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"EFFECTS OF LOW MOLECULAR WEIGHT HEPARIN IN TREATMENT OF ACUTE PANCREATITIS"

Surgery

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ABSTRACT

pancreatitis is a severe and frequently lethal disorder which occurs suddenly and develops rapidly.Acute pancreatitis is usually accompanied with systemic inflammatory cascades and microcirculatory disturbance. Microcirculatory disturbance is a trigger factor in the development of Acute pancreatitis , and plays a key role in the development of multiple organ dysfunction syndrome or multiple organ failure (MODS/MOF) The aim of the study is to look for the role of low molecular weight heparin (LMWH) IN treatment of pancreatitis which improves microcirculation

Patients And Methods: Our study included 100 patients , 50 in each group.

GROUP : A patients will undergo conventional therapy that includes management of shock ,maintenance of water and electrolytes balance, fasting, gastrointestinal decompression , administration of pancreatic enzymes inhibitor(octreotide) , antibiotics (cephalosporins and metronidazole) and oral manganese sulfate and symptomatic treatment.

GROUP : B patients: The treatment included following the methods used in GROUP A patients, plus administering LMWH at 100 micro gram /kg per day subcutaneous injection starting from the admission day and continuing for 7 days.

The APACHE II score was compared in both groups at the time of admission and after 7 adays of treatment.

Results: The results showed that the decline in APACHE-II scores in the observation group was larger than that in the control group and lower values than those in CONTROL group ($p < 0.05–0.01$). There is a significant benefit in terms of mean hospital stay , morbidity and mortality rate in LMWH group.

Conclusion: LMWH can enhance the effect of conventional treatment for acute pancreatitis , and can markedly decrease the mortality of acute pancreatitis . LMWH is a simple, safe, economic and effective method for treatment of acute pancreatitis.

KEYWORDS

PANCREATITIS, LMWH , microcirculatory disturbances, APACHE II, mods

INTRODUCTION

Acute pancreatitis is a disease which has many etiologies. Each etiology seems to affect the pancreatic acinar cell in some way that results in premature activation and retention of potent proteolytic enzymes.

In early stages of pancreatitis, macrophages, neutrophils, endothelial cells are activated. Preinflammatory cytokines are released and inflammation factors re elevated during acute pancreatitis and have been implicated in progression of pancreatitis associated microvascular disturbance and hemorrhagic necrosis. Ischemia, reperfusion injury and tiny thrombosis are closely associated with pancreatic microcirculation disturbance[1].

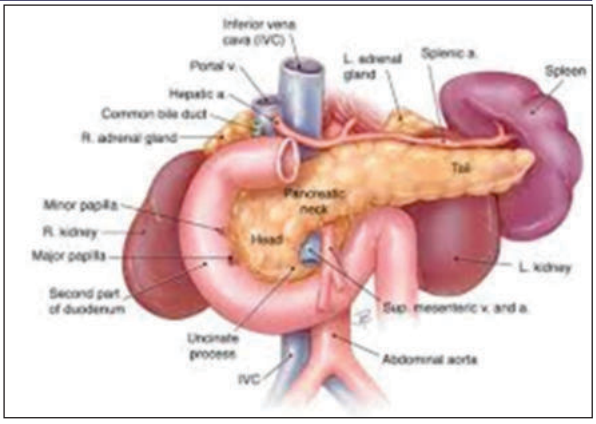
Severe acute pancreatitis [SAP] is severe and frequently a lethal disorder. Its mortality rate reaches upto 25 to 40%.[2].SAP is usually complicated with systemic inflammatory cascades and microcirculatory disturbances – related morbidity due to infected pre pancreatic necrosis.

Microcirculation disturbance is a trigger factor and plays an important role in the development of multi organ failure.[3, 4]. Due to high mortality rate, search for newer modality of treatment is the hot point in the fields of pancreatic surgery.Low molecular weight heparin (LMWH) is known to posses a special anti-thrombin activity which is stronger and safer than unfrationated heparin. LMWH can reduce the release of cytokines and inflammatory mediators, resulting in an improvement of the microcirculation of pancreas.

Our experimental study provides evidence that LMWH can block the initiation of an inflammatory storm, leading to improvement of microcirculation system; and has anti-thrombus effect to reduce the formation of microthrombosis in pancreas. These findings demonstrate the important therapeutic effect of LMWH in the treatment of acute pancreatitis

AIM OF THE STUDY

Effect of LMWH in improvement of microcirculation in acute pancreatitis.



OBJECTIVES OF THE STUDY

To study the effect of low molecular weight heparin (LMWH) in the treatment of acute pancreatitis.

