

## ORIGINAL ARTICLE

**Topical Heparin: A Better Sanative For Burns Patient than Conventional Treatment**

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**Abstract:**

*Background:* Burns trauma represents a major cause of morbidity and mortality. Tackling the pain and providing a better healing with conventional therapies have been compared to that by using topical heparin application in < 40% burns. *Aim and Objectives:* To compare pain score, healing, duration of hospital stay after applying topical heparin and conventional treatment for burns < 40%. *Material and Methods:* A total of 80 patients were included in the study and divided into 2 groups Heparin (H) and Control (C) group with 40 patients in each group. H group received unfractionated Heparin 25,000 IU / 5ml and C group received silver based antimicrobial cream and paraffin gauze. *Results:* Maximum number of patients belonged to the age group (15-35years = 65.5%). The maximum number of patients who sustained thermal injuries was from 11-20% (23 patients) and 31-40% (22 patients). The patients in H group had a significant decrease in their pain score ( $p < 0.001$ ) when compared to C group. The days of hospitalization was reduced significantly in patients receiving topical Heparin therapy when compared with the C group. Majority of the patients in H group (36 patients, 90%) had only 1-2 doses/day of analgesic medication administered to them. Patients in C group (26 patients, 65%) had to be given 3-4 divided doses/day of analgesia. *Conclusions:* From this study it was concluded that topical application of Heparin reduces pain, duration of hospital stay, rates of wound infection, cost and time required for dressing.

**Keywords:** Burns, Pain, Topical Heparin

**Introduction:**

The complexity of burn trauma can never be fully addressed, yet the patients coming to a hospital with a thermal injury are being dealt with a protocol based remedy on a daily basis. Burn trauma causes a significant drain on the physiological and well as psychological system of a person. The disfigurement as well as pain associated with thermal injury makes the sufferer a virtual outcast in the society, though sympathised. Analgesia, speedy recovery with reduction in the days of hospitalisation and early return to work is what the patient suffering from burns expects from his healers. This study uses the help of heparin to achieve the same in turn exploring the various effects of this multifaceted compound [1].

Heparin is an anticoagulant in its natural form. It has been used in the treatment of burns for a couple of decades but due to the lack of controlled documentations and trials its use has not been ubiquitous. The non-anticoagulant effects of Heparin form the rationale for using heparin to treat burn trauma [2]. Recent basic science literature suggests heparin may have a biological role as an anti-inflammatory, anti-proteolytic and neoangiogenic agent. In the immediate post-burn setting, the benefits of heparin's postulated anti-inflammatory and enhanced wound healing properties could include reduced pain, infection,

length of hospital stay, and mortality [1]. Morbidity and mortality associated with burn trauma is dreaded. Our hospital being the only fully equipped and dedicated centre capable of handling burn cases in an area spanning 80 km and treating the patients, who come from a financially challenged and educationally backward class, we have taken up the task to explore the lesser known but equally beneficial effects of heparin in order to treat burn trauma. The aim of this study was to compare the effectiveness of topical heparin treatment with that of conventional therapy in the management of burns.

#### **Material and Methods:**

A total of 80 patients admitted in the department of General Surgery, BLDEU's Shri B. M. Patil Medical College Hospital and Research Centre during October 2015 to May 2018 were included in our study with a sample size of 40 patients in each group. A prospective study was conducted wherein patients with age 15-50 years, with a total burn surface area of less than 40%, with superficial to 2<sup>nd</sup> degree burns presenting to the hospital within 72 hours of burn trauma were included in this study after obtaining clearance from the Institutional Ethics Committee and the patient and/or the relative's consent for the above mentioned study. Patients with hypersensitivity to heparin, with history of heparin induced thrombocytopenia, who are actively bleeding, with low platelet count and altered coagulation profile, with family history of bleeding disorders, with full thickness burns and with infected wounds were excluded from the study.

They were divided into two groups- Heparin Group (H) of 40 patients and Control Group (C) of 40 patients. Group H received topical heparin

therapy from the day of admission and Group C patients were given conventional treatment i.e. with topical silver sulphadiazine cream and paraffin gauze dressing.

