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RESPONSIVENESS IN SHOCK PATIENTS**

EVALUATION OF PASSIVE LEG RAISING TEST FOR PREDICTING FLUID RESPONSIVENESS IN SHOCK PATIENTS

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ABSTRACT

Introduction: Intravenous fluid administration remains the primary therapeutic intervention for haemodynamically unstable patients. However, studies have shown that about 50% of such patients would not respond to fluid therapy only. This study evaluates the predictive value of passive leg raising (PLR) test in predicting fluid responsiveness in shock patients.

Methods: Adult patients who were in a state of continuous shock (systolic blood pressure < 90mmHg) after initial fluid resuscitation in accident and emergency unit in a teaching hospital in Nigeria over a six-month period were enrolled. All the patients underwent passive leg raising (PLR) test, and were then divided into PLR responders (systolic blood pressure >90mmHg) and PLR non-responders (systolic blood pressure <90mmHg) following PLR. This was followed by further re-categorization into two sub-groups; those who responded to fluid therapy to maintain blood pressure (FTG) and those who required cardiotoxic drugs (CTG). The pre-intervention and post-intervention vital signs were then retrospectively analysed between the groups.

Results: Twenty-five patients' results were analysed for the study. The mean age of the patients was 50.6±4.64 years with male to female ratio of 1.2:1. The mean age of the patients in FTG and CTG were comparable (51.67±3.54 vs 49.53±5.28; p= 0.2378). Twelve patients responded to Passive Leg Raising (PLR) test and 13 patients failed to respond to PLR. Nine (75%) out of 12 patients that responded to PLR were successfully managed with fluid therapy as compared to 2 (15.38%) out of 13 non-responders who were successfully managed with fluid therapy only (p=0.0094) giving PLR 75% and 85% positive predictive value and negative predictive value respectively in predicting pre-load dependent circulation.

Conclusion: Passive leg rising can be used as a guide for fluid replacement in patients with shock. Other interventions should be considered early in patients who failed to respond to passive leg raising.

Keywords: Passive leg raising test, fluid responsiveness, critically ill patients

INTRODUCTION

Shock is a state of circulatory collapse resulting in tissue hypo perfusion. It is characterized by fall in systolic blood

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pressure below 90mmHg and mean arterial pressure below 60 mmHg or reduction of mean arterial pressure for more than 30 minutes, oliguria and decreased peripheral perfusion.^{1,2} Shock can be classified into four major groups based on the pathophysiologic mechanism responsible for it: hypovolemic shock, cardiogenic shock, low resistance shock and septic shock.

The initial treatment of shock includes fluid replacement and oxygen support therapy. The aim of fluid administration is to increase preload and subsequently increase cardiac output, however, studies have shown that about 50% of critically ill patients will not respond to fluid therapy and thus are at increased risk of fluid overload if caution is not taken.³ The risk of fluid overload and its adverse effects are more likely to be of great detriment in patients with cardiogenic shock, who are more likely to require guarded fluid therapy to prevent volume overload in an already weakened heart.

Differentiating the type of shock at presentation may be a difficult challenge and even more difficult is knowing when the “tank is full”. In order to determine the effectiveness and adequacy of fluid therapy in patients with shock, it is mandatory to monitor the patient’s hemodynamic response to fluid administration to avoid fluid overload. There are currently various invasive and non-invasive means of monitoring fluid responsiveness in shock; however, the invasive forms such as central venous pressure (CVP) and pulmonary arterial wedge catheter pressure (PAWCP) are becoming less favored, while the non-invasive methods such as transthoracic echocardiography assessment of stroke volume and passive leg raising test (PLR) also known as modified Trendelenburg position are gaining more popularity as means of determining fluid responsiveness in shock patients.

The passive leg raising (PLR) is a simple maneuver that mimics exogenous fluid replacement by mobilizing about 200-300ml of blood from the capacitance vessels of the lower limbs and the splanchnic circulation reservoir to central circulation thus

increasing the preload.⁴⁻⁶ The hemodynamic changes associated with PLR is expected to lead to increase in right ventricle output and stroke volume in patients with pre-load dependent right ventricle and in patients with significant or good left ventricular reserve; this positive response will not be observed or marked in patients with non-preload dependent right ventricle and those with poor left ventricular reserve such as patients with cardiogenic shock. Thus, response to PLR may guide clinicians in determining patients who are likely to respond to fluid therapy without risk of fluid overload.^{7,8} Various high-tech adjunct equipment had been used to assess hemodynamic changes in response to PLR, such as the use of bioimpedance and carotid Doppler to determine volume responsiveness and bioflow using transthoracic echocardiography to measure stroke volume. This study was conducted to evaluate PLR in predicting fluid responsiveness in patients with shock using simple bedside blood pressure and pulse rate as means of assessing fluid responsiveness following PLR as authors are not aware of any such study in Africa.

