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Propofol *Versus* Thiopental for Outpatient Anesthesia

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Propofol (2,6 di-isopropylphenol in lipid emulsion)[1] is a short-acting intravenous anesthetic with high lipid solubility, short elimination half-life, and inactive metabolites. These properties produce rapid onset of anesthesia and quick return of psychomotor function. This study compared propofol emulsion to thiopental with respect to efficacy, side effects, and quality and rapidity of recovery when these drugs were used for induction and maintenance of anesthesia in short gynecological procedures.

METHODS

Ninety-three women (ASA physical status I or II) scheduled for dilation and curettage of the uterus were studied. The protocol was approved by the hospital's Clinical Investigation Committee, and written informed consent was obtained from each patient. Exclusion criteria were age less than 18 or greater than 65 yr, morbid obesity, history of allergy to propofol or thiopental, or an inability to communicate effectively. The two groups were comparable with respect to age, weight, ASA physical status, race, and smoking history (table 1).

Eligible patients were assigned to receive propofol or thiopental using a restricted randomization protocol which assigned two patients to receive propofol for each patient assigned to receive thiopental. This design allowed detection of a 20% difference in response, with a power of 0.44 and a Type-1 error rate of 0.05. Patients and postanesthetic recovery room (PARR) nurses did not know which drug was used. All patients were monitored with an electrocardiogram (EKG), noninvasive blood pressure device, and an end-tidal CO_2 monitor (Engstrom Elisa™) connected at the face mask elbow connection. Blood pressure (BP), heart rate (HR), respiratory rate (RR), end-tidal CO_2, and EKG rhythm were recorded at 1-min intervals, beginning 1 min before induction and ending at the conclusion of the procedure. Occurrence and duration of apneic episodes were noted.

No premedication was used. The patient was asked to count slowly while anesthesia was induced with propofol 2.5 mg/kg or thiopental 4.5 mg/kg given intravenously over 20–30 s. Induction time was defined as the interval from the start of injection to the cessation of counting. The patient was allowed to breathe 100% oxygen for 3 min after induction, then 70% nitrous oxide and 30% oxygen was administered, and the surgery began. Intermittent boluses of 25% of the induction dose were given to maintain adequate anesthesia (judged by increasing HR, BP, RR, or muscle tone). No muscle relaxants were used. At the end of the procedure, the nitrous oxide was discontinued and the patient transferred to the PARR. The patient was asked to open her eyes every 30 s. The time from discontinuation of the nitrous oxide to eye opening on command was recorded by the PARR nurses. Thereafter, the time to orientation (based on knowledge of name, current date, and name of hospital) was measured. Each patient was interviewed before leaving the PARR and questioned about adverse effects. The intravenous site was inspected for erythema or pain before discharge.

All results are reported as mean value plus or minus standard deviation (SD). Wilcoxon rank-sum tests for continuous variables, and chi-square tests or Fisher exact tests for discrete variables, were used to compare outcomes between treatment groups. All P values were based on two-tailed hypothesis testing, and a P value of less than 0.05 was considered significant.

RESULTS

The mean duration of anesthesia was the same in the 2 groups (table 2). The ratio of the average total dose of propofol to the average total dose of thiopental was 1.97. The ratio of the mean rates of administration of the drugs was 1.98. Fifty-three percent of the thiopental patients required more than three supplemental doses, while 60% of the propofol patients required fewer than three supplemental boluses during the procedure.

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TABLE 1. Demographics

	Propofol	Thiopental
Number of patients	60	30
Age (yr)	31.1 ± 11.5	30.3 ± 11.6
Weight (kg)	62.6 ± 11.9	60.3 ± 10.1
ASA Physical Status (%) I	83.3	83.3
II	16.7	16.7
Smokers (%)	62	76

TABLE 2. Anesthetic Details

	Propofol	Thiopental
Duration of anesthesia (min)	10.0 ± 2.1	10.0 ± 1.6
Average total dose (mg)	284.4 ± 63.6	550.0 ± 144.9
Mean administration rate ($mg \cdot kg^{-1} \cdot min^{-1}$)	0.47 ± 0.11	0.93 ± 0.17
Number of supplemental doses	2.4 ± 1.1	3.5 ± 1.3

The mean induction time was longer in the propofol group, 35.7 ± 8.4 s, *versus* 26.3 ± 5.3 s in the thiopental group ($P < 0.0001$). Apnea, defined as the cessation of respiration for more than 15 s, occurred during induction in 47% of the propofol group and 23% of the thiopental group ($P < 0.05$). Seven (12%) of the patients who received propofol were manually ventilated when the duration of apnea exceeded 60 s. No patient who received thiopental was apneic for more than 60 s.

Both drugs had similar effects on HR, BP, and RR (table 3). Two patients in each group developed EKG changes during cervical dilation. One patient in each group developed transient bradycardia, one propofol patient had premature atrial contractions, and one thiopental patient developed bigeminy. The arrhythmias disappeared when an additional bolus of anesthetic was given. Maintenance efficacy was defined as excellent if HR, BP, and end-tidal CO_2 remained within 10% of the initial measurements during the anesthesia; good if HR and BP varied less than 30% from the initial readings and end-tidal CO_2 was less than 55 mmHg; and poor otherwise. Using these definitions, there was no difference between the two groups ($P > 0.05$, Fisher's exact test). The time interval from discontinuation of the nitrous oxide to eye opening on command and to orientation was significantly shorter in the patients who received propofol (table 4).