The treatment meted out to these patients included administration of antibiotics and analgesics systemically along with proton pump inhibitors and sufficient intravenous fluids as per the required dosage calculated for each and every patient (Parkland's Formula). The only difference was that Group H was treated with topical heparin application and the other Group C was regularly dressed with silver based antimicrobial cream and paraffin gauze. The patients presenting to the emergency room within 72 hours post thermal injury were initially evaluated and admitted to the burn unit. The burn size in Total Body Surface Area (TBSA) and the severity of burned areas was determined by clinical assessment and various formulas. Bathing or cleaning with normal saline of contaminated burns was done. Analgesics were administered as and when required i.e. parenteral injections of Tramadol were used for the first five days and later oral analgesics were allowed. Analgesics were administered on demand from 2<sup>nd</sup> week. Daily water baths were given to patients in both groups.

Injection unfractionated heparin 25000IU/5ml i.e. 5000IU/ml was used in the topical application for every patient in Group H. The source being from porcine intestinal mucosa, recommended for use in human burn injuries and trauma, was used. Each vial with 500 ml normal saline was stirred to make heparinised sodium solution fit for topical application on Burn Wounds. The dose of heparin required for topical application was calculated to be 100,000IU/15% Burn Surface Area (BSA) per

day in 3-4 divided doses. The medication was applied to the burnt surface drop by drop with a 20 ml syringe and a 30-gauge needle (Insulin Syringe), until the pain was relieved, repeated for 2-4 times with 10 minute intervals until blanching occurred. Beginning on the 2<sup>nd</sup> day, heparin was applied twice a day, for two days and was used in a diminishing quantity for 1 week. Burn area was observed for neovascularisation and signs of healing i.e. appearance of granulation tissue and epithelisation. Heparin treatment was started as soon as the patient was received in the emergency room or burns ward after the initial assessment and resuscitation was complete and was continued till post burn day 7.

The study data was statistically analyzed to evaluate the differences in Control Group and Heparin Group. Student's 't' test, Chi square test, Paired 't' test and Fishers exact test were used to assess the statistically significant values. Values of  $p < 0.01$  or less were considered to be statistically significant, designated by 'S', those statistically not significant, by 'NS'.

### Results:

Maximum number of patients belonged to the age group 15-35 years (65.5%). Male and female patients were almost equally distributed among both groups wherein there were 22 males: 18 females in Group C (55%:45%) when compared to 18 males: 22 females (45%:55%) in Heparin Group. However, when combined the study and control group had equal number of male to female patient's ratio.

The maximum number of patients who sustained thermal injuries was from 11-20% (23 patients)

and 31-40% (22 patients). Together they made up 57.5%. The least number was in 21-30% (14 patients). Most of our patients reported to the hospital within 4 hours of burn trauma i.e. 68 patients (85%). Most of the patients (95%) sustained burns accidentally, rest (5%) sustained burns due to suicidal cause.

The pain score on Day 1 using Visual Analogue Score (VAS) were compared after administering the dose of heparin a single time for the H group and cleansing the wound with normal saline for the patients in C group. The pain score on day 5 was taken after the final dose of topical heparin administration for the H group and after removing the paraffin gauze dressing for the patients in C group. As our results indicate, the patients in Group H had a significant decrease in their pain score ( $p$  value  $< 0.001$ ) when compared to Group C (Fig. 1).

The days of hospitalization was reduced significantly in patients receiving topical heparin therapy when compared with Group C. Most of the patients in Group H were discharged in the 2<sup>nd</sup> week (i.e. 8 days) whereas most of the patients in Group C were discharged in the 3<sup>rd</sup> week.  $P$  values suggest the same results (Table 1).

Majority of the patients in Group H (36 patients, 90%) had only 1-2 doses/day of analgesic medication administered to them. Patients in Group C (26 patients, 65%) had to be given 3-4 divided doses/day of analgesia. This is significant as heparin acts as an analgesic too. All these were calculated using Fishers exact test. There were no complications seen in any of our patients. There were no mortalities in our study.