METHODS

This prospective study was carried out over a six-month period. Adult patients who were diagnosed of shock in the emergency department and were not out of shock after our routine standard of care involving ABC of resuscitation, which include infusion of 2 litres of normal saline within 30 minutes and ongoing search for, and treatment of background cause of shock were enrolled into the study. Shock was diagnosed when systolic blood pressure (SBP) is less than 90mmHg with one or more other clinical evidence of shock such as pallor, cold skin, and evidence of dehydration: fast thready pulse, yawning and thirst.

Informed consents were obtained from all the rational patients or their relative when patients were considered to be irrational and not competent to give informed consent. Patients who failed to give consent, or those in whom the procedure was considered to be

technically difficult to perform (such as patients with lower limb and pelvic fracture and patients with hip pathology that preclude flexion of hip joint), patient with amputation with little fluid to mobilise and patients with suspected elevated intracranial pressure who may not tolerate sudden increase in intravascular volume were all excluded from the study. The data collected include: patients' biodata, clinical diagnosis, vital signs at various points, mean arterial pressure (MAP) calculated as sum of patient's diastolic blood pressure (DBP) and one-third of pulse pressure (PP) [DBP+1/3PP] and patients' estimated weight using ARDSnet's formulae to predicting body weight.⁹ All patients received initial routine care using ABC of resuscitation with intention to treat.

The procedures of PLR were performed on those patients who failed to maintain systolic blood pressure above 90mmHg after our initial resuscitation with 2L of fluid over 30 minutes. The procedures of PLR were performed by two senior registrars who were previously trained on PLR test. The two senior registrars who performed the procedures were not aware about the nature of the study. The procedure of PLR was performed on each of the enrolled patient by raising the two lower limbs of the patient at the same time (by one senior registrar) from supine position to between 45° and 60° (by flexing the hip joints and keeping the knee joints in full extension). The second senior registrar measured patients' pulse rate, blood pressure, respiratory rate and spO₂ after ten seconds of commencement of PLR while the patient's lower limbs are kept at PLR position.

Enrolled patients that underwent PLR were then divided into two groups based on their haemodynamic response to PLR test: PLR responders and PLR non-responders. Patients whose systolic blood pressure rose above 90mmHg or pulse rate fell by ten/minute or more after PLR were considered as PLR responders. Both groups were then continued on intravenous fluid therapy, oxygen support and other routine care. The

subsequent fluid therapy regimen consists of infusion of 20ml/kg of normal saline over 10 to 20 minutes, following which patients' vital signs were reassessed.

All patients that failed to maintain systolic BP of greater than 90mmHg with other sign of shock after 30 minutes of current regimen had re-infusion of another 20ml/kg of normal saline over 30 minutes. Those patients that maintained systolic blood pressure of greater than 90mmHg after the fluid therapy were considered to respond to fluid therapy only (FTG) while those who still failed after the re-infusion of fluid therapy were considered as those that required cardiotoxic drugs (CTG). Based on response to exogenous fluid therapy, patients were then sub-grouped into two groups; those who responded to fluid therapy to maintain blood pressure (FTG) and those who required dobutamine (at dose of 10 mcg/kg/minute) as cardiotoxic drugs (CTG) to maintain their blood pressure (Figure 1). The pre-intervention and post intervention vital signs were then retrospectively analysed between the groups. Test of significance was by t-test for continuous variable and chi square for categorical variables. P-value was set below 0.05 for statistical significant difference.

