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A Study to Observe Pulse Pressure Variation after Induction with Propofol for General Anesthesia

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Abstract

Background and Aims: Pulse pressure variation (PPV) is a reliable and predictive dynamic parameter presently being utilized for fluid responsiveness. In the operating room, fluid administration based on PPV monitoring helps the physician in deciding whether to volume resuscitate or use interventions in patients undergoing surgery. Propofol is an intravenous induction agent which lowers blood pressure. There are multiple causes such as depression in cardiac output, and peripheral vasodilatation for hypotension. We undertook this study to observe the utility of PPV as a guide to fluid therapy after propofol induction. Primary outcome of our study was to monitor PPV as a marker of fluid responsiveness for the hypotension caused by propofol induction. Secondary outcome included the correlation of PPV with other hemodynamic parameters like heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP); after induction with propofol at regular interval of time. **Methods**: A total number of 90 patients were recruited. Either of the radial artery was then cannulated under local anaesthesia with 20G VygonLeadercath arterial cannula and invasive monitoring transduced. A baseline recording of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and PPV was then recorded. Patients were then induced with predetermined doses of propofol (2 mg/kg) and recordings of HR, SBP, DBP, and PPV were taken at 5, 10 and 15 minutes. Results: Intraoperatively, PPV was significantly higher at 5 minutes and significantly lower at 15 minutes after induction. It was observed that there were no statistically significant correlations between PPV and SBP or DBP. PPV was strongly and directly associated with HR. **Conclusion**: We were able to establish that PPV

predicts fluid responsiveness in hypotension caused by propofol induction; and can be used to administer fluid therapy in managing such hypotension. However, PPV was not directly correlated with hypotension subsequent to propofol administration.

Keywords

Pulse Pressure Variation (PPV), Propofol, Fluid Responsiveness

1. Introduction

Over the last decades, fluid therapy has been considered as first line of therapy during the resuscitation of hemodynamically unstable patients. Although, fluid therapy increases cardiac output (CO) and improves blood pressure; volume overload can also lead to pulmonary edema and interstitial edema which thus increases morbidity and mortality. Accurate prediction of fluid requirement is crucial as it has a great impact on patient outcome. One of the most important concepts in resuscitation is volume responsiveness or the increase in cardiac output in response to a fluid challenge. Central venous pressure (CVP) and pulmonary artery occlusion pressure (PAOP) are static variables to determine the fluid requirement of patients. Dynamic variables, such as pulse pressure variation (PPV), stroke volume variation (SVV), plethysmographic variability index (PVI) and aortic blood flow measured by doppler are more reliable in this regard. [1] [2] These dynamic variables depend on the relation between cardiopulmonary interactions with mechanical ventilation. In the operating room fluid administration based on pulse pressure variation monitoring helps the physician in decision making; whether to volume resuscitate or use interventions. Intra-operative optimization of CO using volume expansion reduces the length of hospital stay, intensive care unit admissions, and complications after major surgery in various settings. [3] [4] [5] In contrast; inappropriate fluid administration can have deleterious effects. [6] CVP is not fully reliable with wide variations in intra-thoracic pressures. It is a poor estimate of preload (as preload depends on ventricular volumes); and the likelihood that CVP can accurately predict fluid responsiveness has been recorded to be unacceptably low (40% - 60%). [7] [8] Although dynamic indices such as pulse pressure variation have been shown to be more trustworthy than CVP in predicting fluid responsiveness with high sensitivity and specificity; they have their own limitations. Numerous studies have shown that a reliable PPV value can be taken only if the patient is on controlled ventilation with tidal volume preset at 8ml/kg; and PPV more than 12 - 13% predicted fluid responsiveness in patients with septic shock or acute respiratory distress syndrome. [9] [10]

It is known that propofol when used as an induction agent lowers blood pressure. Studies have hypothesized that fluid pre-loading prior to propofol administration does not significantly alter the incidence of hypotension post induction.

[11] Thus our aim was to observe the utility of PPV as a guide to fluid therapy after propofol induction.

Although there are only a few studies delineating the utility of using PPV in every hypotensive episode inside the operating room, its role in guiding fluid therapy is well established. Hence the present study was done at our tertiary care centre to examine fluid responsiveness through PPV guided fluid therapy and hemodynamic changes occurring in the operating room after induction and before initiation of any surgical incision. Primary outcome of our study was to monitor PPV as a marker of fluid responsiveness for the hypotension caused by propofol induction. Secondary outcome included the correlation of PPV with other hemodynamic parameters like heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP); after induction with propofol at regular intervals of time.

