remifentanil is a relatively new and ultra-short-acting drug with a half life of 9-11 min and may provide a faster recovery profile [7]. Remifentanil has an ester linkage that makes its metabolism unique compared to other opioids since it is metabolized by blood and tissue esterases [8], independent of hepatic and renal function which may make it also suitable for hepatic and renal patients [9-11].

Therefore the aim of the current prospective randomized study was to determine whether bolus administration of remifentanil-propofol could provide adequate analgesia and similar patient comfort with a faster recovery profile when compared with bolus administration of fentanyl-propofol during dilatation and sharp curettage.

Material and Methods

This prospective study was performed at GATA Academic Military Hospital and Adnan Menderes University Hospital. Women undergoing dilatation and sharp curettage aged 18-60, whose ASA physical status were I or II were asked to participate in the study.

Participation was on a voluntary basis. All participants gave their informed consent. The study protocol was approved by the local ethics committee. Patients with pulmonary, hepatorenal, neuromuscular and neuropsychiatric disease, morbid obesity, and patients undergoing emergency curettage for massive bleeding or hemodynamic instability were excluded from the study. Patients who were unable or refused to give informed consent were also excluded from the study. All patients had undergone dilatation and curettage procedures for evaluation of abnormal uterine bleeding.

Subsequent to transfer to the operating room and before anesthetic induction, IV cannulae were inserted and standard monitoring was initiated, consisting of a five-lead ECG, noninvasive blood pressure, pulse oximetry. Patients were placed supine on the gynecological table with their legs in stirrups. They were randomized to the remifentanil group (Ultiva; GlaxoSmithKline, The Upjohn Company, Belgium) (n = 36) or the fentanyl group (Fentanyl Citrate, USP 50 mcg/ml; Abbott Laboratories, North Chicago, USA) (n = 36) by using a computer-based random number generator program. The remifentanil group received an IV bolus dose of 1 μg kg^{-1} remifentanil over a period

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of 30 sec whereas the fentanyl group received an IV bolus dose of fentanyl 0.5 ug/kg. After obtaining baseline measurements, we administered 1 mg kg^{-1} of lidocaine IV to minimize the burning that accompanies administration of propofol. Then, anesthesia was induced with propofol (Propofol 1% Fresenius, Fresenius Kabi, Australia GmbH]) 2 mg/kg in both groups. Anesthesia was maintained with 60% nitrous oxide (N_2O) in oxygen with a fresh gas flow of 4 l min^{-1} through a facemask. N_2O was discontinued when the gynecologist declared the dilatation and curettage procedure finished.

After the operation, the surgeons were questioned about their subjective evaluation of surgical working conditions during dilatation and sharp curettage (0 = not satisfied, 1 = satisfied, 2 = extremely satisfied). In addition, the patients were questioned at discharge about their anesthetic experience (0 = not satisfied, 1 = satisfied, 2 = extremely satisfied). Recovery of the patients was evaluated using the modified Aldrete scoring system [12].

A verbal pain scale (VPS) was used to evaluate pain intensity, with scores of 0 (no pain), 1 (light pain), 2 (moderate pain), 3 (severe pain). VPS scores were evaluated 5 and 10 min postoperatively. Modified Aldrete scores were evaluated 5 and 10 min postoperatively. VPS scores were queried by a nurse blinded to the opioid administered. Diclofenac sodium (Miyadren 75 mg, Fako Drug Company, Istanbul, Turkey) was administered IM to patients with a score > 1. Blood pressure, heart rate, and oxygen saturation were recorded just before the administration of fentanyl or remifentanil (preinduction), 5-10 min after induction, and five and ten minutes after the end of the dilatation and curettage procedure. Duration of the surgical procedure, duration of anesthesia, awakening time (time from end of the discontinuation of N_2O to spontaneous eye opening), orientation time (time from end of the discontinuation of N_2O to the time the patient is able to recall name and date of birth) and also time from end of the discontinuation of N_2O to the patient's responding to verbal comments were recorded. Also recorded were the frequency of the adverse events during or after surgery (e.g., episodes of nausea, vomiting).

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA), version 14.0; p values < 0.05 were considered significant. Data are presented as mean ± standard deviation (SD). Parametric continuous variables were analyzed using the Student's t-test. Differences between categorical variables were analyzed with the chi-square test and Fisher's exact test. Based on a previous study, a priori power analysis was performed using two-sided analysis with an (alpha) error of 0.05 and a power of 0.8 to detect a difference of 60% for recovery times. Thirty patients were calculated to be needed for each group. Assuming possible dropouts, the sample size was increased to 36 patients per group.

Results

Seventy-two women undergoing dilatation and sharp curettage procedures were included in the study. Both the remifentanil and fentanyl group consisted of 36 patients each. Both groups were found comparable in terms of patient characteristics (Table 1).

No statistically significant difference was found between the groups (Tables 1 and 2) in terms of ASA physical status, duration of the surgical procedure, anesthesia time and hemodynamic variables throughout the study period.

