The use of propofol in a group of older patients undergoing oesophagoscopy

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Summary

Propofol (Diprivan; Stuart) a new, very short-acting intravenous anaesthetic agent, was tested in its aqueous emulsion formulation. Used as an induction and maintenance agent, its anaesthetic properties, dosage requirements and side-effects were compared with those of thiopentone in 40 American Society of Anesthiologists class I and II patients scheduled for routine oesophagoscopy.

Both heart rate and diastolic blood pressure were more stable in the propofol group, and recovery times were significantly shorter. Patients were remarkably clear-headed after propofol. When the quality of anaesthesia was independently assessed by an anaesthetist and a surgeon, propofol was rated good or satisfactory in all subjects, and thiopentone in 80%. Anaphylactoid reactions associated with the previous Cremophor EL formulation were not encountered, and pain on injection was experienced in 10% of propofol subjects as against 5% who received thiopentone.

This new intravenous agent produces safe and predictable anaesthesia followed by rapid recovery, making it especially suitable for outpatient anaesthesia.

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The new intravenous anaesthetic drug propofol (2,6-di-isopropylphenol) (Diprivan; Stuart) has been subjected to considerable recent scrutiny and found to possess certain advantages.[1-4] These include rapid onset of sleep with a very short half-life in the body so that there is rapid recovery, and a degree of analgesia not usually associated with intravenous hypnotics. In its new formulation, dissolved in the oil-in-water emulsion Intralipid, it has produced no sensitivity reactions. The accepted induction dose is between 2,0 and 2,5 mg/kg, after which a sleeping time of 3 - 8 minutes is usual. The maintenance dose is between 0,1 and 0,3 mg/kg/min.[5] It has a large volume of distribution (755 l in a 70 kg body) and a high systemic clearance of approximately 1 800 ml/min.[6]

This paper compares the response to thiopentone and propofol in a series of 40 patients undergoing oesophagoscopy. In 90% this was for confirmation of malignant disease. Although some patients had recently lost weight there was no overt disease, and all could be classified as American Society of Anesthesiologists (ASA) class I or II anaesthetic risks. Hospital ethical committee approval and informed consent from individual patients were obtained.

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Patients and methods

All patients starved for at least 6 hours before the investigation and received lorazepam 1 mg by mouth 2 hours pre-operatively as premedication. They were assigned to one of two groups of 20 to receive either propofol 2 mg/kg or thiopentone 4 mg/kg for anaesthetic induction. The drug was administered via a rapidly running intravenous drip while the patient inhaled 100% oxygen. After 1 minute and the onset of sleep, this was followed by intravenous fentanyl 0,001 mg/kg, suxamethonium 1 mg/kg and intubation with an oral armoured cuffed endotracheal tube without topical analgesia to the pharynx or trachea.

Systolic and diastolic blood pressures and heart rate were measured before induction, 1 minute after induction and before the administration of fentanyl and suxamethonium, immediately after intubation, at the start of the operation, and every 5 minutes thereafter until its end. Ventilation was controlled using 33% oxygen in nitrous oxide to maintain an end-expired partial pressure of carbon dioxide of 4,5 v/v as measured by an infra-red capnograph (Datex).

For maintenance, aliquots of either 10 - 20 mg propofol or 25 -50 mg thiopentone were given as indicated by the cardiovascular or reflex movement responses to the surgical stimulus. If movement still interfered with the surgery, an additional 25 mg suxamethonium was used. Doses and times of administration of drugs were recorded along with any side-effects and abnormal reactions. At the end of the procedure, nitrous oxide was discontinued and 100% oxygen was given. The time in minutes was noted for the periods until breathing restarted, until extubation, and until opening of the eyes on command. The time to full orientation was also measured, using as criteria the correctness of answers on personal details and the ability to sit up unaided. An overall assessment of the quality of the anaesthetic was made by the surgeon and the anaesthetist independently and graded as excellent, satisfactory, or unsatisfactory, based upon a smooth induction, absence of movement and other side-effects, stability of blood pressure and pulse rate, and rate of recovery.

Before leaving the recovery room, patients were questioned about the quality of their anaesthetic, specifically concerning awareness, pain on injection, nausea and vomiting or headache.

