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Induction Characteristics of Propofol and Thiopentone: A Comparative Clinical Study in short day Care Cases

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ABSTRACT

In This Randomized Study, an attempt was made to evaluate clinically and compare Propofol and Thiopentone when used alone in unpremedicated patients undergoing minor surgical and orthopedic procedures like fracture reductions and manipulation for dislocations. The study was conducted to know the side effects and drawbacks of the drug. Premedication was avoided to study the drug as a sole inducing agent and also to avoid the effect of premedication on various parameters. All the parameters studied with Propofol were compared with that of Thiopentone.

Keywords- *Propofol, Thiopentone, induction*

INTRODUCTION

Thiopental,a derivative of Pentobarbital remains the "standard" drug against which other drugs are compared.None of the currently available intravenous anaesthetic agents are ideal. Thiopentone is used widely in current anaesthetic practice. However it has a long half-life which delays recovery in outpatient anaesthesia due to accumulation, if used in repeated doses for maintenance. It is necessary to introduce a new, short acting and effective intravenous anaesthetic agent without cumulative properties. Such a drug will be useful for total intravenous anaesthesia,

and will eliminate pollution . Early discharge of patients is cost effective.

MATERIAL AND METHODS

After obtaining ethical comitee approval, forty ASA class I and II adult patients for short surgical procedures like fracture manipulations were studied. Informed consent was taken. The patients were divided into two groups of twenty each. Group I patients (Study group) were induced with Propofol and the group II (control group) with Thiopentone Sodium. Patients with history of allergy or with history of previous adverse reactions after anaesthesia were excluded. No patients in the group received any premedication,to avoid interference . Study groups of patients were induced with Propofol 1%, 2.5 mg/kg IV and the control group of patients with Thiopentone 2.5 %, 5 mg/kg IV. Repeat doses of either Propofol 25 mg IV or Thiopentone 50 mg IV were given only as and when necessary.All the patients were maintained with oxygen (33%) and nitrous oxide 66% without volatiles.

RESULTS AND ANALYSIS

The obtained data was analyzed using the ANNOVA test and the students 't' test.

Table No. 1 shows that the age, sex and weight of the patients were not statistically significant between the two groups.

PAIN ON INJECTION

Pain on injection was graded as mild, moderate and severe. The incidence of pain on injection was given in Table No. 2. Table No. 2 shows that there was no pain on injection in the Thiopentone group. Two patients out of 20 patients in the Propofol group had mild pain.

Induction time:

Induction time was taken as the time taken for the loss of the eye lash reflex from the start of the injection of the drug. The time taken for loss of verbal contact was also noted.

Table No. 3 shows the mean induction times, and standard deviations. There was no significant difference between Propofol and Thiiopentone regarding induction times.

Table No. 4 shows the incidence of spontaneous movements. Two patients out of twenty had spontaneous movements in Propofol Group with an incidence of 10 %. In Thiopentone Group it was absent.

Excitatory effects:

The incidence of excitatory affects such as spontaneous movements, twitching increased muscle tone, hiccups were shown in Table No. 4

INCIDENCE OF ADVERSE EFFECTS

Respiratory side effects like apnoea, coughing and laryngospam were observed and are shown in Table No. 5

The Table No. 5 depicts that seven patients out of twenty patients of Group I had apnoea with an incidence of 35%. Three out of 20 patients in the Group II had apnoea and the incidence was 15%.Coughing was present in one patient of

Group I, - incidence of 5%. Laryngospasm was not noted in both the groups.

Cardiovascular and Respiratory variables

The heart rate was noted before induction, during induction, and at 2,5 ,10 ,15 minutes intervals thereafter. The data were analyzed using "analysis of variance "(ANOVA) and T-test. The data is depicted in Table No. 6

The changes in the heart rate from the base line are shown in the Table No. 7

In Group I the maximum changes in heart rate were noted at five and ten minute intervals. The mean heart rate in Group I (Propofol) reduced from the base line values by four to six beats from induction to recovery. Whereas in Group II (Thiopentone), the heart rate raised from the base line values from Induction to recovery. The mean raise in heart rate was by two beats up to 10 minutes. Difference in heart rates were not significant statistically.

