

# Bolus Dosing of Remifentanyl with Propofol for Gynaecological Day Case Surgery

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## Abstract:

Short duration, highly stimulating gynaecological procedures provide a significant anaesthetic challenge. We compared induction and maintenance with intermittent boluses of a propofol-remifentanyl mixture with induction of anaesthesia with propofol-alfentanil followed by maintenance with isoflurane in a double-blind randomised controlled trial.

Sixty female subjects undergoing gynaecological surgery lasting less than 10 minutes were recruited. The isoflurane group resumed spontaneous breathing earlier than the remifentanyl group but there were no other differences in surgical conditions. Emergence and recovery were similar in both groups. Mild pain was relatively common in both groups but easily treated with simple analgesia, while nausea was rare with either technique.

One patient was excluded due to a longer than anticipated procedure. Two patients, one in each group, were admitted overnight due to bleeding after termination of pregnancy, but there were no complications attributed to either anaesthetic technique.

Intermittent bolus propofol-remifentanyl is a simple technique which may be more convenient than the use of intravenous infusions for short surgery. However, it was associated with more prolonged apnoea and had no apparent advantages over propofol-alfentanil-isoflurane anaesthesia in these women having procedures of very short duration.

## Introduction

Short duration, highly stimulating procedures with little or no need for postoperative analgesia can provide a significant technical challenge to the anaesthetist. A deep level of anaesthesia is required to attenuate the responses to surgical stimuli, yet patients also require rapid recovery and return to street fitness, ready for discharge. The fact that many techniques have been tried<sup>1-5</sup> suggests that there is currently no ideal technique. The shorter gynaecological day case procedures are one group which typifies these problems.

Remifentanyl is an ultra-short acting opioid, typically administered by infusion. It provides intense analgesia, which is titratable to clinical needs. It has a short and constant context-sensitive half-time<sup>6-8</sup>, giving a rapid and predictable offset. For this reason, it has proved an ideal adjunctive agent for total intravenous anaesthesia (TIVA)<sup>9</sup>. The use of an infusion is, however, expensive, labour intensive and can be inconvenient for the rapid turnover cases described<sup>10</sup>.

One safe and commonly used alternative is to use an inhalation agent to maintain anaesthesia, supplemented with a short-acting opioid such as alfentanil. However, we aimed to exploit the pharmacological properties of

remifentanyl by delivering intermittent boluses of a propofol-remifentanyl mixture rather than the more common infusion. We opted to compare this with an alfentanil-propofol-isoflurane technique in patients undergoing short, day case gynaecological procedures, to determine if either technique had clinical advantages, especially in terms of reducing recovery time or improving time to street-fitness and discharge.

## Patients and Methods

We obtained local research and ethics committee approval for this randomised, double blind, controlled trial. All healthy female patients between the ages of 17 and 60 undergoing routine elective minor gynaecological surgery were eligible for inclusion. Those giving a history of reflux or hiatus hernia, obesity (defined as having a body mass index >30), or cases requiring tracheal intubation for any other reason were excluded from the study. Potential volunteers all

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received a patient information leaflet prior to attending the day case unit for surgery and all recruited subjects gave written informed consent.

Sixty patients were enrolled and allocated, by computer-generated randomisation, into two study groups. The isoflurane group acted as the control and underwent induction of general anaesthesia using alfentanil (10 µg/kg) and propofol (2–3 mg/kg). Anaesthesia was maintained with 67% nitrous oxide in 33% oxygen with isoflurane (1–2% inspired concentration), as required. The remifentanyl group underwent induction of general anaesthesia using remifentanyl (1–1.5 µg/kg) and propofol (2–3 mg/kg). Anaesthesia was maintained with 67% nitrous oxide in 33% oxygen with incremental doses of 10 mg propofol and 5 µg remifentanyl. This was achieved by delivering 1 ml incremental boluses of a premixed solution of 200 mg propofol (20 ml of 1% solution) containing 0.1 mg remifentanyl (5 µg/ml).

All patients were fully monitored throughout with pulse oximetry, an ECG and a non-invasive blood pressure device. No premedication or pre-emptive analgesia was given. Following induction of general anaesthesia, the lungs were ventilated using a facemask with or without an oropharyngeal or laryngeal mask airway, depending on individual patient requirement. The patient was then allowed to breathe spontaneously via facemask or laryngeal mask airway for the remainder of the operation, through a circle breathing system.