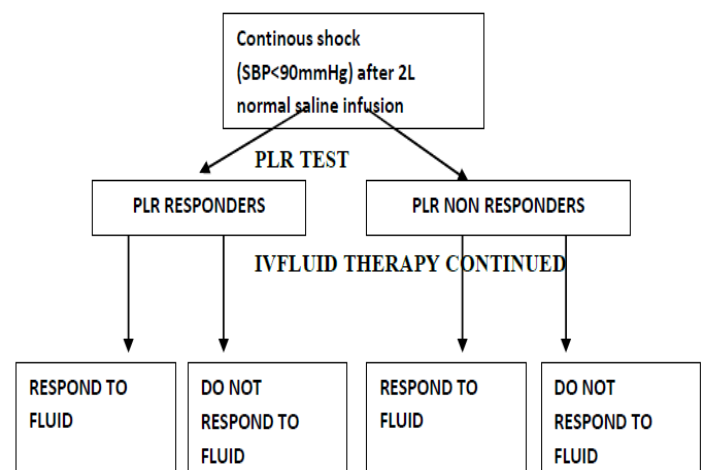


Figure 1: Flow chart showing grouping and subgrouping following PLR test and intravenous fluid therapy respectively. PLR: Passive leg raising

RESULTS

The spectrum of clinical diagnosis in both the responders and non-responders were similar (table 1)

Table 1. The spectrum of clinical diagnosis among the patients

Diagnosis	PLR Responders	PLR Non responders
Blunt abdominal injury	7	5
Thermal burn	1	2
Intestinal obstruction	3	4
Perforated duodenal ulcer	1	2

Twelve (48%) of the 25 patients responded to PLR and 13 patients failed to respond to PLR. Nine (75%) out of 12 patients that responded to PLR were successfully managed with fluid therapy as compared to 2 (15.38%) out of 13 non responders who were also successfully managed with fluid therapy only ($p=0.0094$) giving PLR 75% and 85% positive predictive value (PPV) and negative predictive value of (NPV) respectively in predicting pre-load dependent circulation. Nine (81.8%) out of the 11 patient who responded to fluid therapy alone were PLR responders giving a specificity of 81.2%, while 11(84.6%) of 13 non responders and 2 (22.2%) of the 9 responders to PLR also failed on fluid therapy alone giving a specificity of 78.6% in predicting fluid responsiveness

Pre-intervention pulse rate (PR), systolic blood pressure (SBP) and mean arterial pressure (MAP) were comparable in all groups (Fig 2).

Analysis of vital signs following PLR intervention showed that PR, SBP and MAP had statistically significant differences between those that responded to fluid only therapy (FTG) and those that do not and required cardiotoxic drug (CTG): PR (102.90 ± 13.79 vs 121 ± 16.85 ; $p=0.0076$),

SBP (102.63 ± 3.06 vs 85.14 ± 1.40 ; $p<0.001$) and MAP (82.14 ± 10.92 vs 68.99 ± 5.40 ; $p=0.001$).

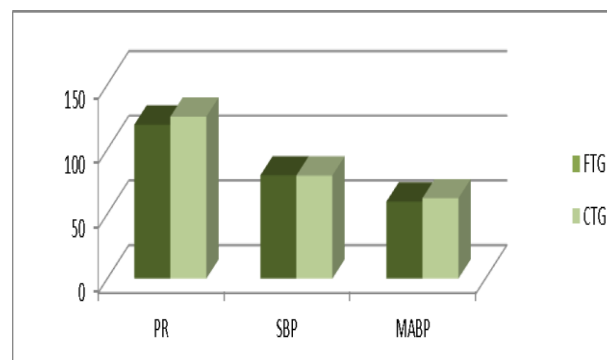


Figure 2: Pre- intervention vital signs among those treated with intravenous fluid therapy only and those that required cardiotoxic drug.

DISCUSSION

Shock is a state of circulatory collapse caused by imbalance between oxygen supply and demand resulting in cellular hypoxia and subsequent end-organ dysfunction. Passive leg raising test is recommended as one of the means of monitoring hemodynamic responsiveness in shock patients based on current international recommendation.¹⁰ This study was thus conducted to evaluate the predictive value of PLR in preload dependent circulation among patients with circulatory collapse using a simple bed side vital signs as means of measuring responsiveness.

Our study found out that PLR induced changes in preload through gravitational redistribution of blood from the lower extremities and abdomen and predict preload dependent circulation in patients who were clinically diagnosed of shock based on low systolic blood pressure.

The study also found out that about 48% of the patients who were in shock responded to rapid endogenous fluid mobilization from lower limbs following passive leg raising test and were considered to be PLR responders.