Table 1: Comparison of Various Parameters between Group H and Group C

Variables	Range	Group H	Group C	P
Age in years N (%)	15-25	18(45)	16(40)	-
	26-35	10(25)	10(25)	
	36-45	8(20)	14(35)	
	46-50	4(10)	0(0)	
Sex N (%)	Male	18(45)	22(55)	0.3711
	Female	22(55)	18(45)	
Percentage of Burns N (%)	5-10	14(35)	06(15)	0.0445
	11-20	14(35)	10(25)	
	21-30	4(10)	10(25)	
	31-40	8(20)	14(35)	
Duration of Burns in Hours N (%)	1-2	18(45)	10(25)	0.2741
	3-4	16(40)	24(60)	
	5-6	4(10)	4(10)	
	>6	2(5)	2(5)	
Type of Burns N (%)	Chemical	0(0)	2(5)	0.0684
	Electrical	6(15)	6(15)	
	Flame	14(35)	22(55)	
	Scald	20(50)	10(25)	
Analgesics Doses/Day N (%)	1-2	36(90)	14(35)	-
	3-4	4(10)	26(65)	

Continued...

Variables	Range	Group H	Group C	P
<b>Pain Score (VAS) according to Percentage of Burns on Day 1 (Mean ±SD)</b>	<b>5-10</b>	7±1.7	8±0.0	0.362
	<b>10-20</b>	7±1.0	8.8±0.4	0.004
	<b>20-30</b>	7±1.4	8.8±0.8	0.080
	<b>30-40</b>	8.5±1.0	9.3±0.8	0.172
<b>Pain Score (VAS) according to Percentage of Burns on Day 1 (Mean ± SD)</b>	<b>5-10</b>	2.3±1.4	5.3±1.2	0.010
	<b>10-20</b>	2±0.0	6.2±1.3	<0.001
	<b>20-30</b>	2±0.0	7.2±1.1	<0.001
	<b>30-40</b>	4.5±1.0	7.7±0.5	<0.001
<b>Duration of Hospital Stay (Days) according to Percentage of Burns (Mean ± SD)</b>	<b>5-10</b>	7.7±1.0	4.3±3.1	0.022
	<b>10-20</b>	7.6±0.8	10.2±2.9	0.041
	<b>20-30</b>	8±0.0	21±10.7	0.166
	<b>30-40</b>	13.5±11.3	23.6±3.4	0.049

Note: \*means significant at 5% level of significance (p<0.05)

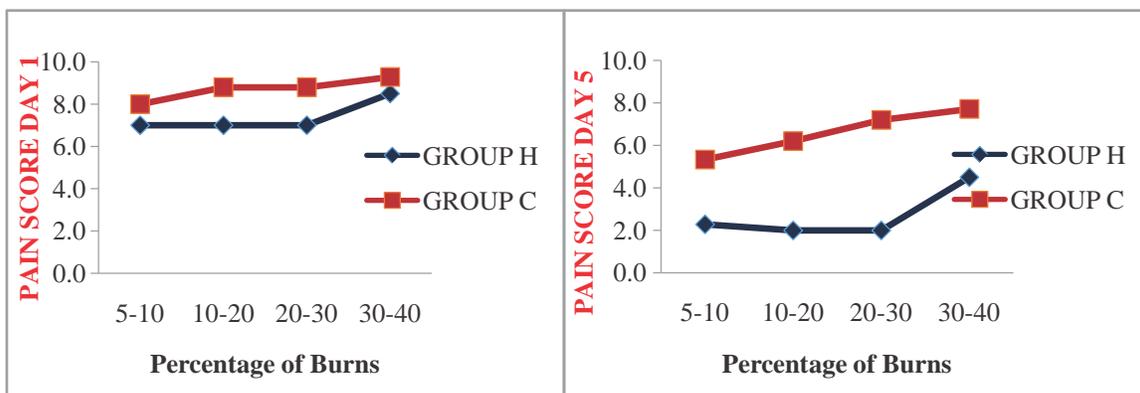


Fig. 1 & 2: Mean Pain Score Day 1 and Day 5 between Study Groups according to Percentage of Burns



**Fig. 3: Healing of Wounds in Heparin Group (H) on (a) Day 1 (b) Day 3 (c) Day 5 (d) Day 40**



**Fig. 4: Healing of wounds in Control Group (C) on (a) Day1 (b) Day3 (c) Day 5 (d) Day 4**

**Discussion:**

Burn trauma represents a major cause of morbidity and mortality, as well as a significant drain on limited health resources. The breached skin barrier is the hallmark of thermal injury [3-4]. Thermal injuries produce coagulative necrosis of the skin and underlying tissues which is very painful and is associated with complex local and systemic pathological process and a high morbidity and mortality.