Table 1. — *Patient characteristics of the groups*.

	Group R (n = 36)	Group F (n = 36)
Age (years)	40.6 ± 9.5	40.3 ± 10.4
Weight (kg)	70.3 ± 10.3	67.9 ± 10.9
Height (cm)	162.4 ± 10.1	160.9 ± 11.2
ASA physical status (I/II)	28/8	29/7
Duration of surgery (min)	6.7 ± 0.8	6.5 ± 0.9
Duration of anesthesia (min)	8.3 ± 0.6	8.5 ± 0.5

Data are means ± SD, or number of patients.
There were no statistically significant differences between the groups.
R = remifentanil; F = fentanyl; ASA: The American Society of Anesthesiologists.

Table 2. — *Hemodynamic parameters of the groups at selected time points*.

	Preinduction	5 minutes after induction	10 minutes after induction	5 minutes postoperative	10 minutes postoperative
HR (bpm)					
Group R	83.0 ± 9.8	68.9 ± 9.6	72.2 ± 8.7	78.8 ± 5.8	75.2 ± 12.9
Group F	83.4 ± 9.4	72.3 ± 7.4	72.5 ± 7.0	80.5 ± 7.5	71.3 ± 9.5
SAP (mmHg)					
Group R	131.4 ± 18.6	118.7 ± 19.1	116.7 ± 16.7	117.1 ± 10.7	123.8 ± 23.5
Group F	130.9 ± 17.3	120.2 ± 17.4	119.5 ± 20.1	119.0 ± 23.9	129.3 ± 19.2
DAP (mmHg)					
Group R	75.9 ± 14.5	70.9 ± 13.1	70.9 ± 10.1	80.5 ± 18.8	76.8 ± 12.4
Group F	82.6 ± 14.2	75.6 ± 12.6	75.4 ± 7.9	78.8 ± 20.9	82.3 ± 12.8
MAP (mmHg)					
Group R	95.8 ± 14.3	84.7 ± 15.2	82.5 ± 12.5	85.8 ± 8.0	94.3 ± 18.0
Group F	99.7 ± 16.8	89.7 ± 13.2	86.3 ± 13.4	86.7 ± 7.5	98.3 ± 13.3
SpO_2					
Group R	99 ± 1	99 ± 1	99 ± 1	98 ± 2	98 ± 2
Group F	98 ± 2	99 ± 1	98 ± 2	98 ± 2	98 ± 2

Data are means ± SD.
There were no statistically significant differences between the groups.
R = remifentanil; F = fentanyl; Bpm = beats per minute; MAP = mean arterial pressure; DAP = diastolic arterial pressure; SAP = systolic arterial pressure; HR = heart rate; SpO_2 = peripheric oxygen saturation.

VPS scores after the operation did not differ significantly between the groups (Table 3). Modified Aldrete scores were higher in the remifentanil group both 5 and 10 min postoperatively (Table 3).

Patients in the remifentanil group recovered from anesthesia earlier. Awakening time, orientation time, and time from the end of anesthesia to response to verbal commands for the patients enrolled in the study was significantly shorter in the remifentanil group compared with the fentanyl group (Table 3). Both gynecologists and patients in the remifentanil group expressed similar satisfaction as compared with the fentanyl group. The frequency of perioperative adverse events (e.g., episodes of nausea, vomiting) did not differ significantly between the groups (Table 4).

Discussion

Dilatation and sharp curettage, among the most frequently performed gynecological surgeries, is a short procedure. In the current study, mean operation time for dilatation and sharp curettage was 7 min, which is within the 9-11 min [13] systemic half-life of remifentanil. Even though it is a short procedure, the pain related with dilatation and sharp curettage is generally considerable due to

Table 3. — *Verbal pain scale (VPS), modified Aldrete scores of subjects at selected time points, recovery profiles of subjects and satisfaction scores of both subjects and gynecologists.*

	Group R (n = 36)	Group F (n = 36)	*p*
Pain score (VPS)			
PO 5 (min)			
0/1/2/3	28/7/1/0	30/6/0/0	ns
PO 10 (min)			
0/1/2/3	26/8/2/0	28/6/2/0	ns
Modified Aldrete score			
PO 5 (min)	9.5 ± 0.8	7.4 ± 1.6	0.001
PO 10 (min)	10.1 ± 0.6	9.2 ± 0.9	0.001
Satisfaction scores of patients			
Very satisfied (2)	32 (88.8%)	32 (88.8%)	ns
Satisfied (1)	4 (11.2%)	4 (11.2%)	ns
Not satisfied (0)	0 (0%)	0 (0%)	
Satisfaction scores of gynecologists			
Very satisfied (2)	31 (86.1%)	32 (88.8%)	ns
Satisfied (1)	5 (13.9%)	4 (11.2%)	ns
Not satisfied (0)	0 (0%)	0 (0%)	ns
Recovery times			
**Time to spontaneous eye opening (min)	2.0 ± 0.6	4.3 ± 1.1	0.01
**Time to responding to verbal comments (min)	3.4 ± 0.9	5.9 ± 1.1	0.01
**Orientation time (min)	4.9 ± 1.2	8.6 ± 1.2	0.01
Analgesic Requirement (n)	10	8	ns

Data are means ± SD, or number of subjects.
* $p < .05$ (significant difference), ns: not significant.
R = remifentanil; F = fentanyl; PO = postoperative; VPS = verbal pain scale.
** Calculated from discontinuation of nitrous oxide.