MATERIALS AND METHODS

Design Of Study:

Randomized prospective comparative clinical study.

Minimum of 100 consecutive patient diagnosed with acute pancreatitis of 72 hrs or less duration.

Inclusion Criteria:

Patients diagnosed with acute pancreatitis based on the following 2 criteria:

1. Abdominal pain characteristic of acute pancreatitis (duration <72 hrs)
2. Serum amylase and/or lipase ≥ 3times the upper limit of normal

Exclusion Criteria: Patients

1. Sensitive to LMWH
2. Pregnant

3. Breast feeding
4. Coagulation disorders
5. Undergoing haemodialysis

Source Of Data

patients admitted in HITECH MEDICAL COLLEGE, BHUBANESWAR from SEPTEMBER 2018 to AUGUST 2020

Methods Of Data Collection

Patients who satisfy the inclusion criteria will be enrolled into the study. Prior informed consent will be taken from the patients and relatives before enrolling them into the study. The particulars of the patient including name, age, gender, admitting diagnosis will be documented.

Patients will be assigned to 2 groups as random number table A and B.

Group A Patients

will undergo conventional therapy that includes management of shock ,maintenance of water and electrolytes balance, fasting, gastrointestinal decompression , administration of pancreatic enzymes inhibitor(octreotide) , antibiotics (cephalosporins and metronidazole) and oral manganese sulfate and symptomatic treatment.

Group B Patients:

The treatment included following the methods used in GROUP A patients, plus administering LMWH at 100 micro gram /kg per daysubcutaneous injection starting from the admission day and continuing for 7 days.

Observation Parameters

Clinical Parameters:

Clinical Severity by Atlanta Criteria(Complication rate, occurrence rate of organ failure), in hospital mortality, curative rate and mean hospital stay in the two groups were observed and compared.

Laboratory Tests:

The APACHE II scores, parameters on admission and at 1 week after treatment were determined:

Statistical Methods

Parametric and non parametric data will be analyzed using students t-test (paired and unpaired) and Chi- square test respectively. A P value<5 will be considered significant.

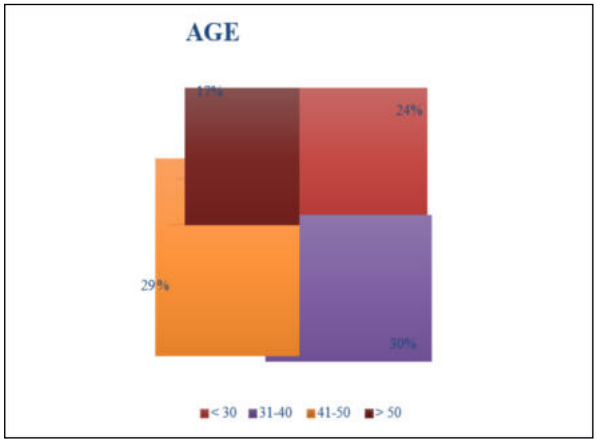
RESULTS

Comparison Between Groups

In our study, there were 50 patients in the observation group (44 men, 6 women; average age 40 years) and 50 patients in the control group (42 men, 8 women; average age 40.04 years). Differences in general data, such as sex and age, between the groups were not statistically significant (p > 0.05). Thus, the groups were comparable.

Age Distribution Table-1

AGE(IN YRS)	NO OF PATIENTS	PERCENTAGE
< 30	24	24%
31-40	30	30%
41-50	29	29%
> 50	17	17%



Age In Years Table-2

	AGE IN YEARS	
TREATMENT	MEAN	SD
WITH HEPARIN	40	9.44
WITHOUT HEPARIN	40.04	11.92
P VALUE - 0.985		
NON SIGNIFICANT		
UNPAIRED T TEST		

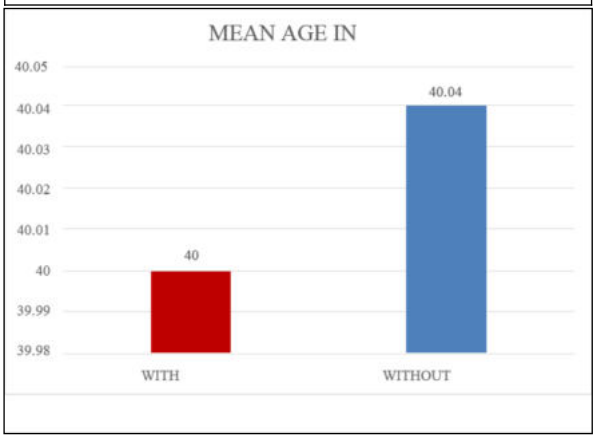


Table-3 Age Distribution Among Groups

	TREATMENT	
AGE(IN YRS)	WITH HEPARIN	WITHOUT HEPARIN
< 30	11	13
31-40	14	16
41-50	16	13
> 50	9	8
P VALUE - 0.880		
NON SIGNIFICANT		
KRUSKAL WALLIS TEST		