Changes in systolic blood pressure

Table No. 8 shows the systolic blood pressure changes at baseline, during Induction, at 2 minutes, 5 minutes, 10 minutes and 15 minutes intervals.

In Propofol Group, fall of systolic blood pressure was observed at all the time intervals. The fall was maximum at 2 minutes after induction. In Thiopentone Group, the systolic blood pressure increased when compared to base line values at 2 minutes and 5 minutes. Though these changes were observed between the two Groups, they were not statistically significant.

Changes in diastolic blood pressure.

Table No. 9 depicts the alterations that occurred in diastolic blood pressure at the stipulated periods of study in both the Groups.

The diastolic pressure decreased slightly from baseline in Group I patients whereas it increased slightly in Group II patients at all intervals.

Changes in mean arterial pressure The mean arterial pressure changes were statistically analyzed to know their significance and shown in Table No. 10

In the Propofol Group there was a slight decrease in the mean arterial pressures after induction and during maintenance. The decrease in mean arterial pressures were not of much significance statistically when compared to base line values. In Group II there was slight increase in the mean arterial pressures from the base line which were also not significant statistically when compared with the base line values. When both the Groups were compared during anaesthesia and analysed statistically, the difference in mean arterial pressures became significant at 2, 5 and 10 minutes intervals $P < 0.05$.

Changes in respiratory rate

Apnoea

Apnoea was considered when spontaneous respiration was absent for 20 sec or more.

Table No. 12 shows that apneas was frequent and prolonged in Propofol Group. In Group I, seven patients out of 20 had apnoea, the incidence being 35%. In Group II, apnoea occurred in three patients out of 30 during induction, - incidence of 15%. The mean duration of apnoea in Group I was 39 sec and in Group II was 22 sec.

Recovery from Anaesthesia

Group I patients took a mean time of 10.08 minutes to open the eyes and Group II patients took 9.52 minutes to open the eyes. There was not much difference statistically between the two Groups regarding the time taken to open the eyes. However, five patients out of twenty in Group I received supplementary doses. This was the reason for the higher mean value in the Group I patients. If these five patients are excluded from consideration, and the mean value is evaluated for fifteen patients only, we get a value of 8.7 minutes for opening of the eyes and 9.2 minutes for protruding the tongue .Group I patients took 10.59 minutes and Group II patients took 10.00 minutes to protrude the tongue .Group I patients took 11.29 minutes and Group II patients took 10.46 minutes for orientation. These values show that there was not much difference in the recovery parameters . However, statistically significant difference was found in the time taken for other parameters like sitting, standing and normal Romberg. Propofol Group of patients were able to perform these activities much earlier when compared to Thiopentone Group of patients. Group I patients took a mean time of 15.31 minutes compared to 18.90 minutes for sitting ($p<0.05$), 17.66 minutes compared to 22.60 minutes for standing ($p<0.01$) and 18.78 minutes compared to 27.30 minutes for normal Romberg ($p<0.01$).

Nausea and Vomiting

None from Group I had nausea. One patient in Group II had nausea, - incidence of 5%.

Drowsiness

All the patients of Group 11 complained of drowsiness even after half an hour compared to none in Group I

TABLE No. 1

	Group I Proporfol	Group II Thiopentone
Number of Patients studied (N)	20	20
AGE (Mean)	30.40	36.05
(S.D)	12.41	15.40
SEX (Male)	17	14
(Female)	3	6
WEIGHT – Mean (Kg)	51.50	55.35
S.D.	9.36	13.18

TABLE No. 2

Drug	Group	Cases (Nos.)	Occurrence of pain in No. of patients & grade	Percentage
Propofol	I	20	2 (Mild)	10
Thiopentone	II	20	Nil	0

