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Case Report Open Access

# A Comparative Study of Paediatric Thermal Burns Treated with Topical Heparin and Without Heparin

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## Abstract

Following reports of heparin use in burn treatment, an ethics-committee-approved prospective randomized study with controls compared results obtained using traditional usual burn treatment without heparin with results in similar patients similarly treated with heparin added topically. The subjects were 100 consecutive burn patients (age, <15 yr) with second-degree superficial and deep burns of 5-45% TBSA size. Two largely similar cohort groups, i.e. a control group (C) and a heparin group (H) with 50 subjects per group, were randomly treated. The 50 C patients received traditional routine treatment, including topical antimicrobial cream, debridement, and, when needed, skin grafts in the early post-burn period. The 50 H patients, without topical cream, were additionally treated, starting on day 1 post-burn, with 200 IU/ml sodium aqueous heparin solution USP (heparin) dripped on the burn surfaces and inserted into the blisters 2-4 times a day for 1-2 days, and then only on burn surfaces for a total of 5-7 days, prior to skin grafting, when needed. Thereafter, C and H treatment was similar. It was found that the H patients complained of less pain and received less pain medicine than the C patients. H needed fewer dressings and oral antibiotics than C. The 50 H patients had four skin gratings' (8%), while the 50 C patients had 10 (20%). Five 5 C patients died (mortality, 10%). No H patients died. The number of days in hospital for H vs. C was significantly less (overall, $p<0.0001$): 58% of H were discharged within 10 days vs. 6% of C; 82% of H were out in 20 days vs. 14% of C; 98% of H vs. 44% of C were out in 30 days; and while 100% of H were discharged by day 40, 56% of C required up to another 10 days. The burns in H patients healed on average in 15 days (maximum period 37 days) vs. an average of 25 days (maximum>48 days) in C ($p<0.0006$). Procedures and costs in H were much reduced compared with C. Photographs of the differences between H and C are presented for the sake of comparison. It is concluded that heparin applied topically for 5-7 days improved burn treatment: it reduced pain, pain medicine, dressings, and use of antibiotics; it significantly reduced IV fluids ($p<0.04$), days in hospital ($p<0.0001$), and healing time ($p<0.0006$); and it reduced skin grafts, mortality and costs.

## Introduction

Ours 1200-bed Indira Gandhi Government General Hospital and Postgraduate Institute, Puducherry, India, admits a total number of 50,000 patients a year, of whom an average of 1.5 patients per day are admitted to the burns unit. Approximately 50% of the burn patients die because they are suicide cases with severe second-degree and third-degree burns covering from 60 to nearly 100% of the Total Body Surface Area (TBSA). As survival is bleak and treatment costs prohibitively high and economically unsupportable, these dire situation patients are generally given narcotics to lessen their suffering until the burn pathology inevitably terminates in death.

Another nearly 50% of the patients admitted have second-degree and third-degree severity burns in less than 50% TBSA. In the three years prior to this study, of the 1344 such patients admitted, 430 died, with a mortality rate of 31.9%. The treatment of burn patients has been onerous and difficult, and needs improvement. Measures and means that might produce new burns therapies have been explored. In this study I am concentrating on advantages of heparin therapy in children.

The present study was therefore designed to evaluate whether the addition of heparin, administered only topically [1] for a limited time and prior to any surgery, could improve burn treatment and reduce burn morbidity and mortality [2] in our hospitalized patients. The Ethics Committee approved the study plan and the use of heparin by protocol.

## Method

### Subjects: selection, characteristics, and distribution

In the six months between September 2009 and February 2010, 226 patients were admitted to our burns unit. The subjects in this study were the first consecutive 100 patients aged <15yr whose superficial and deep second-degree severity burns were below 50% TBSA size (range, 5-45%). Fifty of these randomly selected patients were designated to be the control group (C). C patients received the traditional routine treatment without the addition of heparin. C treatment included pain medications, intravenous resuscitation fluids, oral antibiotics, topical antimicrobial sulphur-base cream, water baths, debridement, tissue-releasing incisions, blood transfusions, and skin grafts. The other fifty randomly selected patients were assigned to the heparin-treated group (H). H patients received the same treatment but without the use of topical antimicrobial creams, so that sodium aqueous heparin solution USP from a bovine intestinal mucosa source (heparin) could be applied topically for the first 5-7 days of treatment, and before skin grafting.