Heparin has shown to be very effective in the treatment of burns [4-7]. A number of studies on burn patients have unearthed the effects of heparin which were anti-inflammatory, neoangiogenic, reduction of tissue edema, epithelializing and anti serotonin, in addition to anticoagulation. Use of heparin in burns patients according to a protocol, maintained blood circulation, inhibited blood clotting and infarctions, relieved pain, limited

inflammation, revascularized ischemic tissue, enhanced granulation and resulted in new skin that was smooth and comfortable with minimum or no scars.

The patients in the present study had the same parameters and characteristics, were limited to an age group of 15-35 years with a variety of burn trauma upto 40% TBSA size. These 80 patients with these parameters were prospectively randomized without bias into two similar 40 patient cohort groups, a control Group labeled C, and a test-variable Group labeled H.

The observations that we made in our study were that the heparin group of patients were receiving analgesics only once or twice a day for 1 week and from the start of 2<sup>nd</sup> week it was only on demand basis and very few patients opted for it. This was in contrast to the patients in control group wherein they received analgesics thrice or more in a day in the first week and in the 2<sup>nd</sup> week it was down to once or twice a day. These findings were consistent with similar observation made in a study conducted by Agbenorku *et al.* [8] who found heparin to be effective in alleviation of pain. Similar study conducted by Masoud *et al.* [9] concluded that application of heparin topically over the burn area in patients with superficial 2<sup>nd</sup> degree burns reduced the pain significantly when compared to the conventional treatment.

The overall quantity of analgesics used and the frequency of administration were less in Group H. Statistical analysis on the basis of Fishers exact test showed a very high significance in the reduction of need of analgesics by patients in Group H than Group C.

Majority of the patients in the heparin group had a hospital stay of 8 days, whereas most of the patients in the control group were discharged in

the 3<sup>rd</sup> week (p value <0.05). Studies conducted by Agbenorku *et al.* [8] and Masoud *et al.* [9] have reported that the patients treated with heparin spent less time in the hospital and were discharged early. The patients in heparin group had an improved outcome when compared with the patients in control group with respect to reduced pain and reduced tissue edema which all translated into reduced duration in their hospital stay.

The acceptable appearance of the new skin was generally better in heparin group (Fig. 2) as compared to control group (Fig. 3) patients in this study. In our part of the world with most of our patients belonging to lower socioeconomic group, a reduced stay in the hospital meant a quick return to work. The mean duration of hospital stay was significantly less in Group H as compared to Group C. The shorter stay increased the cost effectiveness, decreased mental and economic hardship faced by the patient and the patient's family due to loss of man hours. This was at par with results from similar studies worldwide [11-12].

It is glad to state that in our study we did not encounter any complication regarding wound healing or otherwise. Our observation is strikingly similar to one study conducted by Venkat-achalapathy *et al.* [10] wherein patients treated with heparin solution had fewer complications and side effects.

There were benefits to doctors and nurses with heparin use. In Group H patients, the benefits of relieved pain, along with the fewer water baths and dressings and no use of time consuming for applying antibiotic topical creams, rendered the treatment of Group H patients more pleasant and easier than in Group C patients. The burn unit ambience was notably quieter, calmer and more pleasant as well.

In the study that we conducted, we calculated the average cost and expenditure on the intravenous antibiotics (Injection ceftriaxone 1g) and made a comparison between the two study groups and we found that the patients treated with heparin had to spend an average of Rs.910 per day whereas the control group had to shell out Rs.1200 per day. Similar cost benefits were reported in studies conducted by Masoud *et al.* [9] and Venkatachalapathy *et al.* [10].

### Conclusion:

A thorough study conducted in our hospital clearly suggested that Heparin as a topically administered agent for burn trauma significantly improved the general condition of the patient, provided adequate analgesia, reduced complications and decreased the overall cost compared to the patients in the study group. Hence Heparin treatment, which in addition to providing medical benefits, if cost effective, will be readily acceptable by patients and healthcare providers the world over.

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