TABLE No. 3

		Group I (sec)	Group II (sec)
Loss of Verbal	Mean	49.60	45.70
	S.D.	11.67	4.68
	Range	30-80	35-54
Loss of Eyelash	Mean	54.70	51.15
	S.D.	12.69	5.90
	Range	34-86	40-60

TABLE NO. 4

Group	Spontaneous Movements	Twitching	Hypertones	Hiccups
Group I	2	-	-	-
Group II	-	-	-	-

TABLE NO. 5

Group	Apnoea	Coughing	Laryngospasm
Group I	7	1	-
Group II	3	-	-

TABLE No. 6

		Heart rate per min Group I	Heart rate per minute Group II
Baseline	Mean	95	88
	S.D.	10.89	12
	Range	72-110	66-120
Induction	Mean	91.50	89.95
	S.D.	10.14	11.58
	Range	70-110	64-110
2 minutes.	Mean	91.70	90
	S.D.	8.97	11.74
	Range	72-104	64-110
5 minutes.	Mean	89.00	89.50
	S.D.	9.04	11.88
	Range	72-108	64-110
10minutes.	Mean	89.70	89.20
	S.D.	10.51	12.01
	Range	74-108	62-106
15 minutes.	Mean	91.00	87.80
	S.D.	11.14	11.40
	Range	76-110	60-104

TABLE NO. 7

	Group	Group II
Induction	-4	+2
2 minutes after Induction	-4	2
5 minutes after induction	-6	2
10 minutes after Induction	-6	2
15 minutes after induction	-4	-1

TABLE No. 8

		Group I (MM Hg)	Group II (mm Hg)
Baseline	Mean	119.70	121.20
	S.D.	11.03	12.70
	Range	100-140	104-160
Induction	Mean	116.20	121.15
	S.D.	12.50	17.16
	Range	100-140	104-180
2 minutes.	Mean	112.50	127.40
	S.D.	14.45	18.61
	Range	90-130	104-180
5 minutes	Mean	113.50	127.80
	S.D.	15.31	18.56
	Range	90-148	104-176
10minutes.	Mean	113.35	121.40
	S.D.	12.89	11.10
	Range	96-132	110-148
15 minutes.	Mean	115.35	122.50
	S.D.	11.03	10.88
	Range	100-132	100 - 144

TABLE No. 9

		Group I (mm Hg)	Group II (mm Hg)
Baseline -	Mean	77.80	79.80
	S.D.	8.41	9.42
	Range	70-90	50-100
Induction	Mean	76.50	82.20
	S.D.	11.56	9.78
	Range	70-100	70-102
2 minutes.	Mean	75.70	82.95
	S.D.	11.00	9.35
	Range	60-100	70-102
5 minutes.	Mean	74.40	82.10
	S.D.	9.78	8.36
	Range	60-86	70-100
10minutes.	Mean	75.80	81.80
	S.D.	9.75	7.85
	Range	50-94	70-100
15 minutes.	Mean	76.60	82.30
	S.D.	8.51	8.06
	Range	56-90	70-100

