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Intravenous analgesia versus thoracic epidural catheterization in moderately severe pancreatitis: A randomized controlled trial in a tertiary care health facility.

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ABSTRACT… Objective: To evaluate the two most commonly used methods for pain relief in acute pancreatitis i.e. epidural analgesia and I/V analgesia and compared the results. **Study Design:** Randomized Controlled Clinical Trial. **Setting:** Surgical Unit-1 of Holy Family Hospital, Rawalpindi. **Period:** June 2019 to June 2020. **Material & Methods:** Patients presenting with acute pancreatitis with moderate severity were divided into groups A and B. In group A patients, epidural catheter was passed at T9-T10 level epidural space and they received 0.125% Bupivacaine injection every 4 hours, while group B patients received combination analgesia in the form of IV tramadol 100mg TDS and IV Toradol 30mg BD. Pain was assessed by using visual analog scale (VAS) at 12 hour intervals. Rescue analgesia, in the form of IV paracetamol 1g given in the case of >7 VAS score was also recorded. **Results:** Total 100 patients were included according to the inclusion criteria of the study. Patients were randomly divided into two groups; Group A (Epidural) and group B (intravenous). Mean age (years) in the study was 42.39+11.21 whereas there were 37 male and 63 female patients who were included in the study. In our study, mean pain score in group A was 3.16+1.23 which was significantly lower than group B (5.42+1.01), p-value < 0.0001. There was a single mortality in the study. 6 patient's required ventilatory support due to respiratory complications, 5 in group B and 1 in group A. **Conclusion:** Epidural analgesia is superior to I/V analgesics in pain management of moderately severe pancreatitis and it also reduces respiratory morbidity in these patients.

Keywords: Catheterization, Intravenous Analgesia, Pancreatitis, Paracetamol.

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INTRODUCTION

Acute pancreatitis is an inflammatory condition of pancreas whose incidence in United States of America has reached 35/100000 population.[1] In 80% of patients the disease is mild and self -limiting but it is the deadliest disease of hepatobiliary system in 20% of cases in which the mortality reaches up to 30% due to multiorgan failure and pancreatic necrosis.[1] The etiology of acute pancreatitis varies among different areas and cultures but gallstones and alcohol consumption are major causes making 40-70% of cases. Sudden onset of severe abdominal pain is hallmark of acute pancreatitis commonly localized to epigastric region and radiates like a belt around trunk into back.[2] Severity of pain correlates with severity of acute pancreatitis and serum lipase and C reactive protein is diagnostic and prognostic indicator of acute pancreatitis respectively.[3-5]

Besides endoscopic removal of gall stones, treatment of acute pancreatitis is mainly supportive which includes fluid resuscitation, effective analgesia, early nutrition and oxygenation.[2] These approaches do not affect pancreas directly but try to attenuate systemic inflammatory response and multiorgan failure.

Pain relief is mainstay of treatment. Analgesics used mostly for pain relief in acute pancreatitis are parenteral opioids and NSAIDS or their combination.[5,6] Epidural analgesia is now widely used to decrease pain and severity of disease in

moderate to severe acute pancreatitis.[1,3] Epidural analgesia blocks noxious afferent sympathetic nerve which improves pancreatic perfusion and decreases the severity of metabolic acidosis and tissue injury which prevent pancreatic necrosis.[1,2,7]

Although epidural analgesia is known to be far more effective than any IV analgesic, Epidural catheter insertion itself is an invasive procedure with known complications and thus many centers in the world are still reluctant to use it in pancreatitis. This study aims to provide evidence base for the use of epidural analgesia in acute pancreatitis and evaluates its efficacy in pain management of patients with moderately severe acute pancreatitis and compares it with IV analgesia.

