

# Role of Topical Heparin Therapy in Thermal Burns

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## ABSTRACT

**Introduction:** The quest for advancement in burn care continues to reduce mortality and morbidity. Heparin is used mainly in medical specialties for its antithrombotic properties is made utilized in treatment of burns. Study aimed to assess the efficacy and safety of topical heparin therapy in thermal burns.

**Material and methods:** It is a prospective study 100 consecutive thermal burn patients admitted for a period of 2 years. All patients selected with certain specifications like thermal burns of mostly 2<sup>nd</sup> degree, with range 20- 60%% and age group 15-45 yrs of less than 48hrs duration.

**Results:** All the demographic parameters are not significant in the groups. Pain medication required for burn patients is less when heparin therapy is advocated. There is a significant difference in fluids requirements between two groups with H group requiring less amount of fluid ( $p < 0.001$ ). Average duration of hospital stay in C group is 34.72 days and in H group it was 21.36 days with all same facilities and care apart from topical wound care ( $p < 0.001$ ) which is significant. 30% of control group required skin grafts and one contracture release later after discharge. In H group 20% had skin graft and none had any post burn contracture.

**Conclusion:** We conclude that Heparin can improve clinical outcomes in the treatment of burn injury.

**Keywords:** Thermal Burns, Heparin, Topical therapy.

## INTRODUCTION

The history of treatment of burns is over 3500 years old. First evidence was found in cave paintings of Neanderthal man. As time passed many changes, innovations came in type of dressings and wound care all having their own pros and cons. In India with a population of over 1 billion, 70-80 thousand burn admissions occur annually.<sup>1</sup> This high incidence makes burns an endemic health hazard. Significant breakthrough took place in the advanced countries in terms of reducing mortality and controlling morbidity. Many a time the same protocols cannot be applied in our country as the enormous population and limited health care budget poses new challenges. This necessitates the development of newer methods of management within our means to reach the common end point of reducing morbidity and mortality.<sup>2</sup> Also commonest age group afflicted being the productive age group pose a problem to society being the income generating group. Salvageable % and productive age group burn patients given priority with the available resources<sup>3</sup> in burn management. So a cost effective treatment can be made with heparin by using unfractionated heparin in the form of spray. Heparin which is used mainly in medical specialties for its antithrombotic properties is made utilized in treatment of burns and also additionally its other use are

anti inflammatory, immunomodulatory effects, angiogenesis in wound healing.

In the modern era of evidence based medicine, there is every need to study the usefulness or otherwise of a particular method or medication to reach a consensus before it is put to use. Use of heparin in burns is one such initiative which needs to be studied thoroughly and repeatedly. An attempt has been made in this article to reach such logical conclusions.

## MATERIAL AND METHODS

A prospective study 100 consecutive thermal burn patients admitted in King George Hospital, Visakhapatnam, between the year Jan 2013 – Jan 2015 was conducted.

**Inclusion criteria:** Age group 15-45 yrs, thermal burns of 2<sup>nd</sup> degree with range 20- 60%%, with duration of less than 48hrs duration.

**Exclusion criteria:** Medical disorders, pregnant ladies, coagulation disorders other types of burns like chemical, electrical.

In total 100 cases divided as C group 50 patients and Group –H-50 patients. All patients initially evaluated and resuscitated as per ATLS principles. Written and informed consent taken from all patients explaining regarding study. Routine case taking and blood biochemistries performed along with coagulation profile on day 1,3,5 in case H group. Routine pain management protocol and antibiotic given.

**Control group [C]:-** Topical antibiotic cream after resuscitation is applied with conventional 1% silver sulphadiazine after debridement.

**Heparin group[H]:-** Topical heparin spray is prepared by adding 20.8 ml of 5000 IU /ml of heparin to 500 ml of physiological normal saline to make a total of 200 IU/ml concentrated solution. Dose of heparin requirement is calculated based on % of burns taking each 15% 1 lakh IU of heparin and accordingly solution is prepared. With iv needle and set, heparin solution is sprayed on occlusive saline dressing of single layer gauze pads which help by providing adequate moist environment and avoids wastage of heparin.

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occlusive dressing also avoids insensible fluid and heat loss, reduces pain and infection rate.