2. Methods

This was an observational study conducted over two years from June 2016 to June 2018 in the operating room complex of a tertiary care hospital. The study protocol was approved by the Institutional Review Board and Ethics Committee of same hospital. We recruited 80 ASA I and II patients, aged 16 - 60 years who were undergoing elective major surgeries under general anaesthesia (GA) at our hospital. Patients who had cardiac diseases, hypertension, were critically ill, were on vasoactive drugs, positive modified Allen's test and those who required vasoactive drugs during the period of observation were excluded from the study. Pre-anaesthetic check-up was carried out diligently for all patients which included type of surgery planned, detailed past and treatment history, and hematological parameters (especially coagulation profile). After obtaining written informed consent; a modified Allen's test was performed for patency of arterial arches of hands. Patients with positive Modified Allen's test were excluded from the study. Either of the radial artery was then cannulated under local anaesthesia with 20G Vygon Leadercath arterial cannula and invasive monitoring was transduced on Philips Intellivue MP 40 monitors. A baseline recording of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and PPV was recorded. Patients were then induced with predetermined doses of propofol (2 mg/kg) and recordings of HR, SBP, DBP, and PPV were taken at 5, 10 and 15 minutes. If the PPV after induction was found to be more than 15% at any time, a fluid bolus of 10ml/kg over 15 minutes was given; and volume responsiveness was monitored. Any episode of hypotension requiring administration of vasoactive drugs like ephedrine or phenylepherine resulted in the exclusion of the case from the study.

Considering a confidence level of 95% and confidence interval of 11 the number of patients in our study to achieve statistical significance is 79. This was calculated by Survey System (http://www.surveysystem.com/sscalc.htm#one). So, a sample size of 80 was considered adequate for our study. Numerical va-

riables were expressed as mean +/− standard deviation (SD). The categorical variables were presented as absolute values or percentage. ANOVA test was used for analyzing the difference in mean PPV, SBP, DBP and HR at 5, 10 and 15 minutes with the baseline values. For all tests of significance, p-value < 0.05 was considered statistically significant. Pearson's correlation coefficient (r) was used to measure correlation between PPV and HR, SBP, DBP.

3. Results

Majority of the patients (32.5%) were in the age group of 51 - 60 years. The mean age of the patients was 41.25 ± 12.85 years. There were 48.8% male patients while female patients constituted 51.2% of study group. PPV was significantly higher at 5 mins and significantly lower at 15 mins after induction when compared to baseline values (Table 1). There was statistically significant decrease in HR, SBP and DBP after five, 10 and 15 minutes post induction of anaesthesia; when compared to baseline values (Table 2). Further, it was observed that there were no statistically significant correlations between PPV and SBP or DBP (Table 3). However, PPV was strongly and directly associated with HR (r = 0.534; **p < 0.05**).

Table 1. Mean PPV (%) values at different time intervals.

Time intervals	PPV (%) (Mean ± SD)	p Value
Baseline	10.30 ± 2.08	-
05 minutes	13.15 ± 1.92	**p < 0.05**
10 minutes	10.04 ± 1.50	p > 0.05
15 minutes	9.54 ± 1.48	**p < 0.05**

Table 2. Mean heart rate, systolic and diastolic blood pressure values at different time intervals.

Time interval	Heart rate (per minute)		Systolic blood pressure (mm Hg)		Diastolic blood pressure (mm Hg)	
	Mean (±SD)	p Value	Mean (±SD)	p Value	Mean (± SD)	p Value
Baseline	80.44 (±11.61)	-	129.66 (±13.26)	-	78.10 (±8.52)	-
05 mins	67.70 (± 7.86)	**p < 0.05**	109.64 (±8.93)	**p < 0.05**	64.16 (±7.34)	**p < 0.05**
10 mins	75.48 (±7.61)	**p < 0.05**	121.26 (±8.83)	**p < 0.05**	72.71 (±6.68)	**p < 0.05**
15 mins	75.84 (±7.01)	**p < 0.05**	123.81 (±6.02)	**p < 0.05**	73.70 (±6.24)	**p < 0.05**

Table 3. Correlation of Pulse pressure variation with heart rate, systolic and diastolic blood pressure.

