Audit of preoperative fluid resuscitation in perforation peritonitis patients using Physiological and Operative Severity Score for enUmeration of Mortality and Morbidity

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ABSTRACT

Context: Debate continues regarding fluid (crystalloid vs. colloid) of choice for resuscitation. Physiological and Operative Severity Score for enUmeration of Mortality and Morbidity (POSSUM) may be used to compare the benefits of preoperative fluid resuscitation with crystalloids and colloids in peritonitis patients. Aims: The aim of this study is to compare crystalloid and colloid for preoperative resuscitation using morbidity, mortality, length of hospital stay (LOS), and time taken to resuscitate as the outcome parameters. Settings and Design: This was a prospective randomized clinical trial. Subjects and Methods: One hundred and seven peritonitis patients were prospectively randomized to fluid resuscitation by crystalloid (Group A) and colloid (Group B) solutions. Physiological score component of POSSUM was recorded before and after fluid resuscitation; operative score component was recorded at discharge/death. These scores were then used to calculate the predicted morbidity and mortality before and after the fluid resuscitation. Statistical Analysis Used: Effect on morbidity and mortality were compared by repeated measure analysis of variance, and its significance was tested by Tukey's test. LOS and time taken to resuscitate were compared using unpaired t-test. Significance was taken at 5%. Results: Fluid resuscitation improved mean predicted morbidity by 0.095 and 0.137 in Group A and Group B, respectively. Similarly, fluid resuscitation improved predicted mortality by 0.145 and 0.185 in Group A and Group B, respectively. These changes were statistically significant. Improvement in morbidity and mortality appeared greater in Group B. No difference was found in the two groups for LOS and time to resuscitate. Conclusions: Preoperative fluid resuscitation using either crystalloid or colloid solutions decreases morbidity as well as mortality in peritonitis patients.

Key Words: Fluid management, intra-abdominal sepsis, peritonitis

INTRODUCTION

Some degree of hypovolemia always exists in patients with perforation peritonitis, caused by “third space” sequestration of fluid within the peritoneal cavity, gastrointestinal fluid losses, decreased oral intake, and increased insensible fluid losses associated with fever. If not treated in time, it contributes to multiorgan dysfunction syndrome.[1,2]

Therefore, it is uniformly recommended that in patients with perforation peritonitis, surgery should often be deferred until the physiological status improves. However, studies assessing

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How to cite this article: Kumar S. Audit of preoperative fluid resuscitation in perforation peritonitis patients using Physiological and Operative Severity Score for enUmeration of Mortality and Morbidity. J Emerg Trauma Shock 2017;10:7-12.

Received: 01.07.13. Accepted: 20.11.16.
the benefits of preoperative resuscitation in these patients are scanty.[3] Furthermore, the debate regarding the fluid of choice for resuscitation is far from settled.

Audit of benefits using parameters such as crude morbidity and mortality may be misleading because such rates make no allowance for differences in case mix and fitness of patients.[4] Therefore, a risk-adjusted scoring system that predicts both mortality and morbidity, such as Physiological and Operative Severity Score for enUmeration of Mortality and Morbidity (POSSUM) is better. POSSUM has been validated world over.[5]

However, POSSUM has never been used to define the fluid of choice and benefits of preoperative fluid resuscitation in peritonitis patients. Therefore, this study was done.

The aim of this study was to compare the benefits and hazards of crystalloids versus colloid, i.e., hydroxyethyl starch in the preoperative management of the patients with secondary bacterial peritonitis. The outcome parameters were:

1. Time taken to achieve goals of preoperative fluid resuscitation
2. Morbidity
3. Mortality
4. Length of hospital stay (LOS), and
5. Complications attributable to type of fluid administered.

**SUBJECTS AND METHODS**

This prospective, double-blind, noncross over, randomized clinical trial was conducted in Surgery Unit II, Department of Surgery at GTB Hospital and UCMS, Delhi. The study was conducted from October 2006 to April 2009. Consecutive perforation peritonitis patients of either sex and age between 18 and 60 years with secondary bacterial peritonitis were included in the study. Patients were recruited only after obtaining informed written consent. The Ethical Committee of the Institute granted its approval to carry out this study.

**Inclusion criteria**
- Perforation peritonitis cases
- Age between 18 and 60 years.

**Exclusion criteria**
- Patients who denied consent
- Pregnant females
- Patients with known allergies or manifesting symptoms of possible anaphylaxis on administering test dose of hydroxyethyl starch (HES) 6%
- Patients with major coagulation disorders (activated partial thromboplastin time > 80 s, prothrombin time > 30 s)
- Patients with renal failure (serum creatinine > 2.5 mg%, urine output (UOP) <20 ml/h) due to medical renal disease
- Patients with severe hepatic insufficiency
- Patients with congestive cardiac failure at admission
- Patients who had been resuscitated before reaching our surgery emergency unit.

