Bispectral Index Guided Propofol Induction Dose in Patients Preloaded with Crystalloids

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Background: Conventional pharmacokinetic compartment model doesn't include cardiac output (CO) as a variable for calculating drug concentration. Studies have now identified CO and central blood volume (CBV) as significant factors in calculating the loading dose of propofol. According to previous studies (1999, 2001), compared to patients with low CO, the initial arterial concentration of propofol is lower in patients with high CO due to dilution, taking a longer time to reach hypnosis, for a given dose[1, 2]. However, recent studies (2013) have determined CO to be a negative predictive variable for early phase kinetics of propofol[3]. Although a high CO decreases the drug plasma concentration, an increased CO may accelerate its delivery from the injection site to the target site achieving relatively faster onset of action[4,5].Crystalloids are routinely used to improve CBV and CO, and are preferred over colloids unless indicated, due to lesser side effects. Their half-life ($T_{1/2}$) is usually 20-40minutes under physiological conditions but extend to 80minutes or longer in the presence of preoperative stress, dehydration or blood loss[6]. The longest $T_{1/2}$ of NS measured to be between 3-8 hours is during general anaesthesia requiring intubation[6]. We aimed to preload patients with NS to enhance the CBV and CO to determine propofol induction dose requirement guided by Bispectral Index (BIS). We hypothesised that a lower dose requirement in patients preloaded with crystalloids could reduce the detrimental effects of propofol on haemodynamic stability.

Method: A randomized prospective double blind single center study was undertaken over 18 months. After obtaining hospital ethics committee approval and informed consent from patients, the study was conducted in 46 patients under ASA physical status I, scheduled for elective surgeries. The patients were randomly divided into two groups, the study group and the control group. Study group received 20 ml/kg of NS over 2 hours prior to the induction of anaesthesia and control group did not. All patients were premedicated with midazolam and fentanyl according to body weight and were induced with titrated doses of propofol by administering incremental doses of 20mg over 20seconds at 30second intervals until the endpoint was achieved. The induction endpoint was defined as loss of consciousness determined by absence of response to verbal and gentle physical stimulus and BIS value 45-60. Propofol induction dose and hemodynamic parameters (HR, SBP, DBP, MAP) were measured. Awareness during anaesthesia was evaluated using BIS as well as assessed post operatively using Brice questionnaire. Propofol induction dose was calculated as the mean of observations in the study and control groups. The statistical significance of results was analysed using Student t test and Chi-square test for continuous scale and categorical scale respectively between the two groups.

Results: Propofol induction dose in study group was 0.71±0.16 mg/kg and in control group was 1.04±0.30 mg/kg (P value < 0.001) (Table 1 and Figure 1). However, there was no clinically significant change in the hemodynamic parameters between both groups. None of the patients

had awareness under general anaesthesia.

Conclusion: Crystalloid preloading reduces propofol induction dose during general anaesthesia. This may be explained by an increase in CBV and CO following preloading, which enhances the delivery of propofol to brain.

References:

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3. Korean J Anesthesiol. 2013 Aug;65(2):121-126.
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Propofol requirement for induction in study and control groups

Propofol Dose(mg/Kg)	Study		Control	
	No	%	No	%
<1.0	22	95.6	10	43.5
>1.0	1	4.3	13	56.5
Total	23	100.0	23	100.0
Mean ± SD	0.71±0.16		1.04±0.30	
P value < 0.001				

Table 1

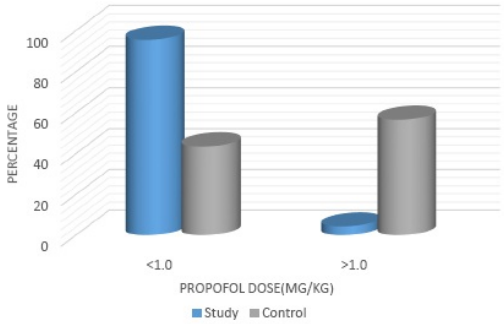

Figure 1