When intravenous fluid therapy was administered to both the responder and non-responder it was found out that majority (75%) of the patients that responded to PLR were successfully managed with intravenous fluid infusion only to maintain blood pressure and thus they were considered as true responder compared to about 15% of the patients who failed to respond to PLR but eventually responded to intravenous fluid infusion. From the study PLR has a sensitivity and specificity of about 81% and 78% respectively in predicting fluid responsiveness in critically ill patients. The sensitivity and specificity from our study were lower than pooled sensitivity and specificity of 86% and 92% respectively in a meta-analysis of 23 trials involving more than 1000 patients.¹¹ This may be due to lag in measurement of patients' vital signs in our study. The higher value quoted in the meta-analysis was probably due to use of stroke volume index as measure of responsiveness in many of such trials; this factor was previously reported to improve predicting value of PLR.^{7,11}

Similarly, the responsiveness to PLR has also been shown to be affected by the method of performing the test; the effect of position on PLR has previously been reported with better fluid mobilization if patient is moved from semi recumbent position before being moved to supine position prior to elevation of the legs.^{4,12}

The first line of management of shock involves fluid replacement therapy through rapid infusion of crystalloids or blood. However continuous infusion of fluid in patients who required other forms of therapy is dangerous, as risk of fluid overload will be imminent, a factor considered as independent risk factor that worsen outcome of patients in septic shock or ARDS.^{13,14} Excessive fluid in form of fluid overload may lead to tissue edema with resultant decrease in blood flow to tissues thus identification of those groups of patients that will respond to further fluid infusion is of importance in critical care and emergency setting as either inadequate or excessive fluid infusion can result in adverse

events.⁷ Therefore, means of predicting fluid responsiveness in shock patients are gaining attention. The use of clinical signs and some other volumetric static measurements are considered unreliable predictor of fluid responsiveness.¹¹ Also dynamic indices such as ventilator-induced variation in pulse pressure and stroke volume which were developed and are considered more reliable, have limited uses in patients with arrhythmia or those with spontaneous breathing or on low tidal volume ventilation.¹⁵⁻¹⁷

The determination of adequacy of fluid infusion and responsiveness in shock patients may be done through invasive monitoring such as measurement of central venous pressure and pulmonary arterial wedge pressure through the use of CVP monitoring device and Swan-Ganz pulmonary artery catheter respectively. These devices have potential harmful effects and there is no current evidence to support their use in monitoring shock patients, more so they are not available in many poor resource settings. Thus there is growing support and paradigm shift toward the use of non-invasive options such as PLR and echocardiography.

PLR has been suggested and currently gaining support as a non-invasive means of predicting fluid responsiveness in patients with hemodynamic instability. Passive leg raising produces a transient and reversible increase in preload volume through mobilisation of the blood from lower extremities and splanchnic circulation, a maneuver that mimic increase in preload without actual exogenous fluid infusion. However, the use of PLR is also theoretically considered to be unreliable in patient with elevated intra-abdominal pressure.⁴ The elevated intra-abdominal pressure (IAP) is hypothesized to compress inferior vena cava, thus increasing resistance to blood flow in PLR.¹⁸ However, the study failed to measure intra-abdominal pressure during the procedure of PLR.¹⁸ Contrary to this hypothesis, it was also theoretically hypothesized that PLR may reduce IAP by pushing the diaphragm up and relieving its weight on the abdominal cavity. This

method is considered safe, as it may prevent patients from receiving unnecessary fluid challenge, which can lead to fluid overload.¹⁹

Thus, PLR should be considered as a means of challenging preload without exogenous fluid administration. Also failure to respond to PLR should raise immediate suspicion of considering non-hypovolemic shock such as cardiogenic shock, obstructive form of shock or decompensated hypovolemic shock that may require escalation of other forms of interventions. Though, PLR is considered to predict fluid responsiveness, the decision to administer further fluid should be individualized and be based on: sign of shock, positive PLR test and risk of fluid overload. The use of PLR should be considered with caution in some clinical conditions such as patients with elevated intracranial pressure that may not tolerate sudden increase in circulatory volume and should be considered of limited use in patients with lower limb amputation with low blood volume in their capacitance vessels, patients on beta blockers and patients with autonomic dysfunction.

Limitation of the study

The study did not measure intra-abdominal pressure which is hypothesized to affect venous return in PLR.

CONCLUSION

PLR is a simple and effective predictor of responsiveness to fluid therapy in shock patients and other interventions should be considered early in patients who failed to respond to PLR. We suggest early use of PLR on arrival as part of the C component of ABC of resuscitation as the procedure will not only predict fluid responsiveness but also assist in effective circulatory volume support.

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