Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v31i6.6847

EFFICACY OF EARLY FLUID RESUSCITATION IN ACUTE PANCREATITIS

Aliya Nasim[1], Hafiz Muhammad Talha Nawaz[2], Saifullah Shafiq[3], Anisa Khan[4], Muhammad Shoaib[5], Aitisam Ullah Shah[6], Muhammad Saad Ahmad[7], Shawwal Amjad[8], Atiq Ur Rehman[9*]

[1]Health Director, The Solar Water Project (Bondh E Shams), Pakistan
[2]Medical Officer, Emergency Medicine Department, Shams Clinic, Rawalpindi, Pakistan
[3]Intern (General Medicine), Northwest General Hospital & Research Centre, Peshawar, Pakistan
[4]Resident Physician, Internal Medicine Department, Lady Reading Hospital, Peshawar, Pakistan
[5]Trainee Medical Officer, General Medicine Department, Lady Reading Hospital, Peshawar, Pakistan
[6]Medical Officer, Critical Care Department, Khalifa Gulnawaz Teaching Hospital MTI, Bannu, Pakistan
[7]Trainee Master of Surgery, King Edward Medical University/Mayo Hospital, Lahore, Pakistan
[8]General Practitioner, General Medicine and Surgery, Khawajgan Trust Hospital, Gujrat
[9*]Faculty of Veterinary & Animal Sciences, Gomal University, Dera Ismail Khan

***Corresponding Author:** Atiq Ur Rehman
*Faculty of Veterinary & Animal Sciences, Gomal University, Dera Ismail Khan
Email Address: atiq_dvm@gu.edu.pk

ABSTRACT

This study intended to assess the influence of early administration of fluids on the clinical results of individuals admitted to the hospital for acute pancreatitis. We conducted a retrospective analysis on a cohort of 701 patients diagnosed with acute pancreatitis at Hayatabad Medical Complex, Peshawar, Pakistan. We included 434 of total non-transferred patients after removing transferred patients and those with incomplete data. We classified patients into two groups, early resuscitation (340 patients) and late resuscitation (94 patients), based on the amount of intravenous fluids administered within first 24 hours. The main outcomes assessed were the occurrence of (SIRS), organ failure, admission to the (ICU), duration of hospitalization, and mortality. The statistical analyses conducted in this study involved t-tests, chi-square tests, and multivariate logistic regression. Early resuscitation resulted in dramatically reduced rates of (SIRS) and organ failure at 24, 48, and 72 hours, decreased (ICU) admissions, and shorter hospital stays. In terms of mortality, intra-abdominal infections, or necrosis, no important differences were detected on CT scans. Subgroup analysis showed that the positive results of early resuscitation were especially distinguished in the groups of patients with interstitial illness on admission but were restricted in those with severe disease: positive response to early fluid intervention was particularly marked in patients with interstitial disease on admission, but patients with severe disease showed a restricted positive response to early fluid intervention. Initiation of fluid resuscitation early in the course of acute pancreatitis is associated with better clinical outcomes, particularly in patients with interstitial disease. That is essential and needs to be done early in any clinical setting.

INTRODUCTION

Acute pancreatitis is a sudden inflammation of the pancreas that varies in severity from minor pain to a severe, life-threatening (Muniraj, 2012). Early fluid resuscitation in managing acute pancreatitis is one of the critical components that aim to stabilize the patient, prevent complications, and improve outcomes. This therapeutic approach involves fluid hydration with the administration of intravenous fluids, maintaining the body's fluid status, optimizing perfusion to the pancreas, and supporting its function. Despite its widespread use, a source of much controversy and ongoing research is the issue of recovery from early fluid in acute pancreatitis. This, therefore, calls for the need to understand the optimal timing, type, and volume of fluids administered, as well as their effect on patient outcomes, in order to get the necessary data to develop evidence-based guidelines and better clinical practice. This introduction highlights the importance of early fluid resuscitation in managing acute pancreatitis, the current evidence, controversies, and the call for further research in taking care of the patients (Aggarwal, 2014).

The use of early fluid resuscitation is rational for the potential to counteract deep fluid shifts, hypovolemic, and the systemic inflammatory response associated with acute pancreatitis (Crosignani, 2022). By restoring circulatory volume and improving pancreatic microcirculation, fluid resuscitation aims to reduce pancreatic necrosis, prevent multi-organ failure, and lower mortality rates. However, despite its theoretical benefits, the practical aspects of early fluid resuscitation, including the optimal timing, type, and volume of fluids, remain subjects of ongoing research and clinical debate (Lira, 2014).