Pain on injection occurred in 27% of the propofol group and 3% of the thiopental group ($P < 0.05$). Pain occurred more often when veins on the wrist or dorsum of the hand were used for injection. The pain was never severe enough to require discontinuation of the drug. No erythema or thrombosis was observed in the short period of postoperative observation. Twitching or jerking of the arms or face were seen during induction in 10% of the propofol group *versus* 6.7% of the thiopental group ($P = 0.53$). Laryngospasm, hiccoughs, or difficulty in obtaining a patent airway did not occur in either group. The incidence of nausea and vomiting postoperatively was the same in the two groups (propofol 10% *versus* thiopental 6.7%, $P = 0.43$). One propofol patient complained of a strange taste on induction. Two thiopental patients and one propofol patient suffered from transient diplopia in the PARR.

DISCUSSION

Outpatient anesthesia requires an agent that produces rapid onset of anesthesia and quick return to a state that allows discharge within a short time. Propofol produced a rapid onset of anesthesia, no airway management problems, and rapid awakening and orientation postoperatively. Thiopental did produce a faster onset of anesthesia; however, the time difference of 10 s is not likely to be clinically significant. Apnea was much more common with propofol than with thiopental in

TABLE 3. Hemodynamic and Respiratory Responses to Anesthesia

		Time from Induction (Min)								
		0	1	2	3	4	5	6	7	8
Heart rate (1.min)	Thio	81.2 ± 17.9	94.1 ± 11.4	85.0 ± 13.2	82.4 ± 12.5	85.3 ± 10.6	84.8 ± 12.5	84.4 ± 11.3	86.0 ± 8.9	87.7 ± 16.3
	Prop	78.0 ± 11.8	92.2 ± 12.6	80.8 ± 11.8	79.1 ± 11.6	81.1 ± 13.2	80.8 ± 13.3	79.9 ± 13.5	78.8 ± 13.4	77.9 ± 12.6
Mean arterial Pressure (mmHg)	Thio	89.5 ± 16.2	82.8 ± 13.3	82.9 ± 16.0	82.0 ± 16.3*	83.0 ± 15.3*	83.0 ± 17.7	83.8 ± 15.6	81.3 ± 13.7	84.4 ± 12.8
	Prop	89.1 ± 14.2	84.6 ± 13.6	79.0 ± 11.7	74.4 ± 14.8	76.0 ± 10.4	77.9 ± 12.2	78.2 ± 12.8	76.8 ± 12.4	79.5 ± 14.2
End tidal CO_2 (mmHg)	Thio	33.0 ± 5.0	26.3 ± 9.0	29.2 ± 6.7	30.8 ± 5.6	28.8 ± 9.5	31.0 ± 7.5	30.8 ± 8.0	31.9 ± 5.8	31.6 ± 6.2
	Prop	21.5 ± 4.9	26.7 ± 6.0	27.9 ± 6.4	29.6 ± 7.0	30.2 ± 5.9	30.6 ± 6.1	32.1 ± 6.7	30.6 ± 6.6	31.0 ± 6.0

* $P < 0.02$, Fisher's exact test.

this study, and nearly identical to the incidence of apnea reported by Cummings,[2] who also used 2.5 mg/kg. In this latter study, the incidence of apnea was reduced to zero when the dose of propofol was reduced to 2.0 mg/kg. However, at this smaller dose, Cummings also reported an unacceptable number of induction failures.

Both drugs produced small but significant decreases in HR and BP, which were well tolerated by the healthy patients in this study. However, this may not be true for the more severely ill or the elderly. Dundee *et al.*[3] has shown that severe hypotension may occur in the elderly with standard doses of propofol.

Recovery, assessed by response to command and time to orientation, was much faster in the propofol group. A subjective finding was the remarkable "clearheadedness" of the patients recovering from propofol. This is corroborated by McKenzie and Grant, who noted a rapid return to baseline of neuropsychological tests administered after propofol anesthesia in a similar group of patients.[4]

The major side effect was pain on injection in 27% of patients receiving propofol, a higher rate than reported by others.[4-6] This may be due to the use of small veins or the absence of a narcotic premedication. No phlebitis was seen in our patients, nor by others who examined their patients 24–72 h after surgery.[4,5]

In summary, propofol, in the dose used in this study, is an effective induction agent which provides good surgical anesthesia in combination with nitrous oxide. Its effects on HR and BP are similar to those of thiopental. Pain on injection is a major significant side effect. However, rapid recovery and return to normal neuropsychological function makes propofol a useful alternative to thiopental for outpatient procedures.

TABLE 4. Recovery Time by Treatment Group

	Propofol	Thiopental	*P* Value
Responds to command (min)	5.8 ± 2.8	10.3 ± 8.2	0.0003
Orientated (min)	7.9 ± 3.0	14.0 ± 9.7	0.0001

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