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Original research article

Usefulness of pulse pressure variation to predict fluid responsiveness in prone position for patients preoperatively screened to show demonstrable autonomic dysfunction: A prospective, controlled, single blinded, clinical investigation

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Abstract

Background: The presence of autonomic neuropathy can potentially blunt the reflex sympathetic response of vasoconstriction to prone positioning, thus possibly influencing changes in pulse pressure variation and its ability to predict fluid responsiveness. A hypothesis that in the presence of co-existing autonomic dysfunction, a fluid challenge in mechanically ventilated patients undergoing surgery in the prone position would fail to produce significant changes in pulse pressure variation was formed and tested.

Methods: An initial preoperative screening for autonomic dysfunction was performed on 60 ASA grade 1 and 2 adult, consenting volunteers who were electively posted for surgery in the prone position using a battery of 5 bedside clinical tests (0-2 tests positive). A fluid challenge of 6% hydroxyl-ethyl starch, 6ml/kg over 10 minutes, was given to patients in both the groups, 15 minutes after surgical incision. Pulse Pressure Variation was monitored after induction, 5 minutes after induction, 5 minute after prone positioning, on initiation of fluid bolus and 15 minutes after starting the bolus. The observer was blinded to the findings of the preoperative screening.

Results: A significant decrease in PPV was seen 15 minutes after starting the bolus (17.72±3.78 vs. 9.80±1.65 and 17.36±2.05 vs. 8.32±1.67) in both the groups, which was comparable between the two groups.

Conclusion: It was determined, in the end, that autonomic dysfunction does not affect the predictive power of PPV for fluid responsiveness in anaesthetized prone individuals.

Keywords: Prone position, fluid therapy, autonomic nervous system

Introduction

The presence of autonomic dysfunction in an anaesthetized patient is known to pose a challenge in hassle free management of goal directed fluid therapy in the supine position [1]. A sudden change in body position in the presence of a dysfunctional sympathetic- parasympathetic system is also known to cause exaggerated hemodynamic variations, for e.g. as seen in orthostatic hypotension [2]. On the other hand, prone positioning of adult healthy human volunteers, under normal conditions, has been demonstrated to show significant hemodynamic changes such as, a decrease in end-systolic and left ventricular volume, a reduction in venous return and an augmentation of left ventricular filling resistance [3]. Consequently, there is a reflex sympathetic vasoconstriction, which results in initial tachycardia followed by control of blood pressure by baroreceptor reflex activation [4]. Alterations in intrathoracic pressure, chest compliance, and lung flow dynamics are also known to occur in this position, which are key determinants of pulse pressure variation. Considering these facts, we assumed that, a major fluid deficit following venous pooling must occur in autonomic neuropathy with prone position, due to blunted sympathetic vasoconstriction. It was also assumed that this fluid deficit could be less responsive to a fluid challenge.

Responsiveness to fluid challenge as seen by changes in pulse pressure variation has gained validity as an accurate method of managing goal directed fluid therapy in anaesthesia. Pulse pressure variation

(PPV) has been validated as a non-invasive, reliable and accurate predictor of fluid responsiveness in the intensive care unit, [5] in the presence of sepsis, [6] in mechanically ventilated patients, [7] in neurosurgical patients [8] and also in patients undergoing surgery in the prone position [9-10]. Its reliability as a predictor of fluid responsiveness in the presence of autonomic neuropathy has not been established so far due to lack of research in this area. A literature search was also carried out to find the influence of autonomic neuropathy on hemodynamic parameters in the prone position, only to find negligible evidence.

The primary objective of this study was to compare the change in PPV before and after giving an intraoperative fluid bolus in mechanically ventilated anaesthetized prone patients who had been screened to have autonomic dysfunction preoperatively, with those who were not found to have autonomic dysfunction. The secondary objective was to compare the changes in heart rate, PPV and mean arterial pressure in patients with and without known autonomic dysfunction in response to the prone position.

Methodology

This prospective, nonrandomized, controlled, single blinded study was conducted from June 2019 to July 2020 at Department of Anesthesiology and Intensive Care Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India, after being approved by the institutional review board. A written informed consent was obtained from all the adult human volunteers participating in this study or from their legal surrogates.

Inclusion criteria

- Between 18-60 years of age,
- 60 ASA grade 1 and 2.
- Patient consent.
- Posted for short duration (estimated time< 200 minutes) surgeries requiring prone position (cervical, thoracic, thoraco-lumbar, lumbar spine discectomies /fixations, lower limb vascular surgeries, gluteal and thigh soft tissue tumors).