This introduction aims to provide the comprehensive overview of the significance of early fluid resuscitation in the management of the acute pancreatitis (Leppäniemi, 2019). This discussion will be based on the existing evidence in support of its use at present, the existing controversies, and will underline the importance of individualized patient care. Importantly, it will outline the critical gaps in knowledge and the future directions of research that are required to optimize clinical outcomes for patients with acute pancreatitis. The introduction thus sets up the stage for a detailed exploration of the therapeutic efficacy of early fluid resuscitation to inform and improve clinical practice. (Malbrain, 2014).

METHODS

Study Overview and Patient Selection

The Council for the Protection of Individual Subjects (#21847) approved the study, which specifically targeted acute pancreatitis patients directly admitted to Hayatabad medical complex Peshawar, Pakistan (uz Zaman, 2022). We identified the patients retrospectively using ICD-9 codes. We included only patients who did not move and had a primary diagnosis of the acute pancreatitis. The early resuscitation group in very ill patients got a significantly higher volume of intravenous fluids within the first 24 hours (p 0.006), but a significantly lower volume between 24-48 hours and between 48 and 72 hours (p 0.027; p 0.002) compared to the late resuscitation group.

Data Collection and Definitions

The primary investigator instructed four personnel to examine electronic and paper health records to extract information regarding patient characteristics, process parameters, and outcomes. The primary data points consisted of age, gender, and Charlson comorbidities score, and the need for interventions such as antibiotics, complete parenteral nutrition, surgery, or ERCP. The evaluated outcomes were the occurrence of Systemic inflammatory response syndrome is a condition characterized by a widespread inflammation throughout the body. It can lead to organ failure, which is the inability of one or more organs to function properly. Intra-abdominal infections are infections that occur within the abdominal cavity, duration of hospitalization, admission to the intensive care unit (ICU), and mortality. The Atlanta Classification established the definitions of SIRS and organ failure (Horeczko, 2014). Severe acute pancreas inflammation is classified according to the presence of (SIRS), organ failure lasting for a period of time exceeding 48 hours, or signs of pancreatic necrosis.

Fluid Resuscitation and Statistical Analysis

The study documented the quantity and nature of intravenous fluids given from the initial emergency room visit until the first 72 hours of hospitalization (Marik, 2017). The early and late resuscitation phases were classified based on the amount of fluid received during the first 24 hours. We kept the abstracters unaware of the study outcomes during data collection. The main measures of interest were the occurrence of organ failure and (SIRS) within 24, 48, and 72 hours, admission to the (ICU), duration of death, and hospital stay. The statistical analysis involved chi-square tests and continuous data, and student's t-tests for categorical respectively. The level of significance was $p < .05$. We estimated the odds ratios using multivariate linear regression models, accounting for age, gender, and Charlson disease score as adjusted variables. We conducted the analyses using Graphpad, Microsoft Excel, and R software.

RESULTS

Hayatabad medical complex Peshawar admitted a total of 701 individuals with acute pancreatitis as their major condition between 1985 and 2009. The study included a total of 434 non-transferred individuals, excluding 222 patients admitted through transfer and there are 45 patients for whom there is no recorded information about the delivery of fluids. We classified 340 of them as "early recovery" and 94 as "late recovery". Baseline patient characteristics and Charlson ratings did not show any notable disparities between the groups. However, the late resuscitation (LR) group had a higher incidence of acute pancreatitis caused by post-ERCP aetiology ($p < 0.03$). The amount of fluid administered for resuscitation varied significantly among the groups. The early resuscitation (ER) group received a greater volume of fluids in the first 24 hours ($p < 0.0001$), while the (LR) group received more fluids duration of the events was categorized into three groups: 24-48 hours, 48-72 hours, and over 72 hours.