Results were analysed with the help of the Statistical Analysis Systems Package. The *t*-test was used for analysing the original data and the chi-square test for nominal data. A value of $P < 0,05$ was regarded as significant.

Results

Demographic data of the 40 patients is given in Table I including the ASA status, age, weight, operating and anaesthetic times. The two groups were not significantly different.

Induction. Sleep, as judged by loss of the eyelash reflex, was induced within 60 seconds in all patients except 1 member of the thiopentone group. There were no excitatory effects.

Dosages. In the propofol group a mean induction dose of 2,07 mg/kg was found adequate to abolish the eyelash reflex in all subjects, with a 70% incidence of transient apnoea. The equivalent induction dose of thiopentone was 4,27 mg/kg, which produced apnoea in 95% of subjects. The maintenance dose for propofol was found to be 0,05 mg/kg/min and for thiopentone 0,14 mg/kg/min.

TABLE I. DEMOGRAPHIC DATA (MEAN ± SD)

	Age (yrs)	Weight (kg)	Duration (min) Operation	Duration (min) Anaesthesia	ASA I	ASA II
Propofol	58,3 ± 10	47,4 ± 12,6	14,2 ± 7,9	19,3 ± 8,6	9	11
Thiopentone	52,5 ± 11,5	52 ± 13,4	12,4 ± 5,2	18,7 ± 5,1	7	13

*20 patients in each group.

TABLE II. CHANGES FROM BASELINE OF BLOOD PRESSURE AND HEART RATE (MEAN ± SD)

	After induction			After intubation		
	Systolic BP (mmHg)	Diastolic BP (mmHg)	HR (/min)	Systolic BP (mmHg)	Diastolic BP (mmHg)	HR (/min)
Propofol	−12 (± 9)	−9 (± 7)	+ 6 (± 9)*	+2 (± 20)	+2 (± 9)*	+18 (± 12)
Thiopentone	−11 (± 20)	−4 (± 12)	+ 14 (± 11)	+7 (± 19)	+9 (± 12)	+24 (± 13)

*$P < 0,05$ v. thiopentone group (20 patients in each group).

TABLE III. RECOVERY TIMES IN MINUTES (MEAN ± SD)

	From end of operation until				
	Breathing	Extubation	Eyes open	Orientated	Sitting up
Propofol	3,1 ± 2,2	4,5 ± 2,4	5,6 ± 3,4	10,9 ± 5,2*	15,3 ± 7,3**
Thiopentone	3,1 ± 2,4	6,1 ± 7,3	8,8 ± 11	17,5 ± 12,7	22 ± 14,8

* $P < 0,05$.
** $P < 0,07$ v. thiopentone group (20 patients in each group).

The propofol group needed an average of 40 mg suxamethonium during maintenance (50 μg/kg/min) and the thiopentone group 25 mg (30 μg/kg/min).

Cardiovascular system. Pre- and postoperative blood pressures were similar in both groups. After injection of either drug the systolic and diastolic pressures fell between 5 and 10%. The pulse rate rose after both drugs, the change being significantly greater after thiopentone ($P < 0,05$). After intubation there was a further rise in pulse rate and recovery of the systolic and diastolic pressures in both groups, with the diastolic pressure increase being significantly greater after thiopentone (Table II).

Recovery. Recovery times in minutes are recorded in Table III. These were short with only small differences between the two groups which were not of significance except for the recovery of orientation ($P < 0,05$) and ability to sit up ($P < 0,07$) which were shorter after propofol. It was noteworthy that during recovery propofol subjects rapidly became well orientated, conversed with staff, showed an interest in their surroundings, and expressed a desire to move about, sit up and drink. This contrasted with the aftermath of thiopentone when patients were more lethargic and tended to drop off to sleep if undisturbed.

Side-effects. Minor side-effects were encountered and these are summarised in Table IV.

TABLE IV. PATIENTS EXPERIENCING SIDE-EFFECTS

	Propofol	Thiopentone
Movements	8	13
Cough	4	2
Stiffness	5	2
Pain at injection	2	1
Postoperative nausea	1	0

Quality of anaesthesia. This was assessed after each case by the surgeon and anaesthetist according to the criteria already listed. The anaesthetic was rated excellent or satisfactory in all the propofol patients, and in 80% of the thiopentone group. Main differences lay in an unacceptably high incidence of movement interfering with the procedure, or marked fluctuations of blood pressure and pulse rate during maintenance. There was no awareness during anaesthesia. The awakening with propofol was judged superior in its rate and clarity.