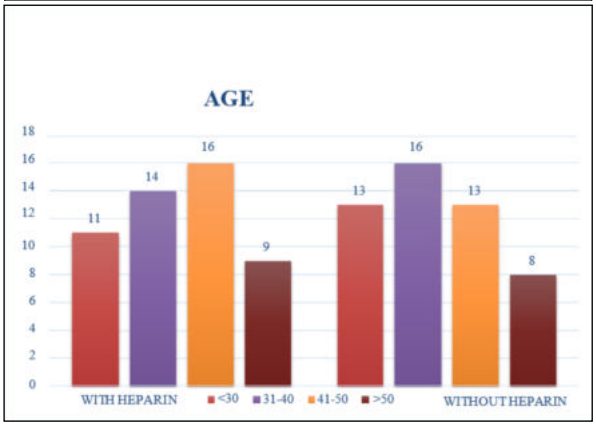


Table-4 Sex Distribution

SEX	NO OF PATIENTS	PERCENTAGE
MALE	86	86%
FEMALE	14	14%

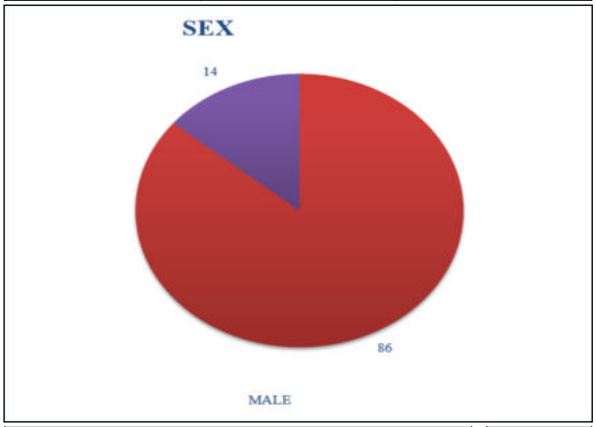
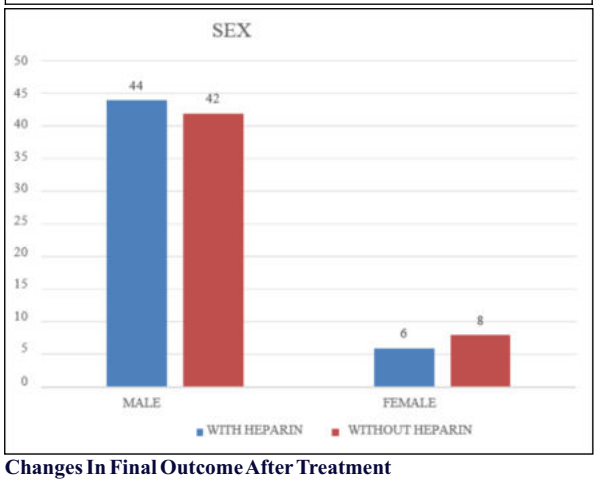


Table-5 Sex Distribution Among Groups

	TREATMENT	
SEX	WITH HEPARIN	WITHOUT HEPARIN
MALE	44	42
FEMALE	6	8
P VALUE - 0.564		
NON SIGNIFICANT		
MANN WHITNEY U TEST		



Changes In Final Outcome After Treatment

In our study out of 100 patients 96 patients recovered and 4 patients died. All the 4 patients were from control group. The final outcome of recovery rate between the two grops were statistically significant with ($p < 0.05$), (Table 7)