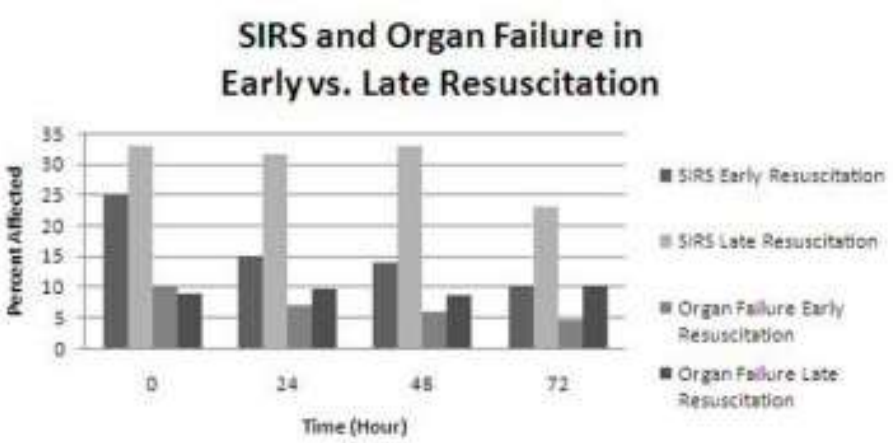

Figure1. Organ Failure and SIRS in LR vs. ER

Table 1: Patient Baseline Characteristics

Characteristic	ER	LR	p-(value)
Patients of (n)	340	94	
Women (%)	179 (53)	50 (53)	0.99
Age (years)	54 ± 20	49 ± 22	0.08
Score Charlson	2.51 ± 2.62*	2.39 ± 2.68	.70
Etiology			
Alcohol %	52 (15)	18 (19)	**.40**
Gallstone %	130 (38)	26 (28)	**.06**
Post-ERCP (%)	18 (5)	11 (12)	**.03**
Triglyceride (%)	8 (2)	2 (2)	0.99
Medication (%)	12 (4)	1 (1)	0.30
Idiopathic (%)	101 (30)	27 (29)	0.90

Tumor (%)	5 (1)	2 (2)	0.70
(Intra-Abdominal Bacterial Infection) %	3	1	0.40
Parenteral Nutrition %	26	46	**0.01**
ERCP %	19	23	0.50
Admission Antibiotics %	18	18	0.99
Fungal Infection of Intra-Abdominal %	1	1	0.90
Surgery	(15) 50	18 (19)	0.40
Necrosectomy %	4 (8)	2 (11)	0.50
Cholecystectomy (%)	37 (74)	12 (67)	0.70
Other %	9 (18)	4 (22)	0.50

*Statistical significance is indicated in bold type.
Mean ± standard deviation

Table 2: Mean of the Intravenous Volumes of Fluid Resuscitation

Volume of Fluid	E R (mL)	L R (mL)	p-value
48-72 Hours	1,841 ± 1,391	3,353 ± 1,615	**.0001**
0-24 Hours	3,493 ± 1,700	2,403 ± 1,216	**.0001**
24-48 Hours	2,571 ± 1,325	578 ± 2,490	**.0001**
Total	7,600 ± 3,574	9,514 ± 4,469	**.0003**

*Statistical significance is indicated in bold type

There was no significant difference in SIRS occurrence at admission across the groups, as indicated by the primary and secondary outcomes ($p < 0.15$). The group that received early resuscitation at admission had significantly lower levels of (SIRS). We categorized the time intervals as 0–24 hours, 48–72 hours, and 24–48 hours. The statistical significance levels for these intervals were $p < .001$, $p < .001$, and $p < .01$, respectively. Similarly, there was no initial disparity in organ failure between the two groups. However, after 72 hours, the group that received early resuscitation showed a statistically significant reduction in organ failure compared the other group ($p < .05$). Early resuscitation group exhibited a lower number of ICU admissions ($p < .001$) and duration is a shorter for hospitalization ($p < .01$); however, fatality rates were comparable between the groups. We detected no disparities in intraabdominal bacterial or fungal infections or necrosis on CT scans.
The subgroup analysis involved a comparison of patients diagnosed with the severe of acute pancreatitis and those diagnosed with interstitial illness upon arrival. There were no significant in the characteristics between the 39 individuals with severe illness and the 364 individuals with interstitial disease. In comparison to the late recovery group, the early resuscitation group of severely ill patients had a higher volume of intravenous fluids within the first 24 hours of life (p 0.006) but a lower volume between 24-48 hours and 48-72 hours (p 0.027; p 0.002). There was no notable disparity in the overall fluid volume over a 72-hour period ($p < 0.27$) among the groups. Patients with interstitial illness exhibited clinical outcome disparities between early and late resuscitation; however, no such disparities were observed in patients with severe disease, save for a greater rate of ICU admission in the (LR) group ($p < 0.02$).