Immediately, after presentation in surgery emergency, a detailed history was taken. A thorough clinical examination was done. Once the clinical diagnosis of secondary bacterial peritonitis was suspected, patients were subjected to following set of investigations: Complete hemogram, blood sugar, kidney function test, i.e., blood urea, serum creatinine, Na⁺, K⁺, coagulation profile, liver function test, i.e., total bilirubin, direct bilirubin, indirect bilirubin, serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, Alk. Phosphatase, arterial blood gas, analysis, chest X-ray, and electrocardiogram (ECG).

Thereafter, an intravenous (IV) line was established using 16–18 Gauge cannula in a suitable peripheral vein. Patients were catheterized and bladder evacuated. Nasogastric (NG) tube was inserted. Patients were given O₂ by mask at the rate of 5 L/min. Central venous pressure (CVP) monitoring was initiated using jugular venous line, setting zero at mid-axillary line. Antibiotics (ciprofloxacin 200 mg intravenously 12 hourly and metronidazole 500 mg intravenously 8 hourly) were started. At this juncture of time, all patients were given test dose (10–20 ml slowly IV) of HES - 6%, 130/0.4 (9.1) while closely observing the patients for pruritus, rashes, or flushing suggestive of possible anaphylactic reaction. Patients presenting with anuria or oliguria were given one liter of crystalloids intravenously within 30–60 min to improve UOP while observing for fluid overloading. If UOP did not improve, patients were given injection furosemide 40 mg IV. If UOP still did not improve, patients were excluded from the study.

At this juncture, physiological component of the Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM) system (annexure-2) was recorded. The physiological component of POSSUM consists of 12 variables: Age, cardiac status, respiratory status, systolic blood pressure (BP), heart rate, Glasgow Coma Scale, serum concentration of urea, K⁺, Na⁺, hemoglobin level, white blood cell (WBC) count, and ECG. Each factor (except WBC count, and ECG which have three grades only) is exponentially allocated 1, 2, 4, or 8.

Expected goals, in the form of improvement in clinical, hematological, or biochemical indices were specified for each patient; however, in general, this consisted of improvement in heart rate, BP, CVP, serum electrolytes, kidney function, and hematocrit.

Patients were randomized with the help of computer-generated random table and administered the fluid therapy according to randomization without knowledge of the observer. Group A patients were given crystalloid solutions. Group B patients were given 6% HES. Ringer’s lactate solution was additionally given
to all patients to compensate for fluid loss by sweating and gastric tube.

Fluid therapies as per random group were commenced as soon as contraindications for colloid infusion had been ruled out. Group A patients were resuscitated by crystalloid solution, the amount and rate of infusion of which were determined by patient’s condition and progress. Group B patients were resuscitated by 6% HES 130/0.4 (9.1) up to total dose of 30 ml/kg body weight, to be infused at the rate of 15 ml/kg body weight/hour. These patients were also given crystalloids according to their needs.

Preoperative fluid resuscitation was deemed complete if the required changes in clinical, hematological, or biochemical status were achieved or if, in the opinion of both the surgeon and anesthetist, further attempt at resuscitation were unlikely to be of any value or would be inappropriate without operative intervention. At this moment, the observer recorded the physiological component of POSSUM score again by appropriate clinical examination and investigations. The amount of fluid infused and time taken to achieve goals of emergency fluid resuscitation were noted.

Thereafter, the patients were subjected to emergency laparotomy at the earliest. A uniform protocol of general anesthesia was used for all patients. The operative procedure was tailored according to the needs and operative findings of the patients.

Postoperatively, the observer closely monitored all patients till death or 30 days after discharge from hospital, for complications and outcome. This included monitoring by clinical methods. Hematological, biochemical, microbiological, and radiological investigations were done as and when required. Blood products if required were given to both groups of patients. Subsequent changes in antibiotics and duration of antibiotic treatment were according to microbiological results and the progress of the patient. All patients were encouraged for oral feeding, commencing after return of bowel activity. Rest of the interventions such as ventilatory support, vasopressor use, dressing of the wound, removal of drain tube, NG tube, and Foley’s catheter were tailored according to the patient’s progress.