One anaesthetist (AH, an experienced anaesthetist familiar with both techniques) was responsible for opening the randomisation envelope and administering anaesthesia to all patients. This anaesthetist also recorded the requirement for airway adjuncts or laryngeal mask airway, time from initiation of induction of anaesthesia to resumption of spontaneous respiration, total dose required for induction of anaesthesia and the total number of bolus doses required for those subjects in the remifentanyl group.

A second anaesthetist (ELH) was blinded to anaesthetic technique using surgical drapes between the anaesthetic machine and the observers. She collected basic patient data, including the total duration of the procedure from surgical draping to end of surgical intervention. She also recorded the surgeons' satisfaction with the operating conditions, based on 10 cm Visual Analogue Score (VAS) ranging from 0 representing worst working conditions to 10 cm representing ideal conditions. The surgeon, who was also blinded to the anaesthetic technique, also evaluated intraoperative blood loss on a three-point scale (less than average, average or more than average).

Postoperative recovery was evaluated by a third investigator (DM) who was also blinded to the anaesthetic technique. She recorded the time from the end of the procedure until the patient could open their eyes, recall their name and were fit for discharge from recovery and the day unit. The Aldrete Score<sup>41</sup> was used as an index of fitness for discharge from the recovery area, with patients required to score more than

eight (Appendix 1). Fitness for home discharge was assessed on the Post-Anaesthetic Discharge Scoring System (PADSS)<sup>42</sup>, with patients required to score nine or more (Appendix 2). Postoperative pain, nausea and vomiting (PONV) were assessed by 10 cm VAS, immediately prior to discharge, and recorded the patient's worst experience up to that point. Prior to discharge home, postoperative analgesic requirements were recorded.

A sample size of 24 per group was calculated to have 80% power to detect a difference in emergence times of 1.2 minutes and we increased the sample to 60 patients in total to allow for incomplete data and drop-outs. Statistical analysis of the results was by 2-sample t-test for continuous data, assuming a normal distribution, and the Mann-Whitney test and Chi-squared test for other data.

**Table 1** Patient, surgical and recovery characteristics in the propofol-alfentanil-isoflurane and propofol-remifentanyl groups

	Isoflurane group	Remifentanyl group
Age (yrs)	28 ± 8	27 ± 8
Weight (kg)	69 ± 12	64 ± 9
Procedure time (min)	5.7 ± 1.05	6.4 ± 1.3
Time to spontaneous breathing (min) <sup>1</sup>	5.8 ± 1.8	8.7 ± 1.7*
Time to recovery discharge (min) <sup>2</sup>	12.5 ± 3.4	13.9 ± 7.0
Time to street-fitness (min) <sup>2</sup>	78.0 ± 16.6	76.6 ± 25.5
Surgeon satisfaction VAS (cm)	10 (6–10)	10 (5–10)
Blood loss (<average, average, >average)	5, 22, 1	4, 21, 4
Pain VAS (cm)	2 (0–6)	2 (0–6)
PONV VAS (cm)	0 (0–2)	0 (0–2)

Results are mean ± SD, numbers or median (range). Two patients, one from each group, were omitted due to admission due to blood loss

\* p<0.05, from isoflurane group

<sup>1</sup> from induction of anaesthesia

<sup>2</sup> from end of procedure

## Results

All subjects were female undergoing minor gynaecological procedures, such as vacuum termination of pregnancy (VTOP), evacuation of retained products of conception (ERPC), or change of intrauterine contraceptive device. These procedures were carried out by one of three surgeons.

Sixty subjects were studied in total, of whom three subjects were excluded. One patient in the isoflurane group underwent a more prolonged procedure, as she required a hysteroscopy and polypectomy taking 21 minutes. Two VTOPs, one from each group, bled leading to prolonged procedures and admission overnight to the gynaecological ward. There were no other complications in either group. The groups were similarly matched with no differences in procedure duration (Table 1).

Patients in the isoflurane group resumed spontaneous

breathing approximately three minutes earlier than the remifentanyl group ( $p < 0.001$ ), but intraoperative surgical conditions and blood loss were similar between the groups (Table 1). There were no differences between the groups in terms of emergence or recovery times or in postoperative pain or nausea (Table 1). Postoperative nausea was uncommon in both groups, with all but four patients having a PONV VAS score of zero; one patient in the isoflurane group had a score of 1 cm, while a further two patients in the isoflurane group and one in the remifentanyl group recorded scores of 2 cm.

The majority of patients required postoperative analgesia, but the requirements were similar in each group (Table 2).