## Contraindications

Patients with liver disease, renal disorders, a blood coagulating diathesis, an allergy to heparin, an active peptic ulcer, a thrombocytopenia, or active or potential bleeding due to trauma were excluded from the study. None of the 100 subjects had a contraindication.

## Procedures

The initial evaluation and procedures on admission to the

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burn unit were the same in all 100 patients. Urgent life-threatening respiratory and/or cardiac emergency were managed first. Vital signs were measured and charted. Intravenous catheters were inserted, blood for laboratory tests was drawn, and intravenous resuscitation fluids were started. TBSA and the severity of the burn areas were determined by clinical assessment. No biopsies for histological determination of burn depth were performed. Patients with burns of more than 40% TBSA had a urinary catheter inserted in order to observe and measure urine in the collecting bag. Personal and family medical histories were recorded. A physical examination was carried out. Bathing or cleaning of contaminated or dirty burns was performed if needed, but not routinely. Fluid intake and output volumes were charted and evaluated, as also laboratory tests. The initial routine laboratory tests were: urinalysis; complete blood count and platelet count; BUN and creatinine; blood bleeding and clotting time, prothrombin time, and partial thromboplastin time. Also, patients received an injection of tetanus toxoid.

## Pain medicine

Pain medication was administered when needed. A parenteral injection of pentozocine and promethazine was used to relieve pain in the first two or three days, after which oral non-steroid anti-inflammatory drugs were used.

## Antibiotics

Penicillins were administered orally as the primary antibiotics for all patients and, in some patients, a third-generation cephalosporin, oral cefotaxine sodium, were added. Amikacin and Metro-gyl injections were used when indicated. In C patients, an antimicrobial sulphur-base cream was applied topically after water-with-antimicrobial baths and debridement of necrotic tissue had been performed. In H, water baths were not routine, and no topical sulphur-base creams were applied, because heparin was being administered topically.

Heparin administration. 20.8 ml of 5000 IU/ml (International Units per ml) of heparin solution were added to 500 ml of physiological normal saline solution in an intravenous fluid bottle to make a total 520.8 ml of 200 IU/ml concentration heparin sodium solution (heparin) [2-6]. Standard intravenous tubing was connected to the bottle and a small gauge (#28 or #30) needle was attached. This 200 IU/ml heparin solution, in an intravenous set-up, was administered only topically, dripped on the burn surfaces, and inserted into the burn blisters. This heparin was administered topically on post-burn day 1 a total of three or four times. The total day-1 topically administered heparin dose was 100,000 IU (1 lakh, in India) of heparin per each 15% of burn surface size which is the dose advocated in the heparin-in-burns protocol in use in burns centres in 13 other countries.16 Burn surfaces were treated with heparin first [7-9]. Approximately 50% or more of the heparin estimated to be needed on day 1 was initially dripped on the burn surfaces repeatedly in the first 10-15 min of heparin treatment, until the patient reported that the burn pain was relieved and the initial burn erythema, if present, was blanched. Then the burn blisters were treated. A hypodermic needle on a syringe filled with 200 IU/ml heparin was introduced into a blister and a small hole was made, out of which the blister fluid spontaneously drained by gravity [10]. Then heparin was inserted through the needle into the blister. The blister was slowly rinsed with heparin three or four times, and then the needle was withdrawn, leaving a residual volume of heparin within the blister.

The blister cover was permitted to settle onto the blister's inner surface. Blisters were not debrided or removed. After the initial treatment of blisters, the burn surfaces were then retreated with heparin at 5-10 min intervals for half an hour. On day 1 the burn surfaces were retreated two or three more times using the remaining amount of the day 1 dose. In the first 24-36 h the few blisters that refilled with burn fluid were retreated a second and rarely a third time with less heparin solution. On post-burn days 2-7, heparin in diminishing doses was dripped on the surface of the burns three or four times a day. During this time no surgery was performed. After day 1 or 2, revascularization of ischaemic areas and the development of granulation tissue were observed, and these signs of healing were utilized to monitor the dose of topically administered heparin [11]. Some blood clotting times were also taken in order to monitor heparin doses. Thus, the clinical signs and laboratory values that were used to determine and monitor the dose and adequacy of heparin applied topically were: relief of burn pain, blanching of burn erythema, reduced swelling and oedema, decreasing burn size, drier burns, revascularization, progressive healing, and blood clotting times in the normal range and up to three times normal.