TABLE NO. 10

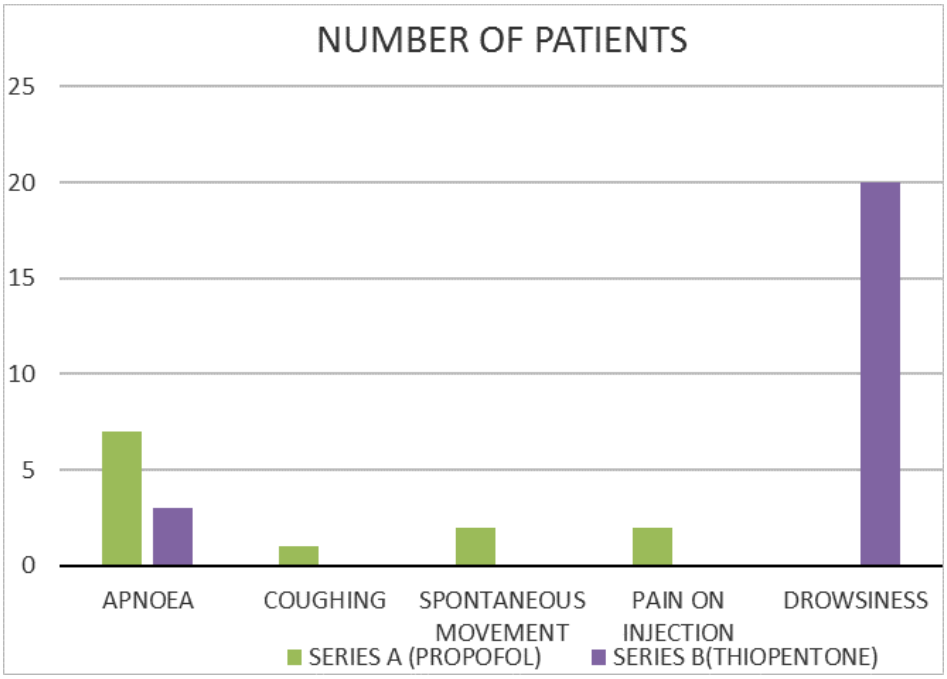
		Group I (MM Hg)	Group II (mm Hg)
Baseline -	Mean	91.40	93.30
	S.D.	8.36	9.83
	Range	70-103	76-120
Induction	Mean	89.50	98.60
	S.D.	10.74	11.86
	Range	70-113	81-128
2 minutes.	Mean	87.65	96.65
	S.D.	10.82	11.36
	Range	73-116	81-112
5 minutes.	Mean	87.75	96.00
	S.D.	10.10	10.15
	Range	66-105	81-125
10minutes.	Mean	87.95	95.70
	S.D.	9.43	9.45
	Range	66-109	83-123
15 minutes.	Mean	89.15	95.50
	S.D.	8.13	9.15
	Range	70-105	81-122