Outcomes were recorded as alive or dead and complicated or uncomplicated. Standard definitions were used for complications. The operative severity elements of the POSSUM for all patients were scored at discharge/death. The elements of operative severity score consist of operative severity, multiple procedures, total blood loss, peritoneal soiling, the presence of malignancy, and mode of surgery. As for the physiological elements, each factor (except for multiple procedures and mode of surgery) is divided into four grades allocating a score of 1, 2, 4, or 8.

**Statistical analysis**

All data were presented as mean. Predicted morbidity and mortality were calculated using POSSUM score and previously given logistic regression equations and exponential analysis. That the two groups (control and study) were similar (or not), to start with, was demonstrated by comparing the physiological component score at admission (repeated measure analysis of variance [ANOVA]), age (Student’s t-test) and sex ratio (Chi-square test). Effect on morbidity and mortality was compared by repeated measure ANOVA and its significance tested by Tukey’s test. The length of stay (LOS) were compared using unpaired t-test. Time taken for achieving goals of emergency preoperative fluid resuscitation was compared by unpaired t-test. Significance was taken at 5% throughout.

**RESULTS**

A total of 1490 patients were admitted to surgery emergency during this period. Out of these 1490 patients, 309 had perforation peritonitis. Of these 309 patients, 202 patients were excluded for various reasons [Table 1], and 107 patients of peritonitis were included in the study: 52 randomized to Group A (RL), and 55 randomized to Group B (HES 6%).

Table 2 shows the final diagnosis in 107 patients included in study. Overall, mean ± standard deviation age was 34.63 (±12.46) years; it was 33.44 (±13.08) years in Group A (n = 52) and 35.75 (±11.84) years in Group B (n = 55). Ninety-seven were males, 47 in Group A, and fifty in Group B.

| Diagnosis | Number of patients (%) |
|-----------|------------------------|
| Ileal perforation | 48 (44.8) |
| Duodenal ulcer perforation | 45 (42.2) |
| Appendicular perforation | 6 (5.6) |
| Prepyloric perforation | 3 (2.8) |
| Gastric perforation | 2 (1.9) |
| Perforation at rectosigmoid junction | 1 (0.9) |
| Ascending colon perforation | 1 (0.9) |
| Jejunal perforation | 1 (0.9) |

**Table 1: Reasons for exclusion (n=202)**

| Exclusion criteria | Number of patients |
|--------------------|--------------------|
| Age (years) <18 | 73 |
| Had received resuscitation before reaching our hospital | 52 |
| Age (years) >60 | 32 |
| Traumatic and iatrogenic (post-MTP) perforation | 26 |
| Nonresponding anuria | 22 |
| Deranged coagulation profile | 3 |
| Positive dengue serology | 3 |
| Wrong preoperative diagnosis | 2 |
22.88 ± 6.14 (range 12–38) for Group A, and 20.67 ± 5.09 (range from 14 to 37) for Group B patients. Overall (for all patients), mean operative severity score was 19.69 ± 2.71 (range 15–33), 19.90 ± 3.73 (range 15–33) for Group A, and 19.49 ± 1.12 (range 17–25) for Group B. Overall (for all patients), mean time taken to achieve goals of resuscitation was 133.36 ± 30.87 (range 90–240) min, 136.8 ± 33.9 (range 90–240) min for Group A, and 130.1 ± 27.6 (range 90–240) min for Group B. Overall (from 107), 87 (81.3%) patients (44 in Group A and 43 Group B) (81.3%) had a total of 189 complications [Table 3]. A total of 17 patients (15.9%) expired, nine (17.3%) in Group A and eight (14.5%) patients in Group B. Mean LOS for all patients was 12.64 ± 7.78 (range 1–32 days); it was 13.83 ± 8.54 (range 1–30) days in Group A, as against 11.51 ± 6.88 (range 1–32) days in Group B.

As per the first requirement of a randomized control trial (RCT), the two groups were evaluated for comparability in terms of age, sex, and preresuscitation physiological POSSUM score. The two groups were found comparable Table 4.

**Effect of resuscitation on predicted morbidity**
The mean preresuscitation predicted morbidity for 107 patients irrespective of groups was 0.863 ± 0.138. It decreased to 0.747 ± 0.153 after resuscitation. This decrease was statistically significant, \( P < 0.001 \) (paired \( t \)-test).

Table 5 shows the comparison of the predicted morbidity between the two groups. The mean predicted morbidity at the time of admission (i.e., preresuscitation) for Group A was 0.867 ± 0.158. After resuscitation, it reduced to 0.772 ± 0.172. This improvement in predicted morbidity was statistically significant \( (P < 0.001) \). For Group B, the mean predicted morbidity at the time of admission was 0.860 ± 0.117. After resuscitation, it decreased to 0.723 ± 0.131. This decrease was significant \( (P < 0.001) \). However, the fall in predicted morbidity following resuscitation was greater \( (0.137) \) in Group B than that in Group A \( (0.095) \).