**Table 2** Postoperative analgesic requirements in the propofol-alfentanil-isoflurane and propofol-remifentanyl groups

	Isoflurane group	Remifentanyl group
Paracetamol	0	1
Diclofenac	17	17
Paracetamol and diclofenac	6	4
Tramadol and diclofenac	3	3

Results are numbers of patients

## Discussion

This report is one of the first describing a general anaesthetic technique using bolus dosing of a propofol-remifentanyl mixture. However, we have found that this mixture has no recovery advantages over the commonly used technique of alfentanil with propofol induction with isoflurane-nitrous oxide-oxygen maintenance for anaesthetising patients undergoing minor day case gynaecological procedures. This is perhaps not surprising, given the very short duration of these procedures.

Many trials have been carried out comparing the recovery profiles between TIVA with propofol and remifentanyl and a more traditional fentanyl or alfentanil-volatile agent technique. Some have found recovery<sup>43,44</sup> and time to discharge home<sup>45</sup> quicker following TIVA with propofol-remifentanyl. Others have found recovery profiles to be similar in the two groups<sup>3,16-18</sup>. Of those trials looking at the functional assessment of patients following anaesthesia with propofol-remifentanyl or a volatile agent, the results are equally inconclusive. Recovery of cognitive function in one trial was shown to be better with sevoflurane-fentanyl compared with propofol-remifentanyl<sup>19</sup>. Other trials have shown psychometric recovery to be better with remifentanyl compared to alfentanil or fentanyl<sup>20,21</sup>. At the time of undertaking this research, there were no reported studies comparing recovery following bolus dosing of a propofol-remifentanyl mixture with an alfentanil-volatile agent technique.

The propofol-remifentanyl bolus technique avoids the time consuming process of priming infusion circuits and

programming an infusion device and may therefore be more convenient than a TIVA infusion when a rapid turnover is required. However, the time from induction of anaesthesia to return of spontaneous respiration was significantly shorter in the isoflurane group, which may represent a safety advantage, particularly with such rapid turnover cases. Nevertheless, all patients in both groups were breathing spontaneously by the time of transfer to the recovery room. There may also be financial benefits from one or other technique, but cost comparisons will vary, depending on the purchasing practices of the individual hospital.

Although not directly relevant to the focus of this study, one incidental finding was a relatively high requirement for simple analgesia in the early postoperative period. We have since changed our practice, with the nursing staff now issuing paracetamol and diclofenac orally to all patients as a premed, unless contraindicated, without a doctor's prescription being required [This is such a simple solution, yet so worthwhile. I cannot stress enough the value of providing prophylactic oral analgesia to most day case patients, either by protocol or by simply encouraging anaesthetists to see their patients early! — Ed].

In conclusion, we have found that the propofol-remifentanyl anaesthetic technique confers no significant recovery benefit over the traditional isoflurane technique in gynaecological minor day case procedures. We have found the main benefit of this technique is its ease of use. Both techniques provide safe, effective anaesthesia, with rapid recovery to street fitness and very little pain or nausea at the time of discharge.

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## Appendix 1

The Aldrete scoring system <sup>11</sup>		
		Score
Activity:	Able to move 4 extremities voluntarily or on command	2
	Able to move 2 extremities voluntarily or on command	1
	Unable to move extremities voluntarily or on command	0
Respiration:	Able to breathe deeply and cough freely	2
	Dyspnoea or limited breathing	1
	Apnoeic	0
Circulation:	Blood pressure $\pm$ 20% of preanaesthetic level	2
	Blood pressure $\pm$ 20–49% of preanaesthetic level	1
	Blood pressure $\pm$ 50% of preanaesthetic level	0
Consciousness:	Fully awake	2
	Arousable on calling	1
	Not responding	0
Oxygenation:	Able to maintain saturation >92% on room air	2
	Needs oxygen to maintain saturation >90%	1
	Saturation <90% even with oxygen	0

Total possible score 10; patients scoring  $\geq 9$  are fit for discharge from the recovery room

## Appendix 2

The Post-Anaesthetic Discharge Scoring System (PADSS) <sup>12</sup>		
		Score
Vital signs:	Blood pressure and pulse within 20% of preoperative baseline	2
	Blood pressure and pulse within 20–40% of preoperative baseline	1
	Blood pressure and pulse >40% from preoperative baseline	0
Activity and mental status:	Orientated and has steady gait	2
	Orientated or has steady gait	1
	Neither	0
Pain, nausea or vomiting:	Minimal	2
	Moderate, having required treatment	1
	Severe	0
Surgical bleeding:	Minimal	2
	Moderate	1
	Severe	0
Intake and output:	Has had oral fluid and voided	2
	Has had oral fluid or voided	1
	Neither	0

Total possible score 10; patients scoring  $\geq 9$  are fit for discharge