The total amount of heparin administered to each patient varied because the nature of the burns and the condition of each patient varied. Between heparin applications, H patients were treated with dressings soaked with physiological normal saline. All C patients were treated with topical applications of a sulphur-base antimicrobial cream. No sulphur-base cream was used in H patients.

Serial photographs were taken of the patients (Figures 1-6).

Statistical evaluation. The study data were statistically analysed to evaluate the differences between the C and the H group. Student's t test and the chi square test derived in Epi Info-6 software were used. Values of $p<0.05$ or less were considered to be statistically significant (designated S, or statistically not significant, designated NS).

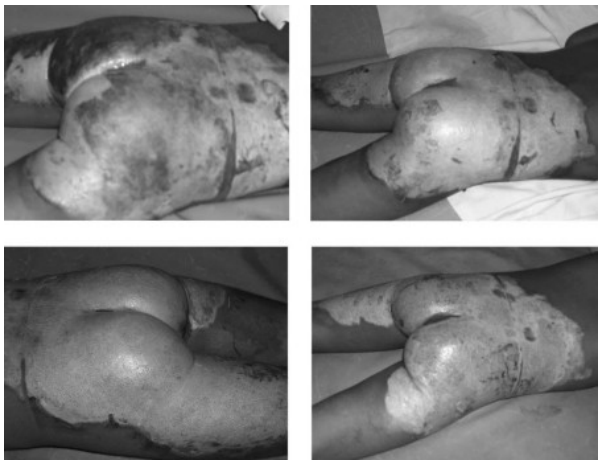

**Figure 1:** Child treated with topical heparin.

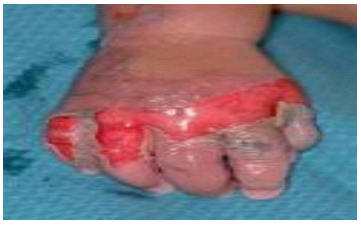

**Figure 2:** Child treated with topical heparin.

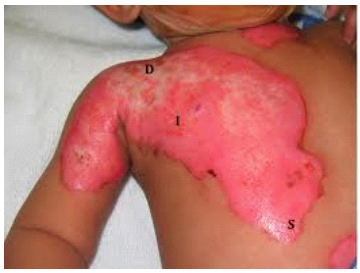


**Figure 3:** Child treated with topical heparin.

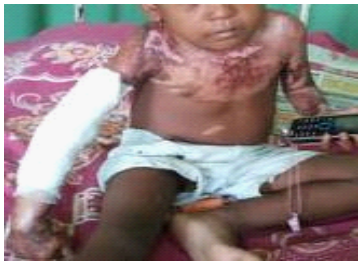

**Figure 4:** Control patient without heparin.

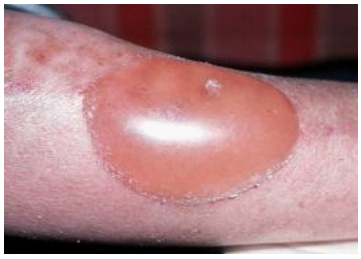

**Figure 5:** Child treated with topical heparin.

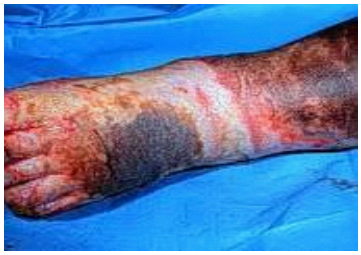

**Figure 6:** Control patient without topical heparin.

## Results

The number of patients was the same in the two groups C and H. The ages were not significantly different. The mode of the scalds and fire mode burns were accidental (Tables 1-5).

All 100 patients had burn pain, which was relieved by pain medicine pain in both C and H. Pain medicine was administered once or at most twice a day to all H patients and to 30% of C patients. Seventy per cent of C patients and essentially no H patients received pain medicine as often as 3-4 times a day (p not calculable) [12,13]. In H patients, the burn surface pain was relieved within 10 to 15 min by topical application of heparin [see Discussion]. In H group children stopped crying immediately after treatment. In H patients recurrent less intense burn surface pain was similarly relieved by another topical application of a smaller quantity of heparin solution. Burn erythema, when present, was blanched by heparin. H patients had less tissue swelling than C patents.