Day 2-7<sup>th</sup> heparin requirement is calculated again according to certain signs of response of heparin spray like blanching of erythema, reduction of edema, formation and separation of eschar, signs of epithelialisation. Dose of heparin is reduced to half and also frequency of spray is reduced depending of pain response. Coagulation profile noted on 1<sup>st</sup>, 3<sup>rd</sup> and 5<sup>th</sup> day. total of 7 day heparin spray is done followed by occlusive saline dressing further till wound healing signs are marked by 10 -15<sup>th</sup> day.

All the hundred patients had pain as a result of burns. Pain medication was given to all by intravenous route followed by oral route when tolerated. Pain medication included routine analgesics like Tramadol, Pentazocine lactate, Paracetamol, Diclofenac sodium etc. All the H group patients required only twice daily doses of intravenous analgesics initially and oral medication later. All C group had to be given intravenous paracetamol apart from twice daily intravenous tramadol (table 1). In H group pain was relieved on topical application of heparin in 10- 15 min and the need for additional parenteral pain medication was not necessary. Burn erythema and edema reduced on topical heparin by 1-2 days further decreasing pain medication usage. Less pain medication made the patients less episodes of gastritis and further anti histaminics. Burn injury itself has the tendency of severe gastritis and curlings ulcers due to ischemic changes in the gastric mucosa. By use of heparin topically ischaemic changes are reduced by its microthrombolytic properties.

**STATISTICAL ANALYSIS**

Results are tabulated and analyzed descriptively in various variables of both control and heparin group patients. Chi square test was done to statistically analyze the data.

**RESULTS**

Hundred consecutive burns patients were selected over a period of two years based on inclusion and exclusion criteria. Of them fifty were treated with topical heparin therapy and the other fifty patients by conventional methods. After initial resuscitative measures patients were allotted to conventional therapy to C group or Heparin therapy to H group. Results of both the groups were compared with various variables to know the effectiveness of topical heparin therapy (table-1). Of these 90% were less than 35 years and 10% between 36-45 years. C group below 35 years is 84%. There is no significant difference in age among these two groups. In H group 48% were males and 52% were females. In C group there were 48% females and 52% males.

Among H group patients 80% were accidental, 10% were Suicidal and 10% were homicidal. C group included 88% of accidental burns, 10% suicidal and 4% homicidal.

Among H group 34% of patients had 20-30% burns, 80% had 31-40% burns, 44% of patients had 41-50% and 4% of patients had 51-60% burns. Similarly among C group patients 30% of patients had 20-30% burns, 28% of patients had 31-40% burns, 42% of patients had 41-50% burns (table-2).

Variable	Control group Number of patients (%)	Heparin group Number of patients (%)	P Value
Age distribution(in yrs)			0.402
15-25	16(32%)	22(40%)	
26-35	26(52%)	23(50%)	
36-45	8(16%)	5(10%)	
Total	50(100%)	50(100%)	
Sex distribution			0.312
Male	26(52%)	24(48%)	
Female	24(48%)	26(52%)	
Total	50(100%)	50(100%)	
Mode of burn			0.43
Accidental	44(88%)	40(80%)	
Suicidal	4(8%)	5(10%)	
Homicidal	2(4%)	5(10%)	
Total	50(100%)	50(100%)	
Percentage of burn			0.51
20-25	21	20	
26-35	15	17	
36-50	14	11	
51-65	-	2	

**Table-1:** Demographic distribution in study

Percentage of burns	No	Heparin dose-no of Vial-(1- vial-5000IU/ml)-average
20-25	17	25.29
26-30	3	30.8
31-35	6	35.9
36-40	11	49.2
41-45	4	52
46-50	7	56.3
51-55	2	63

**Table-2:** Heparin requirement in relation to extent of burns

All the demographic parameters are not significant in the groups.

Requirement of heparin is increased with increase in percentage of burns

Pain medication required for burn patients is less when heparin therapy is advocated

During initial period of resuscitation all C and H groups received intravenous fluids according to the standard protocol using Parkland formula. In 20% and 30% TBSA oral fluids are given along with intravenous as the patients have tolerated oral intake there by reducing the requirements of fluids in H group patients. There was a significant difference in fluids requirements between two groups with H group requiring less amount of fluid (p< 0.001) which was significant (table-3).

