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THE RELATION BETWEEN HAEMOGLOBIN LEVEL AND PLASMA PROTEINS ON INDUCTION DOSE OF THIOPENTONE AND PROPOFOL

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ABSTRACT

Objectives To study the relation between haemoglobin level and plasma proteins on induction dose of thiopentone and propofol so as to decide the difference in doses in anaemic and malnourished indivisuals.

Methodology A randomized, prospective study was carried out to find the effect of haemoglobin level and serum proteins on induction dose of Thiopentone and Propofol. In this study, 100 patients (ASA I-II) of either sex between 12-70 years of age, undergoing elective surgical procedure were randomly divided into two groups (A & B) of 50 each. Group A received thiopentone and group B received propofol as induction agents. They were further divided into 3 groups (1,2 and 3) -1 was control group, 2 was low haemoglobin group (<12 gm%) and 3 was low serum protein group (<6mg%).

Results Requirement of thiopentone was significantly decreased in low haemoglobin group (23.74%) and low protein group (13.03%) ($p<0.05$) as compared to control group. Similarly, requirement of propofol was also significantly decreased in low haemoglobin (30.84%) and low protein group (26.15%) ($p<0.05$) as compared to control group.

Conclusion It was concluded that the dose of induction should be reduced in anaemic and malnourished patients and the dose should be titrated according to clinical effects along with mg/kg dose basis

KEYWORDS : Induction agents; thiopentone; propofol; haemoglobin; serum proteins.

INTRODUCTION

Most frequently used intravenous induction agents arc Thiopentone and Propofol. Both drugs have rapid onset of action because of high lipophilic properties. Both of the drugs have high protein binding. Their distribution and fate ultimately linked to the magnitude of their binding to plasma proteins.

Moderate or heavy drinking increased the induction dose but the use of tobacco did not have any influence. The most important factors governing dosage are the physical fitness of the patient and the premedication used. Patients in ASA grades 1 and 2 required significantly more thiopentone than those in grades 3 and 4. This effect is as great as that of premedication in which an opiate with a phenothiazine or hyoscine markedly reduced the induction dose. It was more important than the patient's pre-operative condition with respect to sedation or apprehension. Small doses of opiates or benzodiazepines do not have as much effect on dosage .

Many times it has been noted that dose requirement for induction is reduced in pale looking and in lean and thin, malnourished patients in comparison to good looking normal patients. So present study was carried out to find the relation between haemoglobin level and plasma proteins on induction dose of thiopentone and propofol.

MATERIAL AND METHOD:

The study was carried out on 100 patients of either sex, 12-70 years of age, belonging to ASA grade I and II undergoing elective surgery. Informed consent and institutional approval was obtained prior to study. Patients with gross cardiac, respiratory and gastrointestinal disorders were excluded from study.

Pre operative base line parameters were recorded 5 cc blood was withdrawn and collected in vials. Haemoglobin estimation was done by Sahli's method while serum protein by Biruet method.Patients were randomly allocated into two major groups (A & B). Group A (n=50) received thiopentone and group B (n=50) received propofol as induction agents. They were further divided into three sub groups; 1,2, and 3.1 was control group (having (Hb>12 gm%) and 3 was low protein group (S. Protein<6gm%).

An intravenous drip of 5% dextrose was started and patient was premedicated with glycopyrrolate 0.2 mg IV five minutes before induction.For induction with thiopentone 2.5%, it was given in a dose of 2 mg/kg body weight into a large forearm vein. After 30 seconds, eyelash reflex was tested and if present further 25 mg was given. This dose was repeated at 15 seconds interval until eyelash reflex disappeared. The amount then given was noted and termed as minimum induction dose (MID). For induction with propofol 1%, it was given in a dose of 1 mg/kg into large forearm vein. The dose was increased by 20 mg every 10 seconds until eyelash reflex disappeared then this dose was noted.

Orotracheal intubation was done with succinlycholine (1-2 mg/kg). Maintenance of anesthesia was done with O2, N2O, Halothane and non depolarizing muscle relaxant with controlled ventilation. Patients were monitored carefully throughout and after procedure.

OBSERVATION TABLES

A randomized, prospective study was carried out to find the effect of haemoglobin level and serum proteins on induction dose of Thiopentone and Propofol. In this study, 100 patients (ASA I-II) of either sex between 12-70 years of age, undergoing elective surgical procedure were randomly divided into two groups (A & B) of 50 each. Group A received thiopentone and group B received propofol as induction agents. They were further divided into 3 groups (1,2 and 3) -1 was control group, 2 was low haemoglobin group (<12 gm%) and 3 was low serum protein group (<6mg%).