Exclusion criteria

- Unwillingness to participate
- History of allergy to starch solutions
- Renal, hepatic, cardiac or pulmonary dysfunction as evidenced by laboratory investigations or history.

Statistical Analysis

The statistical software SPSS version 22.0 (Armonk, NY: IBM corp. released 2013) was used to analyze the collected data with Student’s T test, chi square test, ANOVA and Fischer Exact test (with a probability value of less than 5% as level of significance).

Results

Table 1: Demographic distribution

Demographic variables	Group I (n=30)	Group II (n=30)	P Value
Mean Age (years)	50.16±11.40	44.84±11.98	0.114
Mean Height(cms)	160.76±8.62	164.88±9.81	0.086
Mean Weight(kg)	60.16±6.95	60.64±7.85	0.820
BMI(kg/m2)	23.55±1.99	22.48±3.77	0.216
Male: female ratio (M:F)	17:8	17:8	1.000
ASA class (1:2)	16:9	18:7	0.544

Values in mean ± SD, Categorical data in ratio. $p<0.05$*

Demographic variables were evenly distributed in both the groups ($p>0.05$) (Table1).

Group A (n=30) had 21 patients with history of long standing diabetes (> 10 years), 3 patients with high preoperative glycosylated haemoglobin values of >6.5, 5 patients with long standing diabetes and high glycosylated haemoglobin values both, 1 patient had received chemotherapy for prostate cancer and was posted for lumbar vertebral fracture fixation, none of the patients had history suggestive of any co-existent autoimmune disease. In Group B (n=30), 9 patients had history of long standing diabetes (>10years), 1 patient had high glycosylated haemoglobin levels, none of the patients in this group had received chemotherapy nor did they have history related to any other autoimmune disorder.

Table 2: Mean pulse pressure variation in percentage in both the groups at different time intervals

	Group 1	Group 2	P value between the groups
Baseline (T_0)	6.80±1.29	7.32±1.37	p=0.085
5 minutes after induction (T_1)	6.96±1.56	7.32±1.43	p=0.256

T_0-T_1	(p=0.51) (p=0.732)		
5 minutes after prone (T_2)	14.63±2.86*	15.12±2.52*	p=0.064
T_1-T_2	(p=0.034)* (p=0.025)*		
Initiation of bolus (T_3)	17.72±3.78	17.36±2.05	p=0.56
T_2-T_3	(p=0.06) (p=0.082)		
15 minutes after bolus (T_4)	9.86±1.65*	8.32±1.67*	p=0.075
T_3-T_4	(p=0.012)* (p=0.021)*		

Values in mean±SD and in percentage %

PPV increased significantly five minutes after positioning the patient from supine to prone. There was also a significant drop in PPV fifteen minutes after initiation of fluid bolus. This change was similar in both the groups (Table 2).

Table 3: Change in mean heart rate per minute at different time intervals in both the groups

	Group 1	**Group 2**	**p value between the groups**
Baseline (T_0)	81.52±13.78	88.52±11.97	p=0.074
5 minutes after induction (T_1)	79.92±13.07	78.76±11.19	p=0.136
T_0-T_1	(p=0.12)	(p=0.16)	
5 minutes after prone (T_2)	87.04±16.12*	84.80±15.90*	p=0.29
T_1-T_2	(p=0.048)*	(p=0.051)*	
Initiation of bolus (T_3)	86.72±16.04	87.84±16.35	p=0.068
T_2-T_3	(p=0.31)	(p=0.36)	
15 minutes after bolus (T_4)	82.96±12.93	83.44±13.80	p=0.077
T_3-T_4	(p=0.08)	(p=0.063)	

Values in mean ±SD as heart rate per minute

Table 4: Change in mean arterial pressure at different time intervals in both the groups

	Group 1	**Group 2**	**p value between the groups**
Baseline (T_0)	103.20±18.75	99.72±13.63	p=0.089
5 minutes after induction (T_1)	92.04±17.88	89.00±14.49	p=0.18
T_0-T_1	(p=0.071)	(p=0.068)	
5 minutes after prone (T_2)	107.00±15.89*	104.84±17.62*	p=0.09
T_1-T_2	(p=0.056)*	(p=0.046)*	
Initiation of bolus (T_3)	97.76±15.31	91.00±13.38	p=0.064
T_2-T_3	(p=0.074)	(p=0.06)	
15 minutes after bolus (T_4)	95.84±10.37	95.40±10.92	p=0.2
T_3-T_4	(p=0.09)	(p=0.076)	

Values in mean ±SD (Between the groups *p*>0.05) (values in mmHg)

Hemodynamic recordings were comparable in both the groups at all-time intervals (Table 3 and Table 4). There was a rise in mean heart rate (p=0.046, p=0.039) and fall in mean arterial pressure (p=0.0372, p=0.044) from the time of induction to five minutes after giving prone position in both the groups. There was also a significant drop in heart rate (p=0.048, p=0.042) fifteen minutes after the fluid challenge in both the groups. However these changes were comparable in between the two groups.