Duration of hospital stay is comparatively less in H group. Average duration of hospital stay in C group is 34.72 days and in H group it was 21.36 days with all same facilities and care apart from topical wound care (p< 0.001). Which was significant.

30% of control group required skin grafts and one contracture

release later after discharge. In H group 20% had skin graft and none had any post burn contracture (figure-1).

Heparin administered topically for a limited time in burns patients was studied as a modality of improved treatment. The duration of study was two years. The same doctors, nurses and ancillary staff treated all the C and H groups patients in the same burns unit using same facilities. During the period of two years a total number of 833 patients were admitted to the unit. The subjects in the study were the first hundred consecutively admitted burn patients (figure-2). Out of the 833 total admissions who had the same characteristics as regards age (20-45yrs), cause of burns and severity of burns the survival rates are high and also patients will be cooperative with these burns for the study.

The numbers, ages, gender of the patients, as also the mode of burn was comparable in both the groups which were insignificant. The majority were accidental (80% in H and 88% in C). Rest of them were suicidal and homicidal. The cause of burns had no significant in the treatment, all are treated as per protocol and all are thermal burns.

The heparin is diluted in a concentration of 200IU/ml in order to provide large volumes of less concentrated heparin solution, in view of prevailing weather which is hot and humid and fluids evaporate quickly. Also the total calculated doses are equally distributed throughout day without waste of calculated dose of heparin<sup>3,14,15</sup>. Intermittent spray of heparin throughout the day is performed to have continuous period of freedom from pain to the patient so that they can resort to early ambulation. The continuous spray made the patients satisfied as the burn wound is taken care of round the clock. Most of the times the chief complaint is pain and that is relieved with heparin spray. Topical antibiotic cream on the other hand is applied either once or twice a day and its application is very painful to the patient. Heparin spray which is sprayed on occlusive saline dressing make the patient comfortable and pain free. Also occlusive dressing reduces insensible water loss and reduces hypothermia. Early ambulation makes the patient feel better, makes early range of motion, improves circulation leading to better wound healing were the general observations made in the present study were also observed by other studies<sup>3</sup>

The pain, erythema, swelling, heat signs characteristically associated with inflammation were reduced in patients who received heparin. Pain medication was reduced<sup>4,5,6,7,8,9</sup>. Thus in this study anti inflammatory effects were evident with the usage of heparin.(Table-1). The finding was similar to comparative study of conventional and topical heparin treatment for burn analgesia made by Marcos Buithume. There was less erythema and swelling. The relief of pain with heparin use was remarkable. The coagulation profile was tested on days 1<sup>st</sup> 3<sup>rd</sup> 5<sup>th</sup> days respectively, no significant coagulation changes noted and no bleeding complications seen as heparin used here is by topical spray with little systemic absorption.<sup>10,11</sup>

One assumption is that heparin's anti-inflammatory effects are dose related and dose dependent.<sup>12,13</sup> The reduced use of pain medication and reduced side effects due to pain

Requirements of IV fluids – liters	Control group Number of patients (%)	Heparin group Number of patients (%)	P-Value
5-15	14(28%)	17(34%)	<0.001*
16-25	5(10%)	18(36%)	
26-35	10(20%)	10(20%)	
36-45	6(12%)	5(10%)	
46-55	10(20%)	-	
56-65	5(10%)	-	
Days of hospital stay			
Days	No(%)	No(%) NS or S	<0.001*
5-15	2(4%)	15(30%)	
16-25	16(32%)	21(42%)	
26-35	16(32%)	13(26%)	
36-45	14(28%)	1(2%)	
46-55	1(2%)	0	
56-65	1(2%)	0	
*Significant P < 0.001			
<b>Table-3:</b> Distribution of patients by requirements of IV fluids and Hospital stay			