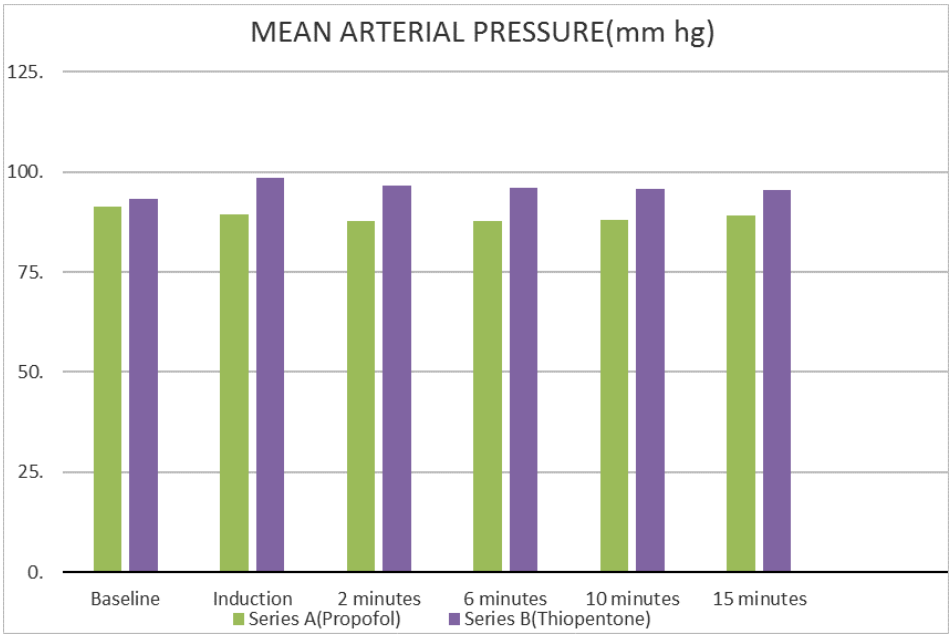
TABLE No. 11

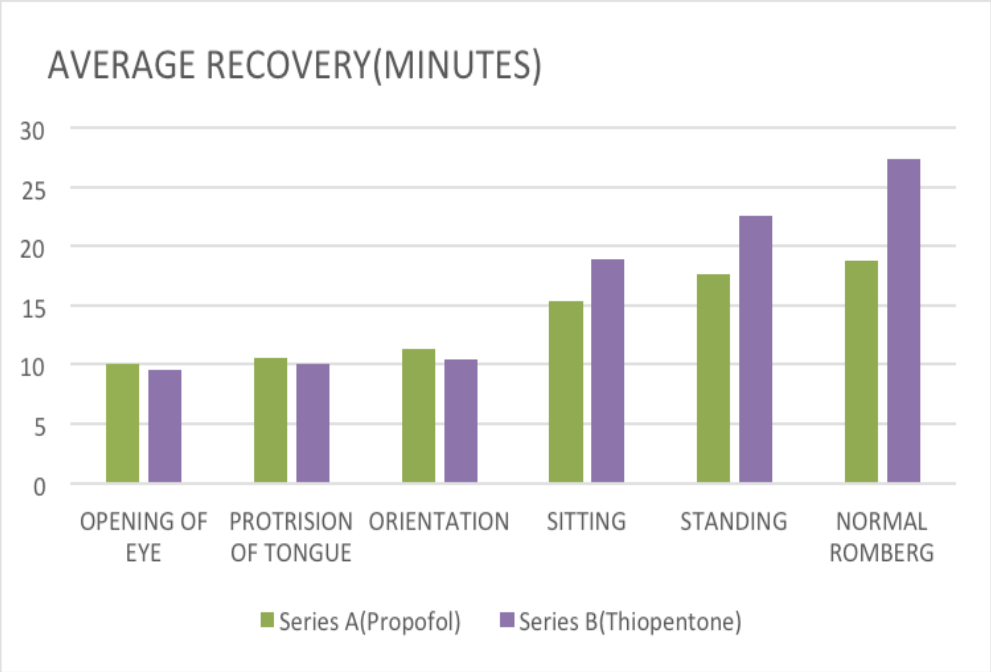
		Respiratory Rate per minute	
		Group I	Group II
Baseline -	Mean	23.20	22.80
	S.D.	3.87	449
	Range	14-28	14-28
Induction	Mean	17.10	18.18
	S.D.	13.48	9.55
	Range	18-32	14-36
2 minutes.	Mean	26.00	23.95
	S.D.	5.58	5.13
	Range	14-32	15-38
5 minutes.	Mean	26.35	23.95
	S.D.	4.67	4.50
	Range	22-38	14-34
10minutes.	Mean	29.65	23.15
	S.D.	5.67	4.33
	Range	20-36	14-34
15 minutes.	Mean	25.35	23.15
	S.D.	4.39	4.06
	Range	18-34	14-30

TABLE No. 12

	Group I	Group II
Number of Patients	7	3
Mean Deviation	39 sec	22 sec







DISCUSSION

The ED95 of the current formulation of Propofol has been estimated as 2.5 mg/kg (Cummings G.C and Collegues, 1984).[1]

In our study, pain on injection occurred only in 10% of patients with Propofol. Pain was not noted with Thiopentone.

In contrast, E. Major et al (1981) noted pain in 80% of patients with ICI 35868 (Disoprofol) when administered in the dorsum of the hand and in 20% when administered in the antecubital fossa.[2,3]

It was observed that the incidence was further reduced when this lignocaine mixed Propofol was given into an anticubital fossa vein. R.D.Stark et al (1985) reported an incidence of 6% when Propofol was injected into veins in the antecubital fossa.[4]

In our study, the mean induction times noted were 54.70sec (Range 30-80 sec) for group I and 51.15 sec (Range 35-54 sec) for group II , when injecting the drug over a period of 30 sec. N. Mackenzie and I.S. Grant (1985) were able to induce the patients with a mean induction time of 30 sec by injecting the drug over 20 sec,[5] G. Rolly and Versichelen (1985) noted a mean induction time 33.3 sec with 1.5 mg/kg of Propofol and 30.5 sec with 2 mg/kg of Propofol, 34.6 sec for Thiopentone (4mg/kg)when given over a period of 2. Sec. There was not much change in the induction times when Propofol 2.5 mg/kg was given instead of 2 mg/kg.[6]

The induction time increased with the duration of the injection of the drug. In our study, we injected the drug over a period of 30 sec instead of 20 sec. Propofol compared favourably with other I V induction agents acting within one arm-to-brain circulation time and with loss of consciousness.