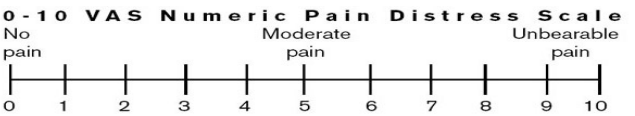
MATERIAL & METHODS

The study design was randomized controlled clinical trial carried out in surgical unit 1 of Holy Family Hospital, Rawalpindi for a period of 1 year i.e. from 16th June 2019 to 15th June 2020. Sample size was calculated using WHO sample size calculator, which came out to be 50 in each group. All the patients, male and female between 18 and 60 years with clinical features of acute pancreatitis, having serum amylase or lipase level greater than 3 times the upper normal limit with CTSI (CT scan severity index) between 4-8 (moderately severe), were included in our study. Patients having chronic pancreatitis, pancreatic cancer, hypersensitivity to bupivacaine, having any contraindication of epidural catheter placement (coagulation disorders, skin infection of vertebral site, spinal surgery etc.), breast feeding or pregnant and those who were referred from other centers after treatment were excluded from this study.

After approval from Institutional Ethics Research Forum Rawalpindi Medical College (RMC) (R-18-RMH), all the patients fulfilling the selection criteria reporting at surgical unit-I, Holy Family Hospital, Rawalpindi were informed about the study and written informed consent was taken.

A random number list was generated for 100 patients randomly allocating them in two groups group A or Group B (50patients in each) using SPSS software. CT scan abdomen with pancreatic protocol was performed in patients presenting with epigastric pain with raised amylase or lipase and CT severity index was assessed. Patients with CT severity index of 4-8 was included in the study. Standard treatment of acute pancreatitis which include IV fluids, antibiotics and PPI's remained same for all the patients.

Epidural catheter was passed by anesthetist in epidural space (T9-T10) in group A patients. These patients were given 0.125% bupivacaine via epidural route every 4-6 hourly and in group B patients, pain relief was done by combination of intravenous opioids and NSAIDS i.e. injection tramadol 100mg IV TDS and injection Toradol 30mg IV BD. Pain was assessed on visual analog scale at 12-hour intervals. Rescue analgesia in the form of IV paracetamol 1g was given if the VAS score exceeded 7 and requirement of rescue analgesia for each group was also recorded and analyzed. Data was analyzed using SPSS version 22.0.



RESULTS

Total 100 patients were included in this study which were divided into two groups. Mean age of the patients in group A and B was 43.08+11.53 and 41.70+10.96 respectively. Out of the 100 patients, 37 were males and rest were females. Males formed 32.0% (n: 16) patients in group A while in group B, they were 42% (n: 21). (Table-I and II)

Mean pain (VAS 24 hours) in both the groups was 3.16+1.23 and 5.42+1.01 respectively. Independent sample t-test was used to compare mean pain (VAS 24 hours) in both the groups which was statistically significant (p-value 0.000), as shown in Table-III.

Effect modifier like age was stratified. Among patients with age 18 – 40 years, mean pain (VAS

24 hours) in both the groups was 3.14+1.10 and 5.54+0.94 respectively (p-value 0.000) whereas among patients with age 41 – 60 years, mean pain (VAS 24 hours) in both the groups was 3.16+1.12 and 5.42+1.01 respectively (p-value 0.000). Among male patients, mean pain (VAS 24 hours) in both the groups was 3.19+1.32 and 5.67+1.06 respectively (p-value 0.000) whereas among female patients, mean pain (VAS 24 hours) in both the groups was 3.15+1.20 and 5.24+0.95 respectively (p-value 0.000).

There was a single mortality in the Study group B. 6 patients needed ICU care with ventilatory support due to respiratory complications (pleural effusions, ARDS, etc.), 5 were of IV analgesia group and one was of epidural group. The rescue analgesia requirement in both groups was similar and no significant difference in requirement was observed (18% VS 20%) (Table-IV).

DISCUSSION

Effect of EA on pain management in patients with predicted severe Acute Pancreatitis has been well established.[5,12] Furthermore, the safety of EA has been widely documented in the literature.[19,20] and its benefit on postoperative morbidity and mortality are well known.[23] Pancreatitis severity has been studied at a microscopic level and various mechanisms have been proposed to explain in pathogenesis and various reasons for the conversion of mild disease to severe disease have been evaluated.

GROUPS	n	Mean Age (years)	Std. Deviation
	100	42.39	11.21
Group A (Epidural Analgesia-EA)	50	43.08	11.53
Group B (Intravenous Analgesia)	50	41.70	10.96

Table-I. Age distribution.