**Effect of resuscitation on predicted mortality**
The mean preresuscitation predicted mortality for all patients irrespective of group was 0.448 ± 0.210. It decreased to 0.282 ± 0.168 after resuscitation. This decrease was also statistically significant, \( P < 0.001 \) (paired \( t \)-test).

Table 6 shows the impact of resuscitation on predicted mortality in the two groups. The mean predicted mortality at the time of admission for Group A was 0.469 ± 0.219. After resuscitation, it decreased to 0.324 ± 0.194. This decrease was significant \( (P < 0.001) \). The mean predicted mortality at the time of admission for Group B was 0.428 ± 0.210. It decreased to 0.243 ± 0.129 after fluid resuscitation. This decrease in predicted mortality was also significant \( (P < 0.001) \). This decrease was more in Group B \( (0.185) \) than in Group A \( (0.145) \).

**Time taken to achieve the goals of resuscitation**
The mean time taken to achieve the goals of resuscitation in Group A was 136.8 ± 33.9 min as against 130.1 ± 27.6 min in Group B. The difference was not statistically significant, \( P = 0.446 \) (unpaired \( t \)-test).

**Operative severity score**
The mean operative severity score for Group A was 19.90 ± 3.73 and that for Group B was 19.49 ± 1.12. The difference was not statistically significant, \( P = 0.446 \) (unpaired \( t \)-test).

**Length of hospital stay**
Mean LOS in Group A was 13.8 ± 8.5 days as against 11.5 ± 6.9 days in Group B, the difference being statistically not significantly \( (P = 0.127) \); unpaired \( t \)-test).

**DISCUSSION**
Perforation peritonitis patients may benefit from preoperative fluid resuscitation as they always tend to present with varying degree of hypovolemia. However, there are scanty studies worldwide to assess the benefits of preoperative resuscitation in perforation peritonitis case; therefore, this prospective, randomized, observer-blind large study in patients with perforation peritonitis was conceived. Audit of benefits of preoperative fluid resuscitation is additional problem. This may be done using parameters such as crude morbidity and mortality. However, comparison of crude mortality and morbidity is misleading because such rates make no allowance for differences

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**Table 3: Complications**

| Morbidity                  | Total patients \( (n=107) \) | Group A \( (n=52) \) | Group B \( (n=55) \) |
|---------------------------|-------------------------------|----------------------|----------------------|
| Wound infection           | 72                            | 35                   | 37                   |
| Wound dehiscence          | 35                            | 20                   | 15                   |
| Hypotension               | 22                            | 14                   | 8                    |
| Chest infection           | 15                            | 11                   | 4                    |
| Respiratory failure       | 17                            | 10                   | 7                    |
| Deep infection            | 15                            | 10                   | 5                    |
| Anastomotic leak          | 6                             | 5                    | 1                    |
| Wound hemorrhage          | 3                             | 3                    | 0                    |
| Impaired renal function   | 1                             | 1                    | 0                    |
| Pyrexia of unknown origin | 1                             | 0                    | 1                    |
| Cardiac failure           | 2                             | 0                    | 2                    |
| **Total**                 | ***189***                     | 109***               | 80***                |

*87 complications were seen in 87 patients, **109 complications were seen in 44 Group A patients, ***80 complications were seen in 43 Group B patients.

**Table 4: Comparison of two groups**

| Age, mean±SD (years) | Group A \( (n=52) \) | Group B \( (n=55) \) | \( P \)   |
|----------------------|----------------------|----------------------|---------|
| Male:female ratio    | 47.5                 | 50.5                 | 0.341 (unpaired \( t \)-test) |
| Preresuscitation physiological score, mean±SD | 28.33±7.37 | 27.73±7.50 | 0.697 |

SD: STANDARD DEVIATION
in case mix and fitness of patients. Therefore, to audit the benefits of fluid resuscitation, we needed a risk-adjusted scoring system that predicts both mortality and morbidity. Copeland developed POSSUM as an audit tool for comparing outcome in surgical patients. Subsequently, it has been validated world over. Moreover, it is very simple to use. Thus, it can be said that POSSUM is one such excellent tool of audit. Hence, we choose POSSUM to compare outcomes.

There were two objectives of this study. The first objective was to quantify the benefits of the preoperative resuscitation in terms of morbidity and mortality, using POSSUM, in patients with perforation peritonitis. The second objective was to find the fluid of choice, between crystalloids and colloid solution, for preoperative resuscitation.