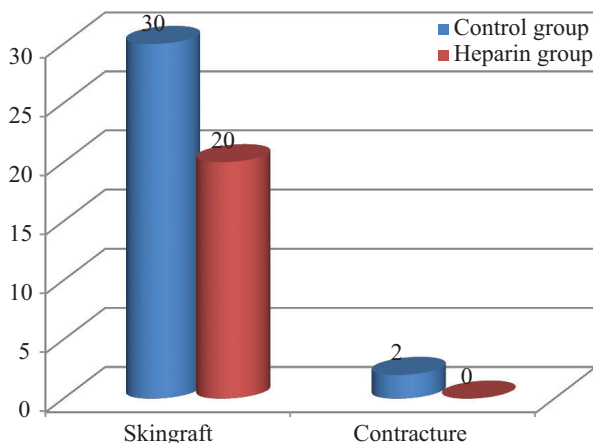


Figure-1: Secondary Procedures done in study



Figure-2: Clinical cases in study

medicine enabled H group patients who were more alert, cheerful, breath, eat, move and participate in their burn treatment more easily compared to Control group.

There were advantages to hospital staff like doctors nurses, ancillary staff in heparin use the number of visits to patients are reduced there by optimizing the associated human

resources. In heparin group pain reduction has led to ease of change of dressing and the change of dressings included with pain in control group. Early separation of eschar by about 9-10 day while that in C group took more than 15 days<sup>8,9</sup>. A study by Ehrlich, H.R., Griswold, T.R., Rajaratanam, J.B.M.<sup>14</sup> showed the same feature – with heparin and noticed eschar separation by 7-9 days earlier and the periods necessary to prepare burn wound for surgical repair was shortened by 5 days.

The use of IV fluids was significantly less in H than C group ( $p < 0.001$ ). T.S Venkata chalopathy<sup>14</sup> study found that requirements with of I.V fluids was reduced significantly. Early ambulation due to reduced pain made patients feel better and early intake of enteral feeds led to less usage of IV fluids and less chances of mucosal sloughing of gastrointestinal tract and reduced rates of tranlocation of gut bacteria and thus reducing septic episodes. Thrombolytic effect of heparin makes the microthrombolysis of intestinal microvasculature and perfusion of intestinal mucosa is improved. The chances of curlings ulcer of gastric mucosa are less., the finding was found in the other studies.<sup>14</sup> The revasculariation of ischaemic tissues and the improved quality and greater quantity of vascular granulation tissue were noteworthy. This is a consistent and early sign of healing in heparin group.<sup>11,12</sup> By using heparin, the areas to be skin grafted were prepared earlier to enable early surgery and better graft take. These improvements were presumed to be function of heparin's neoangiogenic. With heparin, thrombus already formed due to burn insult get lysed and patency of microvasculature is restored. Increase in blood flow and growth factors like vascular endothelial growth factor, epidermal growth factor cause early epithelialisation and neoangiogenesis. This restores blood flow to ischemic areas and early eschar separation. The revascularization makes zone of stasis converted to zone of hyperemia there by making wound to heal faster. Wound healing starts with peripheral epithelialisation and from remnants of dermal appendages. As the study group included second degree burns, most of the wounds healed by epithelialisation with areas of full thickness burns needing skin graft. 30% of control group and 20% of heparin group had skin grafting. The average hospital stay was significantly reduced and number of secondary procedures were reduced, This makes cost of burn treatment less with fewer IV fluids, antibiotics, secondary procedures and late post burn sequel. The scar was supple, early maturation due to immunomodulating effects of heparin. In 2002 a session was conducted on burns at Kanchi Kama Koti Child trust Hospital Chennai<sup>3</sup> and discussions about scar in heparin treated patients was done with certain conclusions that heparin having immunomodulating properties. Follow up patients had fewer complaints regarding scar pigmentations and fewer visits thereafter. Control group had complaints of hypertrophied scars and intense itching. The number of patients of follow up for scar assessment is not documented as all the patients in the study haven't had regular visit and further no specific parameter for scar assessment are available.

## CONCLUSION

Intravenous fluid requirement was less in patients treated with heparin compared to conventional treatment ( $P < 0.001$ ). Pain medication required for burn patients is less when heparin therapy is advocated. Average hospital stay was less for patients treated with heparin ( $P < 0.001$ ). Secondary procedures like skin graft, post burn contractures release were fewer in burn patients treated with heparin.

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