Our study showed spontaneous movements in 10% of the patients of group I;other excitatory effects such as twitching, and hypertonus were not

present. Spontaneous movements were high with Propofol compared to none in Thiopentone. Spontaneous movements have been reported in 14% to 33% of adults by Stark et al[4] and by Fathy et al[7] In our study, these spontaneous movements of a minor nature appeared for few seconds after the completion of injection lasting no longer than 25 sec. It was reported by A. Borgeat et al (1990) that the influence of premedication and the speed of injection on the incidence of spontaneous movements were not clear and further studies were needed to evaluate whether inadequate anaesthesia and central or peripheral stimulation with Propofol.

In our study, Apnoea was present in 35% of patients of Propofol group compared to 15% of patients of Thiopentone group. Mc collum et al[8] noted aponea of more than 30 sec in 17.5% of patients receiving 2mg/kg Propofol and 34 % of patients receiving 2.5mg/kg Propofol. Our results regarding Propofol correlated with the above findings. However, Mc collum et al noted apnoea in 40 % of patients receiving 5 mg/kg of Thiopentone. Grounds et al (1985) observed a very high incidence of aponea in Propofol group of patients (100%) compared to the Thiopentone group of patients (50%).[9] Thus findings in our study in our study were supported by the above observations by both Mc collum and Grounds J.S.C. Mc collum and J.W. Dundee also noted that Propofol was remarkably free from respiratory side effects.[10] None of our patients had any hypersensitivity reaction. Briggs et al reported a case of anaphylactoid reaction in one of the patients who received disoprofol (ICI 35868) 2.5 mg/kg over 20 sec.[11] Because of the associated anaphylactoid reactions with the cremophor EL, the drug was reformulated into the present drug "Propofol" using soya bean oil, glycerol and purifier egg phosphatide.

In our study there was slight decrease in the heart rate in the Propofol group which was not statistically significant. In the Propofol group heart rate did not increase though there was a fall in the blood pressure. In thiopentone group, there was a slight increase in the heart rate which was not statistically significant. Our findings were similar to Grounds and Dubois et al who found that in Propofol cases heart rate was not raised though there was a significant fall in the blood pressure. Rolly noted that heart rate changed little in Propofol group, but it increased in Thiopentone group.[6]

In our study there was a fall of systolic blood pressure at all the time intervals with Propofol and there was a raise in systolic blood pressure at 2 minutes and 5 minutes with Thiopentone. Maximum fall off systolic Blood pressure in the Propofol group was by 2 minutes. Similar changes in the systolic blood pressure were noted by Briggs et al[12] The fall in systolic blood pressure was related to the dose of the drug. Stephan et al noted less pronounced fall in the systolic (18%) and diastolic (4%) when compared to that reported by Prys-Roberts and collagues, who observed a fall of systolic blood plessure (31%) & a fall of diastolic (21%).[13] Martin Gold et al observed that Propofol decreased the systolic blood pressure at 1

min post induction.[14] The systolic blood pressure in the Thiopentone group increased after intubation. Our study findings were similar to that of Martin I Gold et al who observed that there was a raise in systolic blood pressure with intubation in the Thiopoentone group, whereas in the Propofol group it remained at baseline. In our study we found, that systolic blood pressure in Thiopentone group increased with the surgical stimulation whereas it had little effect on the blood pressure in the Propofol group. Thus patients of Propofol group were protected from marked increase in systolic blood pressure during surgical stimulation. We observed similar decreases in the diastolic and mean arterial pressures with Propofol. Grounds found a fall of mean arterial pressure, which was much more with Propofol than with Thiopentone.[10] Similar changes were noted by Rolly, Mackenzie and Grant[15] and Mirakhur et al.[16]

Induction with Propofol was associated with greater fall in blood pressure, which was not much of concern in normally fit patients. Though the maximum fall was at 2 minutes it increased towards baseline afterwards. However, it should be used carefully in hypovolaemic and elderly as suggested by Mc collum[17]

The alterations in mean respiratory rates from baseline were not statistically significant in Thiopentone group. In propofol group, it increased more than that of baseline values at 2 minutes, 5 minutes, 10 minutes. These changes were not statistically significant.