TABLE 1: COMPARISON OF INDUCTION DOSE OF THIOPENTONE IN CONTROL AND STUDY GROUPS

	Haemoglobin		Protein	
	Control A1	Test A2	Control A1	Test A2
Mean dose mg/kg	4.17	3.18	3.76	3.27
P value	<0.001	<0.05		

This table shows statistically significant decrease in mean dose of induction of Thiopentone in low haemoglobin (<0.0001) and in low

protein groups (<0.05).

TABLE 2: COMPARISON OF INDUCTION DOSE OF PROPOFOL IN CONTROL AND STUDY GROUPS

	Haemoglobin		Protein	
	Control B1	Test B2	Control B1	Test B2
Mean dose mg/kg	2.14	1.48	1.96	1.44
P value	<0.0001	<0.0001		

This table shows statistically highly significant decrease in mean dose of induction of Propofol in low (<0.0001) and in low protein groups (<0.0001).

TABLE 3: COMPARISON REDUCTION IN INDUCTION DOSE OF THIOPENTONE AND PROPOFOL IN LOW HB AND LOW PROTEIN GROUPS

	Low Hb<12 gm%		Low protein <6 gm%	
	Thiopentone	Propofol	Thiopentone	Propofol
	A2	B2	A3	B3
Decrease in dose mg/kg	0.99	0.66	0.49	0.51
Percentage decrease	23.74	30.84	13.03	26.15

There was greater reduction in the induction dose of propofol (30.84% and 26.15%) then thiopentone (23.74% and 13.03%) in low haemoglobin and low protein groups respectively.

RESULTS There were significant decrease in mean dose of induction of thiopentone by 23.74% to 3.18 mg/kg in low haemoglobin group when compared to control (4.17 mg/kg) (p<0.0001). There was also significant decrease in induction dose by 13.03% to 3.27 mg/kg in low protein group when compared to control (3.76 mg/kg) (P,0.05) (table-1 and 3). There was significant decrease in mean dose of induction of propofol by 30.84% to 1.48 mg/kg in low haemoglobin group when compared to control (2.14 mg/kg) (P<0.0001). There was also significant decrease in induction dose of propofol by 26.15% to 1.44 mg/kg in low protein group when compared to control (1.96 mg/kg) (P<0.0001) (table-2 and 3).

STASTISTICAL ANALYSIS-

Data was analyzed using SPSS 20 statistical package. A descriptive analysis was done on all variables to obtain a frequency distribution. The mean + SD and ranges were calculated for quantitative variables. Continuous variables were compared by the Student t test. Proportions were analyzed with the chi-square test. A P value of 0.05 or less was considered statistically significant .Statistical analysis was done. Dose of thiopentone and propofol were compared between control and study groups. Significance was assured at P<0.05

DISCUSSION:-

This study was a randomized, prospective study was carried out to find the effect of haemoglobin level and serum proteins on induction dose of Thiopentone and Propofol. In this study, 100 patients (ASA I-II) of either sex between 12-70 years of age, undergoing elective surgical procedure were randomly divided into two groups (A & B) of 50 each. Group A received thiopentone and group B received propofol as induction agents. They were further divided into 3 groups (1,2 and 3) -1 was control group, 2 was low haemoglobin group (<12 gm%) and 3 was low serum protein group (<6mg%).

Propofol is a widely used i.v. anaesthetic agent. However, its binding properties to blood components have not been fully studied. Study of the minimal dose requirements for induction of anaesthesia poses great problems which are solved by the use of a standard administration technique and the abolition of the eyelash reflex as an endpoint.

Dundee JW et al did their study on the 'induction'dose of thiopentone . This has been used in 2206 consecutive unselected inductions, in which variables considered to be likely to influence the dosage were recorded. Milligram per kilogram is the most acceptable method of expressing the average dosage of thiopentone. Doses follow a right skew distribution. Women required a significantly lower average dose of thiopentone than men, while obese patients required less than others. Moderate or heavy drinking increased the induction dose but the use of tobacco did not have any influence. The most important factors governing dosage are the physical fitness of the patient and the premedication used. Patients in ASA grades 1 and 2 required significantly more thiopentone than those in grades 3 and 4. This effect is as great as that of premedication in which an opiate with a phenothiazine or hyoscine markedly reduced the induction dose. It was more important than the patient's pre-operative condition with respect to sedation or apprehension. Small doses of opiates or benzodiazepines do not have as much effect on dosage. Dundee and Hassard (1983) also observed a significant (P<0.001) direct relationship between the induction dose of thiopentone and haemoglobin level.[1]