Discussion

If thiopentone is the bench-mark for intravenous anaesthetics, the emulsion formulation of propofol matches the criteria well. From this and other studies it has been found to have double the potency of thiopentone, with a similar time to onset after intravenous injection. Stability of circulation is at least as good, respiratory depression less, side-effects are minimal, and pain on injection no worse.

The relatively low induction dose which was found to be adequate requires comment. The effectiveness of 2 mg/kg in this series is probably related to the greater age of the patients, premedication, the risk factor — the majority were classed ASA II — and the fact that 90% had carcinoma of the oesophagus.[7] For the same reasons the maintenance dose found effective in this study was less. In addition, propofol has analgesic properties,[8] and the level of stimulation during oesophagoscopy is generally low.

The incidence of apnoea on induction is also higher than previously reported[4] despite the reduced dose. It would not have been influenced by the fentanyl which was given subsequently. The duration of apnoea was not measurable as a

relaxant was used. The consistent smoothness of induction with both test drugs is not always seen with other intravenous agents. The cardiovascular changes on induction and maintenance were minor with both drugs, the heart rate remaining more stable in the propofol group.

The one area where propofol was clearly superior was in the awakening process, where orientation returned more quickly ($P < 0,05$) and motor co-ordination was regained sooner ($P < 0,07$), in contrast with the findings of Bahar *et al.*[9] Some patients showed very long recovery times after thiopentone, which is reflected in the greater standard deviation. A consistently shorter recovery time, which here seems to be a positive attribute of propofol, would be of special importance in outpatient anaesthesia.[10]

During maintenance there were slight to moderate movements in 40% of the propofol subjects, and in 65% of those receiving thiopentone. Such movements were easily controlled with small increments of either agent. It was an observation of the surgeon that stiffness of the jaw and neck was more noticeable in the propofol group (5 patients — 25%) than after thiopentone (2 patients — 10%). This needed small increments of suxamethonium for control, with the propofol group requiring 1,6 times as much as the thiopentone group. This may be related to the shorter action of propofol.

In summary, propofol appears to be a valuable new intravenous anaesthetic agent the potential of which can be fully exploited in its unique form. It compares favourably with thiopentone, with the advantage of more rapid awakening. Its use in this special group of older and sicker (60% ASA II) patients, 90% of whom had confirmed malignant disease, proves to be safe. Propofol, therefore, may well become the drug of choice in total intravenous and outpatient anaesthesia.

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Parkinson's disease in blacks

Observations on epidemiology in Natal

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Summary

Black patients with idiopathic Parkinson's disease (PD) present for neurological consultation much less frequently than white or Indian patients. That this is due to true rarity of PD among blacks is suggested by the observation that blacks with motor neuron disease and secondary parkinsonism are treated in numbers comparable with whites and Indians. These conclusions are derived from a series of 2 638 inpatient neurological consultations and from data on levadopa usage in three major hospitals in Durban. Lower life expectancy and failure of old people to attend hospital may be factors in the apparent low prevalence of PD among blacks, but other undetermined factors must play a part.

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Most physicians and neurologists who work among black people in southern Africa believe that idiopathic Parkinson's disease (PD) is rare in this population group.[1,2] Our experience is in accord with this belief. A recently formulated hypothesis[3] proposes that PD, and some other chronic neurological diseases, are the end-result of an earlier subclinical neuronal insult and subsequent age-related neuronal attrition. In the light of this hypothesis study of the epidemiology of PD gains importance and urgency. If there is a population group which enjoys relative immunity to PD this knowledge might focus attention on possible genetic or environmental influences in the pathogenesis of the disease.

There are several obstacles to the epidemiological study of chronic neurological disease in the Third World. Facilities for accurate diagnosis are usually only available in metropolitan hospitals, but the catchment area of any hospital is vague, the population at risk is uncertain and the proportion of patients who attend hospitals rather than traditional healers is unknown. Field studies and door-to-door surveys are logistically impossible. Nevertheless, there is need for information regarding the prevalence of this and other chronic neurological diseases. We cannot afford to ignore evidence just because the basic data do not meet the full requirements for statistical proof. The evidence must be taken at its face value.