	Two Groups		Total
	Epidural Analgesia (EA)	Intravenous Analgesia	
Male	16	21	37
	32.0%	42.0%	37.0%
Female	34	29	63
	68.0%	58.0%	63.0%
Total	50	50	100

Table-II. Gender distribution.

	Two Groups	n	Mean	Std. Deviation	P-Value
Pain score	Epidural Analgesia (EA)	50	3.16	1.23	0.000
(VAS as 24 hours)	Intravenous Analgesia	50	5.42	1.01	

Table-III. Comparison of Mean Pain (VAS 24 hours) among patients in both the groups.

		Two Groups		Total
		Epidural Analgesia (EA)	Intravenous Analgesia	
Analgesia Requirement	Yes	9	10	19
		18.0%	20.0%	19.0%
	No	41	40	81
		82.0%	80.0%	81.0%
Total		50	50	100

Table-IV. Rescue analgesia requirement.

The activation of pancreatic enzymes leading to edema and necrosis, vasoconstriction and pancreatic ischemia are few of those. EA increases blood flow and delays metabolic acidosis. These effects have been attributed to a sympathetic nerve blockade that redistributes blood flow to non-perfused regions.[4,11] EA has a beneficial effect on the severity of AP, suggesting that EA leads to an improvement in pancreatic blood flow with a concomitant decrease in the severity of metabolic acidosis and diminished tissue injury.

Development of pancreatic necrosis is a critical event in AP that determines patient prognosis because it is often accompanied by infection and multiple organ dysfunction syndromes and, thus, is associated with a high mortality.[12] Therefore, early detection of necrosis is important for the appropriate treatment of predicted severe AP. The literature supports the use of CT scan perfusion studies to measure blood flow and diagnose necrosis in the pancreas.[16] Pancreatic perfusion showed significant improvement of the parenchymal blood flow within the pancreatic gland in the group treated with EA when compared to the control group on admission and at 72 hrs. This observation substantiates the theory that the severity of AP may be related to a vasoconstriction phenomenon, which can be attenuated by EA.[1,16] It also suggests that the use of EA decreases progression from edematous to severe necrotizing pancreatitis caused by early ischemia of the gland and thus could reduce the severity of the disease. This observation is also reflected in our study with lesser ICU admissions and no mortality in test group.

Our study primarily compared the mean pain scores in patients receiving epidural analgesia and those receiving intravenous analgesia in moderately severe acute pancreatitis. Mean pain (VAS 24 hours) in both the groups was 3.16+1.23 and 5.42+1.01 respectively. Comparing it to a study conducted by Sadowski et al, the pain scores were 0.57 vs 2 at 24 hours which are significantly lower in both groups than our study.[1] The reason could be the differences in expression of pain in different cultures and races and pain being a subjective phenomenon. Nevertheless, the scores were significantly lower in the test groups in both studies.

One of the major limitations of this study was the lack of blinding between the two groups. The major reason for this was the invasive procedure (epidural catheter placement) being done on the test group with its attendant risk of complications and subjecting this procedure to the control group just for the sake of blinding would have raised ethical issues. So, there is a chance of patient as well as observer bias in the pain scores recording. Nevertheless, the lesser rate of respiratory complications, reduced pulse rate etc. show some objective evidence of effective pain relief in the test groups. This study also proposes multicenter trials on this topic so that epidural analgesia becomes a norm in the management of acute severe pancreatitis, rather than a luxury offered to a select few patients.

CONCLUSION

Epidural analgesia significantly improves pain scores in moderately severe pancreatitis compared to IV analgesia. It also decreases respiratory complications in these patients and decreases progression of disease and thus also improves morbidity and mortality.

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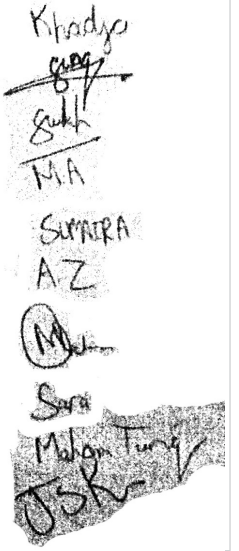
1	Ghulam Khadija	Concept design.	
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