Propofol was first used clinically in 1977 [1]. The original Cremophor formulation was changed to an aqueous emulsion [2-4], which is thought to be less likely to produce anaphylactoid reactions [5]. It is metabolized rapidly by the liver, and possibly by the lungs, with excretion of the metabolites in urine [6]. After an i.v. injection, propofol has a short distribution phase and a rapid metabolic clearance from blood which approximates to liver blood flow. The terminal elimination half-life is between 300 and 500 min. Thus propofol is potentially useful for induction and maintenance of anaesthesia in ambulatory surgical patients.

Thiamylal is a commonly used ultra short-acting barbiturate with a potency 1.1 times that of thiopentone and clinical properties virtually identical to those of thiopentone. The present study was designed to evaluate the safety and efficacy of propofol compared with thiamylal when used for the induction and maintenance of anaesthesia in elective terminations of pregnancy. Observations during anaesthesia were carried out in an open, “unblinded” manner, while recovery observations were “blinded”.

PATIENTS AND METHODS

Forty female patients, ASA class I or II, aged between 18 and 37 yr, were studied during elective termination of pregnancy on an outpatient basis. Patients gave written informed consent to the study, which had been approved by the Institutional Review Board. Patients were excluded with hepatic, renal, haematological, cardiac, respiratory or metabolic disease, gross obesity, or if they gave a history of allergy or any previous adverse response to general anaesthesia.

On arrival of the patient in the operating room a three-lead electrocardiograph was attached and arterial pressure measured using an automated machine. An 18-gauge catheter was inserted into a convenient vein on the forearm or hand and an infusion of lactated Ringers solution in 5% dextrose started. All patients were premedicated with glycopyrrolate 0.2 mg i.v. 5 min before induction of anaesthesia. The patients were assigned randomly to receive either propofol or thiamylal.

Propofol 2.5 mg kg⁻¹ or thiamylal 4.0 mg kg⁻¹ was administered over 20-30 s to induce anaesthesia. The patient was observed for the next 3 min while spontaneously breathing 100% oxygen.
Observations of heart rate and arterial pressure were made at 1-min intervals. If the patient failed to lose consciousness (as defined by loss of eyelash reflex and lack of response to verbal command), the induction was considered unsatisfactory. When necessary, repeat boluses of 25% of the induction dose were administered to complete induction.

Anaesthesia at the commencement of surgery was maintained with 70% nitrous oxide in oxygen. Repeat injections of 25% of the induction dose for maintenance of anaesthesia were administered as indicated clinically by the level of anaesthesia. Indication for repeat boluses included increased ventilation, vocalization, swallowing or movement in response to surgical stimuli. Arterial pressure, heart rate, electrocardiogram and rate of ventilation were monitored throughout. The duration of apnoea was recorded if it occurred. During the procedure, oxytocin 10 units was injected i.v. after evacuation of the uterus.

Recovery time was assessed by a second observer who was unfamiliar with the type of anaesthesia given. This observer measured the elapsed time from the termination of anaesthesia (discontinuation of nitrous oxide) to the time of spontaneous eye-opening, to response to verbal command, and to full orientation (as defined by the patient being able to give her correct birth-date). In the recovery room, observation was continued and arterial pressure and heart rate changes at 5-min intervals were recorded. The occurrence of nausea, vomiting, drowsiness, headache, shivering or any venous complication was noted.

Unless otherwise indicated, data are presented as mean and standard deviation (SD), and the two groups were compared by the unpaired Students' t test and the Fisher exact test, with a significance level of \( P < 0.05 \).

**RESULTS**

Forty female patients were studied in random order, 19 receiving propofol and 21 thiamylal. There was no significant difference between the two groups with regard to mean age, weight or duration of pregnancy (table I).

Anaesthesia induction times from the beginning of the bolus injection, were not different clinically or statistically between the two groups (table II). Propofol 2.5 mg kg\(^{-1}\) induced anaesthesia more reliably than did thiamylal 4.0 mg kg\(^{-1}\) (\( P < 0.05 \)).