Table 3: Primary and Secondary Clinical Results

Results	ER (%)	LR (%)	P-(value)	Relative Risk Reduction(RRR)
SIRS				
Admission	25	33	0.15	-
72 Hour	10	23	**.01**	2.3
48 Hour	14	33	**.001**	2.4
24 Hour	15	32	**.001**	2.1
Failure Organ	8 ± 9.68*	11 ± 10.2*	**.01**	-
Admission	10	9	0.80	-
24 Hour	7	10	0.40	1.4

48 H	6	9	0.40	1.5
72 H	5	10	**0.05**	2.0
ICU	6	17	**.001**	2.8
Length Stay	8 ± 9.68	11 ± 10.2	**.01**	-
Mortality	3	4	.70	1.3

The Statistical significance is indicated in bold type
Mean ± standard deviation

Table 4: Adjusted for (Primary and Secondary) Outcomes of Charlson Score Gender, and Age.

Outcome	Adjusted the Odds Ratio	Confidence Interval 95%	P(value)
Organ Failure			
24 Hour	.70	0.30–1.61	0.3976
48 H	.68	0.27–1.67	0.3966
72 H	.39	.16–0.98	**.0460**
SIRS			
24 Hour	.39	.22–0.67	**.0007**
48 H	.32	.19–0.56	**.0000**
72 H	.40	.21–0.76	**.0050**
Mortality	.80	.24–2.64	.7085
ICU	.30	.15-0.63	**.0013**

The use of bold type shows the presence of statistical significance.

Table 5: Analysis Subgroup: Severe Pancreatitis vs Interstitial Admission

Outcome	ER (%)	L R (%)	P-(value)	RRR (Relative Risk Reduction)
(INTERSTITIAL ADMISSION)				
(SIRS)				
Admission	22	29	.20	1.4
(24) Hour	10	30	**.001**	3.1
(48) Hour	10	31	**.001**	32
(72) Hour	6	20	**.002**	3.4
Organ Failure				
Admission	0	0	-	
(24) Hour	1	4	.15	4.1
(48) Hour	2	3	.30	2.2
(72) Hour	1	5	**.05**	5.1
Stay Length	"7 ± 7.83"	"11 ± 10.6"	**.001**	-
ICU	4	12	**.01**	4.0
Mortality Outcomes	1	1	.99	1.0
(SEVERE ADMISSION)				
(SIRS)				
Admission	46	51	.91	1.1
(24) Hour	61	50	.60	0.8
(48) Hour	46	52	.92	1.3
(72) Hour	51	49	.99	1.0
(Failure Organ)				
Admission	101	101	-	
(24) Hour	65	73	.71	1.2
(48) Hour	63	76	.52	1.3
(72) Hour	44	64	.41	1.6

Stay Length	14 ± 17.5*	13 ± 6.94*	.92	
Admission of ICU	39	88	**.02**	2.3
Mortality	23	38	.40	1.7

The use of bold type shows the presence of statistical significance.
Mean ± standard deviation

DISCUSSION

This presents study evidence patients diagnosed with acute the pancreatitis who receive prompt fluid the resuscitation experience reduced rates of (SIRS) and organ failure (Wei, 2016). Additionally, they have shorter hospital stays and a decreased need for intensive care unit (ICU) admission compared to individuals who do not receive aggressive resuscitation. Patients with interstitial illness upon admission mostly experience the positive impact, indicating that early intravenous fluid administration may not significantly influence the progression of severe disease. These findings remained consistent even after accounting for potential factors that could influence the results, such as the Charlson combination gender, and score, age, (Rattanasompattikul, 2012). Patients suffering from acute pancreatitis may exhibit hypovolemia as a result of variables such as vomiting, decreased oral consumption, fluid accumulation in the third space, and excessive sweating. Experts recommend that a person weighing 70 kg requires a minimum of 6 litres of intramuscular fluid within the first 48 hours after admission, without accounting for fluid loss within blood vessels. In acute pancreatitis, the inflammatory response causes an increase in blood vessel permeability, resulting in reduced blood flow and fluid accumulation in areas outside the blood vessels. This process creates a continuous cycle of vascular dysfunction and inflammation. In order to fix hypovolemia and keep enough blood flow to the pancreas (McClave, 2012), which stops serious problems like pancreatic necrosis from happening, intravenous fluid resuscitation must be started right away.