In the present study, time taken to open the eyes was 10.08 minutes .In Propofol group compared to 9.52 minutes of Thiopentone group. There was not much statistical difference between the two groups. However, five patients out of twenty in group I received supplementary doses. This was the reason for the higher mean value in the group I patients. Our observations were similar to that of Mackenzie and Grant, who reported a mean time of 9.3 minutes for Propofol group to open the eyes.[15] Group I patients took 10.59 minutes and group II 10.01 minutes to protrude the tongue. 11.29 minutes and 10.46 minutes were taken for orientation by group I and group II patients respectively. These values show that there was not much difference between the groups regarding recovery parameters.

If patients in Propofol group with supplementary doses were excluded from consideration, the mean time taken for opening of the eyes was 8.7 minutes; and the mean time taken for protruding the tongue was 9.2 minutes. This findings shows that Propofol group of patients took less time than the Thiopentone group for recovery.

However statistically significant difference was found in the time taken for other parameters like sitting, standing and normal Romberg. Propofol group of patients who received supplementary doses also were able to perform these activities much earlier when compared to Thiopentone group, group I patients took a mean time of 15.31 minutes compared to 18.90 minutes for sitting ($P<0.05$); 17.66 minutes compared to 22.60 minutes for standing ($P< 0.01$) and 18.76 minutes

compared to 27.30 minutes for normal Romberg (P< 0.01). This rapid recovery from anaesthesia with Propofol was observed by many workers. They compared Propofol with other intravenous anaesthetic agents and noted that recovery from anaesthesia was smooth and patient was "clear headed". Randall and Paul noted that Propofol group had less of a requirement for analgesics in the recovery room. Since the drug had no analgesic activity, this observation may be a function of clearheadedness associated with Propofol anaesthesia (Johnston R. Noseworthy T and co-workers 1987)[18] G. Rolly and L. Versichelen (1985)[19] studied premedicated patients and found that recovery from anaesthesia was quicker after Propofol than after Thiopentone. Dubois concluded that recovery from Propofol anaesthesia was rapid and of excellent quality.[20]

In our study, none of the patients of Propofol group had nausea; one patient of Thiopentone group had nausea, with incidence of 5%. Health noted 5% incidence of nausea with Propofol and 10% incidence of nausea with Thiopentone.[3] Our findings correlated with that of Briggs, who noticed almost total absence of emetic sequelae with Propofol.[11]

In summary, Propofol is a smooth, rapid acting, sedative-hypnotic compound that would appear to be a useful alternative to the currently available intravenous agents like thiopentone in situations where early ambulation and discharge are indicated.

CONCLUSION

1) Propofol is very useful in day cases surgery.
2) Propofol provides smooth and rapid induction with less respiratory complications.
3) Recovery from Propofol is rapid without significant postoperative sequelae even with supplementary doses.

The desirable features of Propofol like rapid clear emergence from anaesthesia and lack of cumulation allows the drug to be given as a prospective total I V agent. The rapid recovery and low incidence of side effects with Propofol can result in earlier discharge in day case surgery. In addition, the low incidence of side effects associated with Propofol during maintenance suggest that Propofol may be an acceptable alternative to the volatile anaesthetics and / or nitrous oxide. The rapid recovery of consciousness and orientation result in safer recovery with less likelihood of aspiration and makes the patient street-fit early. Significant cardio vascular depression may occur with Propofol and hence the drug should be used carefully in hypovolaemic patients and in patients with heart diseases.

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