All patients receiving propofol were anaesthetized after a single induction dose, while in the thiamylal group, two patients required an additional bolus before losing consciousness, and two additional patients receiving thiamylal awoke during the 3-min observation period while breathing 100% oxygen. Side effects during induction and the 3-min observation period totalled 16 in the propofol group and 10 in the thiamylal group, but there was no statistically significant difference between the groups (table III). Small and weak spontaneous movement of the limbs occurred in four patients in the propofol group and in one patient in the thiamylal group. These movements were easy to control and did not interfere with surgery. Pain on injection occurred in four patients in the propofol group who all had an i.v. cannula on the back of the hand.

During the 3-min observation period (breathing
THIAMYLAL AND PROPOFOL

100 % oxygen with no surgical stimulation) haemodynamic variables were different between the propofol and the thiamylal groups (fig. 1). A small decrease in systolic arterial pressure was noted in both groups, but was more significant in the propofol group where it reached 11 % below baseline at 3 min. Diastolic pressure was significantly lower with propofol, being 15 % below baseline at 2 min and 22 % below baseline at 3 min. Heart rate increased significantly in both groups at 1 min and remained higher with thiamylal. During maintenance of anaesthesia, heart rate and arterial pressure were stable with both agents, without a significant difference between the groups. No arrhythmias or other electrocardiographic changes occurred during induction or maintenance of anaesthesia with either agent.

There were no reports of awareness or untoward effects during maintenance of anaesthesia in each group. The mean times between supplementary doses of drug and the mean duration of anaesthesia were not different significantly between the two groups (table IV). Recovery from discontinuation of nitrous oxide was significantly more rapid in the propofol group than in the thiamylal group (fig. 2).

Side effects within the first 2 h after surgery were few in both groups, but there was a significantly higher incidence of nausea and vomiting in the thiamylal group (table V).
DISCUSSION

Propofol is a suitable agent for the induction and maintenance of general anaesthesia for ambulatory surgical patients. Propofol 2.5 mg kg\(^{-1}\) induced general anaesthesia more reliably than did thiamylal 4.0 mg kg\(^{-1}\). Induction with propofol was rapid and smooth with a low incidence of coughing or laryngospasm. However, in the propofol group mild pain on injection and spontaneous small movements of the limbs were more common. Apnoea during induction occurred more frequently with propofol, but was of short duration (less than 30 s) and presented no difficulty clinically. Apnoea did not occur with either agent during anaesthesia maintenance. Both systolic and diastolic pressures decreased more with propofol than with thiamylal during the 3-min observation period. The hypotension with propofol was accompanied by a small increase in heart rate, less so than the increase in rate with thiamylal.

These findings with propofol represent probably a dose-related cardiovascular depression, although they were not clinically significant in this group of healthy patients. This effect, which has been demonstrated with both the original formulation and the aqueous emulsion, results primarily from a decrease in systemic vascular resistance and possibly in cardiac output [7–9]. Several authors have reported hypotension in the majority of patients receiving doses of propofol greater than 2.0 mg kg\(^{-1}\) [2, 10]. It is possible that the 2.5-mg kg\(^{-1}\) induction dose, used in our study, represented a relative overdose as all patients were anaesthetized successfully with this single dose of propofol, and only two of the 19 required a 25% supplement for slight limb movements towards the end of the 3-min observation period. However, many authors have used a propofol induction dose of 2.5 mg kg\(^{-1}\) when comparing this drug with other induction agents [11–14].

Recovery was rapid following propofol anaesthesia. Time to eye-opening, response to verbal command and orientation (as determined by correct birthdate) were all significantly faster than with thiamylal. However, the clinical significance of this is debatable as, within 20 min, the patients in both groups were clear-headed with very little drowsiness and there was no difference between the groups in time to discharge. Absence of nausea or vomiting following propofol was also noteworthy, especially considering the nature of the surgical procedure. No thrombosis occurred at the injection site with either agent, although a second 24-h follow-up may have revealed some instances.

In conclusion, both propofol and thiamylal provide a smooth, rapid induction of anaesthesia with minor side effects. Maintenance is easy to control using nitrous oxide and intermittent doses of either agent. Recovery from propofol is more rapid, with significantly less postoperative nausea or vomiting than with thiamylal. Propofol appears to be a suitable i.v. anaesthetic agent for ambulatory patients.

ACKNOWLEDGEMENT

Supported in part by a grant from Stuart Pharmaceuticals.

REFERENCES