McCleane GJ et al inferered that factors that influence the induction of anaesthesia with propofol Patients were investigated in a prospective study of 1000 patients. Pre-operative albumin and urea concentrations correlated with the minimum induction dose of propofol, but less strong correlations were found with haemoglobin, globulin and total protein concentrations. Age was an important influence on the induction dose of propofol (r = 0.34) which was also closely related to ASA grade. Induction of anaesthesia with propofol is dependant on a number of variables, and this study suggested that pre-operative albumin and urea concentrations are important.[2]

Mazoit JX et al studied binding of propofol to blood components and saw the implications for pharmacokinetics and for pharmacodynamics .They studied the binding of propofol to erythrocytes, to human serum and to isolated serum proteins. Because propofol bound to ultrafiltration and equilibrium dialysis membranes, they used a co-binding technique with dextran coated charcoal and with erythrocytes.They concluded that hypoalbuminaemia may increase propofol free fraction particularly during prolonged administration. Since propofol is non-restrictively cleared, no change in clearance is expected to occur, and the increase in free fraction will not be compensated by a parallel increase in clearance. It is also noted that many in vitro studies used concentrations 50 to 500 times the concentration expected to be encountered in the immediate cellular environment.[3]

Edwards R et al studied clinical significance of thiopentone binding to haemoglobin and plasma protein. In their study the minimum dose of thiopentone required to induce anaesthesia was determined by giving thiopentone incrementally until verbal counting and eyelash reflexes were abolished. Males required 2.75 mg/kg (±0.11 SE) and females 2.16 mg/kg (+ 0.10 SE) to abolish verbal counting. Thiopentone requirement correlated positively with haemoglobin concentration (P<0.001) but not with plasma albumin, OI globulin, total globulin or A/G ratio. The presence of sickle-cell haemoglobins did not influence thiopentone requirements.[4]

Ghoneim MM et al did their study on plasma protein binding of thiopental in patients with impaired renal or hepatic function .They studied binding of thiopental to proteins in plasma from healthy, cirrhotic, and uremic subjects .It was studied using equilibrium dialysis. In plasma from healthy volunteers 28.0 plus or minus 0.9 per cent of thiopental was unbound. In plasma from patients with hepatic disease 53.0 plus or minus 2.1 per cent was unbound, while in patients with renal disease 55.7 plus or minus 1.5 per cent

remained unbound. The decreased binding in uremia could not be explained completely by competitive displacement by nitrogenous end products or by hypoalbuminemia, although hypoalbuminemia may account for the decreased binding in cirrhotic patient. There was reduced dose of induction agents in low protein patients. This was explained by the fact that reduction in binding capacity of plasma proteins leads to more amount of drugs free to pass blood brain barrier so decreased dose requirement (Ghoneim and Pandya 1975).[5]

Altmayer P et al studied propofol binding in human blood.It was observed that viscocity of whole blood determined by concentration of red blood cells. Thus a shorter circulation time a patients with low haemoglobin may be the reason for an increased sensitivity to induction agents in anaemic patients. Edward and Ellis (1973) also observed a reduction in thiopentone requirement to abolish eyelash reflex in cases of anaemia. Altmayer et al (1994) observed similar observations regarding propofol binding to serum proteins.[6]

Like the above studies in our study also it was found that there was significant decease in induction doses of thiopentone and propofol and propofol in low haemoglobin and low protein groups.It was observed that in anaemic anoxia cerebral cells may become more sensitive to narcotics so there was lower induction dose of induction agents in anaemic patients.

To conclude that there was significant decrease in induction dose of thiopentone and propofol in low haemoglobin and low protein groups. So dose should be reduced in anaemic and malnourished patients and dose should be titrated according to clinical effects along with mg/kg dose basis.

Conclution Requirement of thiopentone was significantly decreased in low haemoglobin group (23.74%) and low protein group (13.03%) ($p<0.05$) as compared to control group. Similarly, requirement of propofol was also significantly decreased in low haemoglobin (30.84%) and low protein group (26.15%) ($p<0.05$) as compared to control group.It was concluded that the dose of induction should be reduced in anaemic and malnourished patients and the dose should be titrated according to clinical effects along with mg/kg dose basis.

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