Table-6 Final Outcome

FINAL OUTCOME	NO OF PATIENTS	PERCENTAGE
RECOVERED	96	96%
DIED	4	4%

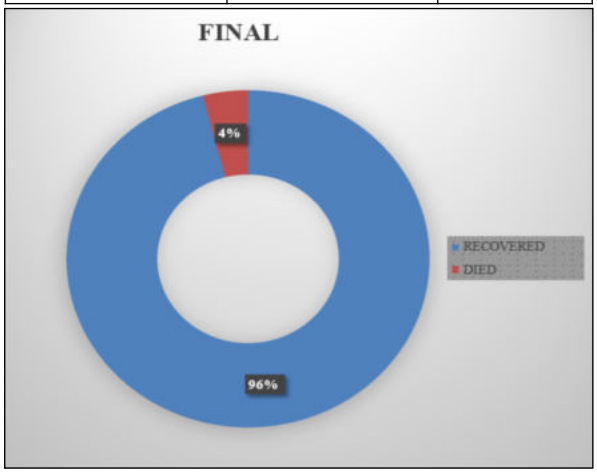
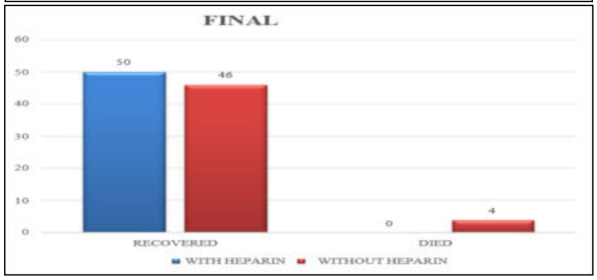


Table-7 Final Outcome Among Groups

	TREATMENT	
FINAL OUTCOME	WITH HEPARIN	WITHOUT HEPARIN
RECOVERED	50	46
DIED	0	4
P VALUE - 0.041		
SIGNIFICANT		
CHI SQUARE TEST		



Changes In APACHE Scores After Treatment

The APACHE II scores at admission were not significantly different between the groups ($p > 0.05$), (Table 8). After 7 days of treatment, the APACHE II scores in the observation group (i.e. patients treated with heparin) were significantly lower than those in the control group with ($p < 0.05$), (Table 9)

Table-8 Apache Score - On Admission

	APACHE SCORE - ON ADMISSION	
TREATMENT	MEAN	SD
WITH HEPARIN	12.56	5.85
WITHOUT HEPARIN	12.58	6.83
P VALUE - 0.987		
NON SIGNIFICANT		
UNPAIRED T TEST		

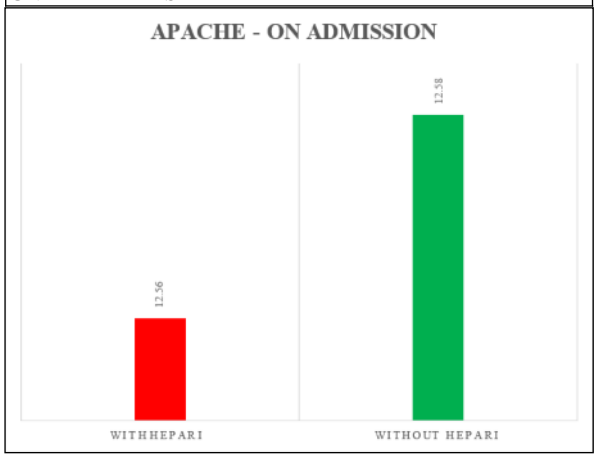


Table-9 Apache Score- On Day 7

	APACHE SCORE- ON DAY 7	
TREATMENT	MEAN	SD
WITH HEPARIN	5.22	3.79
WITHOUT HEPARIN	7.96	4.65
P VALUE - 0.002		
SIGNIFICANT		
UNPAIRED T TEST		

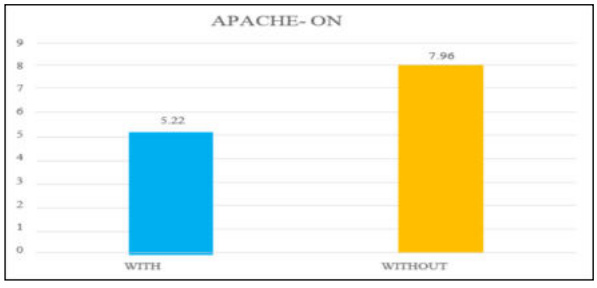
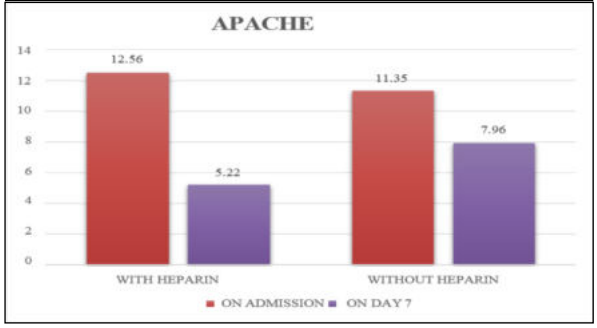