**The benefits of preoperative fluid resuscitation**

McIlroy et al. were probably the first one to audit the benefit of preoperative fluid resuscitation in emergency situations. They studied 148 patients suffering from acute gastrointestinal pathology. Using POSSUM as the tool, they demonstrated that fluid resuscitation improved predicted morbidity and mortality by 4.3 ± 0.7% and 4.2 ± 0.8%, respectively. However, in their study, the patients were largely elderly (mean age being 61 years), and only 30% had perforation peritonitis. Further, the authors did not document time required for achieving goals of resuscitation. Last, and importantly, it was a nonrandomized trial. Nonetheless, they not only demonstrated that resuscitation can be audited and quantified but also proved that resuscitation helps in improving mortality and morbidity.

Our study provides level I evidence of the beneficial role of preoperative fluid resuscitation in perforation peritonitis patients irrespective of the type of fluid used; the predicted morbidity and mortality were reduced by 11.6% and 16.0%, respectively. These findings assume great importance as our trial was an RCT, included a large number of patients with age ranging from 18 to 60 years, focused entirely on perforation peritonitis, and the benefits were more pronounced. Thus, our study overcame the shortcomings seen previously (in McIlroy et al. study).

**Choice of fluid**

There have been numerous trials to find out which is the fluid of choice for resuscitation. A major disadvantage of crystalloid solutions is that relatively large volumes have to be infused to restore an intravascular volume deficit (the classical 3:1 replacement rule). This can lead to interstitial edema which may worsen gas exchange in the lungs and impair wound healing in the skin.

Recently, hyperosmolar crystalloid fluids in the resuscitation of critically ill patients have been used. Hyperosmolar crystalloid fluids act by drawing fluid from the intracellular and interstitial space to intravascular volume. Hence, it is believed that only small volume (and consequently shorter infusion times) is required to achieve the resuscitation end-points. This is the main advantage of these types of fluids.

Colloid solutions are essentially crystalloid solutions with biologically inert colloid particles added. The colloid particles act as oncotic agents to retain fluid in the intravascular fluid compartment. The normal colloid oncotic pressure is 25; it is now possible to administer fluids that have colloid oncotic pressures of up to seventy. In the absence of capillary leakage of colloid particles, these hyperoncotic solutions can expand the intravascular volume by up to 2–3 times their infused volume.

Albumin is a human product, biological colloid, carries with it the risks of infection transmission. Volume for volume, albumin is up to ten times as expensive as other synthetic colloids.

HES appears valuable and significantly cheaper alternative to albumin even for prolonged (5 days) volume therapy in critically ill. HES has been found to be better than modified...
gelatin as volume preload before spinal anesthesia for cesarean section.

HES has been found to inhibit endothelial activation, thus preventing neutrophil adhesion during sepsis syndrome. HES attenuates hypoxia-induced increase in vascular leakage and acute inflammation. Its infusion has no adverse effect on standard coagulation parameters.

Cochrane Database Systematic Review 2007 studied 53 trials comparing crystalloids and colloid for fluid resuscitation for hypovolemia. Pooled relative risks fail to show a mortality benefit for resuscitation with any type of colloid.

Our study shows that the resuscitation with either type of fluid decreased predicted morbidity and mortality. The benefit was greater in colloid-treated patients. These findings are contrary to recent observations derived from meta-analysis wherein it has been stated that the colloids had no beneficial effect on pooled relative risk for mortality. Moreover, this study demonstrates that the time taken to fluid resuscitate is same irrespective of the type of fluid used. Importantly, however, LOS remains unchanged by the type of fluid employed. The findings of this study assume greater importance in view of the fact that there were no side effects attributed specifically to a particular type of fluid. There was no instance of anaphylactic reaction with HES.

CONCLUSIONS

Preoperative emergency fluid resuscitation is associated with statistically significant improvement in predicted morbidity and mortality, irrespective of the fluid use. This improvement in predicted morbidity and mortality is more in patients receiving HES, without increasing the time taken to achieve the goals of the resuscitation. However, the LOS is not impacted by the preoperative fluid resuscitation.

The benefits of preoperative fluid resuscitation in patients with perforation peritonitis have been audited through this study for the first time. Recently, the need for fluid resuscitation has been re-emphasized. In view of this, it is recommended that adequate time should be invested in preoperative fluid resuscitation to favorably impact the predicted morbidity as well as the mortality. However, the choice of fluid may not matter much. Hence, all patients with perforation peritonitis must be resuscitated using IV fluids (either crystalloids or colloids) early and adequately. However, care must be exercised to avoid fluid overloading as the same has been linked with increased severity of organ dysfunction and worse outcome.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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