Discussion

Healthful human bodies' cardiac autonomic drive is affected by position and posture while sedated. The changes following prone position have been extensively studied. Pump *et al.* (2002) [15] observed a rise in heart rate and sympathetic nerve activity in addition to a significant fall in stroke volume six hours after giving prone posture to adult healthy volunteers. Transoesophageal echocardiography in prone surgical patients under general anaesthesia was shown by Dharmavaram *et al.* (2016) [3] to show a reduction in end-diastolic left ventricular area and left ventricular volume. These alterations were attributed to compression of the inferior vena cava, which reduced venous flow, compression of the thorax, which increased left ventricular filling resistance, decreased central blood flow, which caused pooling, and increased blood volume in peripheral vessels, which triggered a reflex sympathetic response. Thus, in an intact autonomic nervous system, the response of prone positioning would be transient hypotension due to peripheral venous pooling, followed by tachycardia and hypertension.

In autonomic neuropathy, absence of this reflex sympathetic response usually manifests itself as orthostatic hypotension or as exaggerated hemodynamic variations following changes in intrathoracic pressure during the valsalva manouver (1). A similar response to a sudden change in position or an increase in abdomino-thoracic pressure following prone position can thus be hypothesized. Negligible research has been carried out so far in this area, particularly in patients with pre-existing autonomic dysfunction who are subjected to prone position under anaesthesia, thus validating the need to study hemodynamic changes and fluid responsiveness in the above stated conditions.

It was therefore, hypothesized that on prone positioning the study group patients (with autonomic dysfunction), there would be less fluid responsiveness due to vasodilatation (as seen by minimal or insignificant changes in pulse pressure variation after fluid challenge). This was the primary outcome measure under investigation in the study. Similarly it was also hypothesized that prone positioning of the study group patients would not bring about a significant rise in heart rate, which was the secondary outcome measure.

Defying our assumptions, the results of this study demonstrated a significant decrease in pulse pressure variation after 15 minutes of fluid challenge, in both the groups. Also, a rise in heart rate, fall in mean arterial pressure and an increase in pulse pressure variation 5 minutes after prone positioning was seen in both the groups, indicating that the presence of demonstrable preoperative autonomic dysfunction in the study group did not alter the haemodynamics with change in position any differently than the control group.

These results were at par with findings from earlier studies showing similar alterations in hemodynamic variables after prone position from supine and after fluid bolus [3-4, 9-10].

The possible explanation for the results that we found in our study is the presence of mechanisms other than the sympathetic-parasympathetic system coming into play after a patient is given the prone position. In a prone posture, the heart may be regulated in a variety of ways, including by neuronal, renal, and endocrine systems, each of which operates on a somewhat different time scale [16]. The trigeminal afferents are thought to regulate heart activity, and there is evidence to imply that the prone posture causes face tissue compression that does not occur in the supine posture. Vessel myogenic activity, which is unrelated to the cardiac autonomic nervous system, is another non-neural component that may play a role [17].

The decrease in pulse pressure variation after bolus and increase in heart rate on prone positioning a patient with autonomic dysfunction can probably be explained by these mechanisms.

This study is not devoid of limitations. For accuracy in measuring PPV for fluid responsiveness, some authors [20] have limited intravenous fluid from the time of induction until the onset of the fluid bolus by administering a diuretic. Secondly, bedside clinical tests for autonomic dysfunction were used to screen the study population because these were found to be reliable, easy to explain and less time consuming. The use of other noninvasive and invasive tests could have optimized our screening process, albeit, at the expense of increasing the cost of surgery and delaying the surgical intervention. Our limitations leave scope for further research in this area.

We thus conclude that, pulse pressure variation is able to predict fluid responsiveness in anaesthetized patients operated in prone position irrespective of the presence or absence of autonomic dysfunction and that autonomic dysfunction does not influence prone position induced tachycardia.

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Conflicts of interest
Nil.

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