Table-10 Treatment

	TREATMENT	
APACHE SCORE	WITH HEPARIN	WITHOUT HEPARIN
ON ADMISSION	12.56	11.35
ON DAY 7	5.22	7.96
MEAN DIFFERENCE	7.34	3.39
P VALUE -0.005		
SIGNIFICANT		

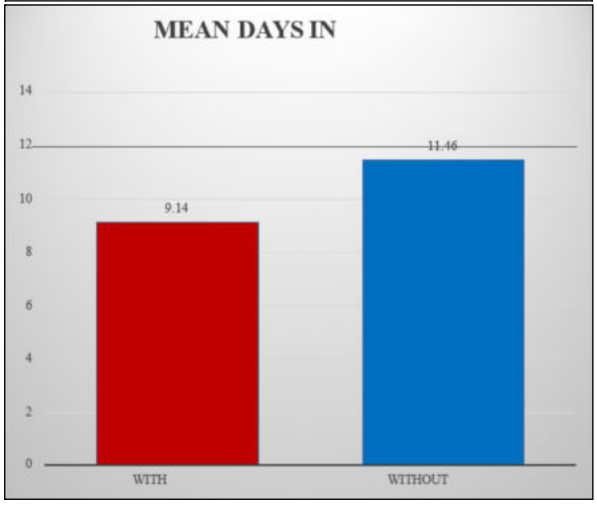


Changes In Duration Of Hospital Stay

In our study mean duration of hospital stay in patients treated with heparin was 9.14 days and in patients treated without heparin was 11.46 days. Which were statistically significant between the two groups with ($p<0.05$), (Table 11).

Table-11

	DAYS IN HOSPITAL	
TREATMENT	**MEAN**	**SD**
WITH HEPARIN	9.14	2.68
WITHOUT HEPARIN	11.46	5.41
P VALUE - 0.008		
SIGNIFICANT		
UNPAIRED T TEST		



DISCUSSION

Although research on the pathogenesis and mechanisms of severe acute pancreatitis has progressed in recent years, the primary cause of the high mortality remains unknown. In early stages of pancreatitis, macrophages, neutrophils, endothelial cells are activated. Preinflammatory cytokines are released and inflammation factors re elevated during acute pancreatitis and have been implicated in progression of pancreatitis associated microvascular disturbance and hemorrhagic necrosis. Ischemia, reperfusion injury and tiny thrombosis are closely associated with pancreatic microcirculation disturbance[1].

As an anticoagulation drug, LMWH can effectively restrain the activity of thrombin and blood coagulation factor Xa, inhibit platelet aggregation, and improve the microcirculation. LMWH can also reduce inflammation by lowering the expression of pro-inflammatory factors, inflammatory factors, adhesive factors.

In this study, the curative effects of adding lmwh alone in the treatment of acute pancreatitis were compared with conventional strategy. The results showed obvious improvements in laboratory indices, much higher cure rate, and lower incidence of complications in the observation than in the control group, suggesting that LMWH safe and effective for treatment of severe acute pancreatitis.Furthermore, the results showed that the decline in APACHE-II scores in the observation group was larger than that in the control group and lower values than those in C group ($p < 0.05–0.01$). The results of our study is on par with other international studies[5,6,7]

APACHE-II scores show an obvious increase in the early stage (0 – 48 h) and the increase becomes faster at 24 to 48 h. A continued increase in APACHE-II scores after discharge usually indicates disease progression. In this study, the APACHE-II scores in the observation group were much lower than those in the control group after treatment, suggesting that LMWH can relieve acute pancreatitis-related inflammation and reduce the incidence of complications.

Limitations Of The Study

This study found that LMWH had a marked effect in the treatment of acute pancreatitis. However, our study is a small, population based study from a single institution, from among patients admitted during a brief time-frame. Larger, multi institutional studies with larger sample size and longer time frames are needed to conform validity and accuracy my results.Patients were followed up till the time of discharge. Further follow up; to analyze further complications of acute pancreatitis did not fall under the parameters of our study. Pediatric patients were not include in our study.

CONCLUSION

Findings From Our Study Found that use of LMWH in treatment of Acute pancreatitis, which acts by improving microcirculation is an effective drug in the non-surgical treatment of acute pancreatitis

As per our study, the APACHE II Scores reduced considerably in the group treated with LMWH, suggesting that there was a considerable improvement in laboratory values, higher cure rate and lower complication. Such as Necrosis, Abscess, sepsis and Organ failure etc.Thus LMWH can effectively relieve acute pancreatitis related inflammation and reduce incidence of complications.

LMWH can rapidly relieve abdominal pain, halt the progression of diseases, reduce the severity and complication, shorten the length of hospital stay and enhance the cure rate**.**

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