Research measuring the specific impacts of intravenous fluid resuscitation, widely acknowledged as an essential element in the early management of acute pancreatitis, is scarce. Banks and colleagues have emphasized the harmful effect of hem concentration on outcomes in cases of acute pancreatitis. A study revealed that individuals who did not receive enough fluids to restore their body's fluid balance, as indicated by an ongoing increase in blood concentration after 24 hours, had a severe form of pancreatitis called necrotizing pancreatitis. In Sweden, Eckerwall's study revealed that patients diagnosed with severe acute pancreatitis who received more than 4000 ml of fluids within the initial 24-hour period showed a higher incidence of respiratory problems compared to those who received a lower volume. Patients with severe acute pancreatitis in the late resuscitation group at the Mayo Clinic had higher fatality rates and showed a tendency towards more organ failure, but this trend was not statistically significant. (Cecconi, 2019).

CONCLUSION

This study emphasizes the crucial importance of promptly administering fluids to treat acute pancreatitis, especially for patients with interstitial illness. Patients who got prompt and intensive intravenous fluid resuscitation were less likely to get organ failure and (SIRS). They also stayed in the hospital longer and didn't need to be admitted to the intensive care unit as often as patients who didn't get as much intensive resuscitation. These benefits were not as evident in the patients with admission at severe disease, that suggesting early fluid resuscitation may not significantly alter the clinical course in these cases. Despite the retrospective design and limitations such as reliance on accurate fluid administration data and evolving care practices over the study period, the findings support the importance of early intervention. Until more targeted pharmacologic treatments are available, early and optimized intravenous fluid resuscitation remains a key intervention for improving outcomes in acute pancreatitis.

REFERENCES

1. Aggarwal, A. M. (2014). Fluid resuscitation in acute pancreatitis. *World Journal of Gastroenterology: WJG*, 20(48), 18092.
2. Cecconi, M. H. (2019). Fluid administration for acute circulatory dysfunction using basic monitoring:narrative review and expert panel recommendations from an ESICM task force. *Intensive care medicine*, 45, 21-32.
3. Crosignani, A. S. (2022). Intravenous fluid therapy in patients with severe acute pancreatitis admitted to the intensive care unit: a narrative review. *Annals of Intensive Care*, 12(1), 98.
4. Horeczko, T. G. (2014). Epidemiology of the systemic inflammatory response syndrome (SIRS) in the emergency department. . *Western Journal of Emergency Medicine*, 15(3), 329.
5. Leppäniemi, A. T.-L. (2019). 2019 WSES guidelines for the management of severe acute pancreatitis. *World journal of emergency surgery*, 14, 1-20.
6. Lira, A. &. (2014). Choices in fluid type and volume during resuscitation: impact on patient outcomes. . *Annals of Intensive Care*, 4, 1-13.
7. Malbrain, M. M. (2014). Fluid overload, de-resuscitation, and outcomes in critically ill or injured patients: a systematic review with suggestions for clinical practice. . *Anestezjologia Intensywna Terapia*, 46(5), 377-396.
8. Marik, P. E.-Z. (2017). Fluid administration in severe sepsis and septic shock, patterns and outcomes: an analysis of a large national database. *Intensive care medicine*, 43, 625-632.
9. McClave, S. A. (2012). Drivers of oxidative stress in acute pancreatitis: the role of nutrition therapy. *Journal of Parenteral and Enteral Nutrition, ,* 36(1), 24-35.
10. Muniraj, T. G. (2012). Acute pancreatitis. *Disease-a-Month*, 58(3), 98-144.
11. Rattanasompattikul, M. F.-Z. (2012). Charlson comorbidity score is a strong predictor of mortality in hemodialysis patients. *International urology and nephrology*, 44, 1813-1823.
12. Warndorf, M. G. (2011). Early fluid resuscitation reduces morbidity among patients with acute pancreatitis. *Clinical gastroenterology and hepatology*, 9(8), 705-709.
13. Wei, A. L. (2016). Early complications after interventions in patients with acute pancreatitis . *World Journal of Gastroenterology*, 22(9), 2828.