Table 4. — *Perioperative adverse events.*

	Group R (n = 36)	Group F (n = 36)
Nausea/Vomiting	1/1 (2.8%)	1/1 (2.8%)
Hypotension (SAP < 90 mmHg)	3 (8.3%)	2 (5.6%)
Bradycardia (HR < 50 bpm)	4 (11.1%)	3 (8.3%)

Data are means ± SD, or number of patients.
There were no statistically significant differences between the groups.
R = remifentanil; F = fentanyl; bpm = beats per minute; HR = heart rate.

cervical dilatation and tissue extraction [14]. Bolus doses of remifentanil, with its short half-life and rapid action, appears to be a good candidate for intraoperative analgesia during such short procedures as dilatation and curettage. Remifentanil infusion for such procedures has been shown to be effective and safe [15]. However when compared with the easy use of bolus fentanyl, remifentanyl infusions necessitated setting up an infusion pump which was not practical for such a brief procedure. Remifentanil in bolus administrations would eliminate the need for setting up an infusion pump apparatus for such a brief surgical procedure, thus making the procedure easier and simpler. However, there is limited data concerning the use of bolus-dose remifentanil. Bolus-dose remifentanil has been studied and found useful in various limited clinical settings, such as preventing unwanted hyperdynamic cardiovascular response during laryngoscopy, intubation, and craniotomy procedures [16-21]. In gynecologic settings, Castillo *et al*. compared different bolus doses of remifentanil in dilatation and sharp curettage but did not compare bolus-dose remifentanil versus the standard drug, fentanyl [22]. To the best our knowledge, the present study is the first study that compares bolus doses of remifentanil with fentanyl for the dilatation and sharp curettage procedure.

We found in the current study that patients in the remifentanil group recovered from anesthesia earlier. Satisfaction scores for both patients and gynecologists were similar between the groups. Adverse effects reported perioperatively were similar in both fentanyl and remifentanil groups. In addition, patients in the remifentanil group reported higher modified Aldrete scores.

Hemodynamic responses in both groups were comparable in the present study. In both the remifentanil and fentanyl groups the frequency of hypotension and bradycardia was consistent with previous studies [22, 23]. Previous researchers have actually reported conflicting results for nausea and vomiting [24, 25] in the use of remifentanil. In the current study, only one case of nausea and vomiting was observed in the remifentanil group, an outcome which was found comparable to the fentanyl group. It should be taken into account in this context that in the current study, propofol, with its antiemetic effect, was co-administered with both remifentanil and fentanyl [26].

VPS scores after the operation did not differ significantly between the groups. Previous studies have recorded conflicting results regarding postoperative analgesic requirements in remifentanil-based intraoperative analgesia. Although some studies suggest a requirement for increased postoperative analgesia [27, 28], others have not found an increased analgesic demand in remifentanil-based intraoperative analgesia [29]. No significant difference in analgesic requirement was found between the groups in the current study. We think that for such a short surgical procedure, the administration of bolus injections of remifentanil is effective. Bolus injections of remifentanil have also been reported to be effective in providing analgesia for extracorporeal shock wave lithotripsy, a very painful procedure [16].

We have further found that awakening time, orientation time, and time of response to verbal comments after anesthesic gas is discontinued were shorter with remifentanil. Attaining faster recovery times from anesthesia is much more important for brief outpatient surgical procedures such as dilatation and sharp curettage. Moreover, patients in both the remifentanil and fentanyl groups expressed similar satisfaction scores. The satisfaction scores of the surgeons also did not differ between the groups and administration of bolus doses of remifentanil did not adversely affect the satisfaction scores of both patients and gynecologists during the dilatation and sharp curettage procedure.

In summary bolus administration of remifentanil would be a good alternative for dilatation and sharp curettage procedures for patients with hepatic and renal diseases as metabolism of remifentanil independent of hepatic and renal function. Moreover when compared with infusion of remifentanil, remifentanil in bolus

administrations would eliminate the need for setting up an infusion apparatus for the dilatation and sharp curettage procedure, thus making the procedure easier and simpler.

Conclusion

In conclusion, remifentanil provided faster recovery times with similar VPS scores and satisfaction scores for both patients and gynecologists. The analgesic requirement also did not increase with remifentanil. Thus, bolus injections of remifentanil appear to be a safe and effective alternative to fentanyl with faster recovery times in providing analgesia during the dilatation and sharp curettage procedures. Further studies are needed.

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