Parameters	Pulse pressure variation	
	Pearson's coefficient (r)	p Value
Heart Rate	0.534	**<0.05**
Systolic Blood Pressure	0.086	>0.05
Diastolic Blood Pressure	0.183	>0.05

4. Discussion

The present study was undertaken with 80 patients to observe the PPV after use of propofol for induction of GA. Determination of the intravascular volume status based on clinical parameters alone can be difficult, as well as misleading in patients undergoing major surgery. Traditionally, estimation of cardiac filling pressure to guide fluid therapy has been done with central venous and pulmonary artery catheters. However, several studies performed in recent times have challenged this traditional concept and have demonstrated that cardiac filling pressures are by and large inaccurate in predicting fluid responsiveness. [7] [8] [9] In addition, several dynamic tests of intravenous fluid responsiveness have been reported. These tests essentially monitor the change in stroke volume (SV) after any manoeuvre that alters the left ventricular preload. These tests usually monitor the alteration in SV during mechanical ventilation to assess the intravascular volume status and predict fluid responsiveness.

In concordance with our study, several authors have demonstrated that PPV/SVV (derived from pulse contour analysis), and plethysmographic variation(derived from the change in the amplitude of the pulse oximetry waveform); are highly predictive of fluid responsiveness. [12] [13] [14] Both these variables have been used effectively to evaluate fluid responsiveness in a number of clinical studies and proved to be sensitive in predicting the ventricular response to fluid loading. However, Michard F *et al.* study found PPV to be superior to SPV because it accurately reflects changes in transmural pressures and is less affected by extramural pressures changes like pleural pressure. [10] Denault AY *et al.* found that SPV cannot be explained by only left ventricular volume changes and other factors as intrathoracic and airway pressure changes also affect SPV. [15] Further, Pinsky MR *et al.*, in their study while probing the limits of arterial pulse contour analysis to predict preload responsiveness observed both these variables may be affected by changes in the vasomotor tone. It is understood that multitude of independent factors may cause increased PPV and decreased SBP/DBP. This might explain the absence of correlation between PPV and SBP/DBP.

Intraoperatively throughout the study, heart rate values were significantly lower when compared to baseline value and so were systolic and diastolic blood pressure values which were also significantly lower when compared to baseline

value as per ANOVA test ($\mathbf{p < 0.05}$). Intraoperatively pulse pressure variation was significantly higher at 5 mins and significantly lower at 15 mins after induction when compared to baseline values as per ANOVA test ($\mathbf{p < 0.05}$). These findings are comparable to the studies of Rathore A *et al*., and Khwannimit B *et al*. [16] [17]

The most noteworthy effect of propofol is a decrease in arterial blood pressure during induction of anesthesia. Independent of the presence of cardiovascular disease, an induction dose of 2 to 2.5 mg/kg produces a 25% to 40% reduction of systolic blood pressure. Similar changes are seen in mean and diastolic blood pressure. The decrease in arterial blood pressure is related to a decrease in cardiac output and cardiac index (±15%), stroke volume index (±20%), and systemic vascular resistance (15% to 25%). Left ventricular stroke work index also is decreased (±30%). [18]

Although the decrease in systemic pressure after an induction dose of propofol is caused by vasodilation, the direct myocardial depressant effects of propofol are more controversial. High concentrations of propofol abolish the inotropic effect of α-but not β-adrenoreceptor stimulation. Clinically, the myocardial depressant effect and the vasodilation depend on the dose and on the plasma concentration. Propofol is a vasodilator because it reduces sympathetic activity. [19] [20] The mechanism of this activity is a combination of a direct effect on intracellular smooth muscle calcium mobilization, inhibition of prostacyclin synthesis in endothelial cells, reduction in angiotensin II-elicited calcium entry, activation of potassium ATP channels, and stimulation of nitric oxide. The stimulation of nitric oxide may be modulated by multiple other factors rather than propofol itself. Pharmacodynamic profile of propofol, thus explains the lack of correlation between PPV and SBP/DBP.

Furthermore, heart rate does not vary significantly after an induction dose of propofol. Propofol either may reset or may inhibit the baroreflex, thus reducing the tachycardic response to hypotension. This explains the consistent relation between increasing PPV and decrease in HR.

5. Conclusion

In current practice, PPV can assist with fluid therapy and hemodynamic optimization in patients under GA and receiving positive pressure mechanical ventilation. With new and improved algorithms the PPV has the potential to help us guide the fluid management. The vasodilatory and hypotensive properties of various induction agents are well-known and such a situation is managed in part with intravenous fluid therapy peri-operatively. We were able to establish that PPV predicts fluid responsiveness in hypotension caused by propofol induction; and can be used to administer fluid therapy in managing such hypotension. However, PPV was not directly correlated with hypotension post propofol administration; which emphasizes the fact that independent factors may cause increased PPV and decreased SBP/DBP.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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