All 50 C and all 50 H patients had superficial and deep second-degree burns in less than 50% TBSA (range, 5-45%).

The time interval between the burn injury event and the time the patient arrived at the burns unit and commencement of treatment ranged from 1 to 8 h. Twenty-eight H patients (56%) presented 5-8 h post-burn, compared with 7 C patients (14%) (p<0.0001, S). Although the time of presentation was longer or delayed in H compared with C, mortality was lower in H than in C. Five C patients died (mortality rate, 10%). No H patient died.

The number of days of hospitalization was significantly greater in C than in H. Twenty-nine patients (58%) in H were discharged from hospital in 10 days or less compared with three patients (6%) in C (p<0.0001, S)[12]. Forty-one of the 50 H patients (82%) were

| | Control group | Heparin group |
|---|---|---|
| **Age distribution (yr)** | No. (%) | No. (%) NS or S |
| **<5 yrs** | 18 (36) | 22 (44) NS |
| **6-15** | 32 (64) | 28 (56) NS |

**Table 1:** Distribution of patients by age.

| Requirement of analgesic per day | Control group | Heparin group |
|---|---|---|
| | No. (%) | No. (%) |
| **1-2 times** | 15 (30) | 50 (100) probably S |
| **3-4 times** | 35 (70) | Nil (no calculation) |

**Table 2:** Patients' requirements of analgesics.

| Percentage of burns | Control group | Heparin group |
|---|---|---|
| | No. (%) | No. (%) NS or S |
| **5-15** | 9 (18) | 10 (20) NS |
| **16-25** | 14(28) | 15(30) NS |
| **26-35** | 14 (28) | 16(32) NS |
| **36-50** | 13 (26) | 09 (18) NS |

**Table 3:** Distribution of patients by percentage of burns (p<0.01).

| Degree of burns | Control group | Heparin group |
|---|---|---|
| | No. (%) | No. (%) NS or S |
| Superficial second | 30 (60) | 35 (70) NS |
| Deep second | 20 (40) | 15 (30) NS |

**Table 4:** Distribution of patients by severity of burns (p<0.08 NS).

| Type of burn | Control group | Heparin group |
|---|---|---|
| | No. (%} | No. (%) NS or S |
| **Flame** | 40 (80) | 45 (90) NS |
| **Scalds** | 10 (20) | 5 (10) NS |

**Table 5:** Distribution of patients by type of thermal burn.

| Type of treatment | Average cost of treatment per patient (rupees) | Cost benefit less (%) | |
|---|---|---|---|
| | Control | Heparin | |
| **IV fluids** | 34.80 | 18.80 | 46 (p<0.04 S) |
| **Analgesics, antibiotics, others** | 1720 | 540 | 69 (p<0.04 S) |

**Table 6:** Cost of treatment (p<0.04).

discharged in less than three weeks compared with seven C patients (14%) ($p<0.0001$, S). Forty-eight out of the total number of 50 H patients (96%) were out of hospital in 30 days, vs. 12 patients (24%) in C in the same period ($p<0.0001$, S). When all 50 H patients were out of hospital, in 40 days, fewer than half the C patients (22, or 44%) had been discharged ($p<0.0001$, S). The remaining 56% of C patients required a variable additional 10 days to be discharged, with a non-calculable p value because zero H patients remained in hospital.

The overall mortality of the 100 consecutive randomly selected patients in this study was a relatively low 5% compared with previous years. The five deaths were in the 50 patients in C (10%). It is of interest and important that all five C deaths were in the 35-45% TBSA size [see Discussion]. None of the 50 H patients died, meaning that p and S values were not calculable.

The patients treated at the Indira Gandhi Government General Hospital and Postgraduate Institute, including our Burns Unit, receives totally free treatment without any cost to the patients. In this study the average cost to the hospital for IV fluids, analgesics, antibiotics, and other items for the C patients was 1754.8 Indian rupees (INR),significantly more than the average cost of 558.8 INR for H patients, with a 68.2% cost benefit reduction ($p<0.05$, S) (Table 6). The total amount of heparin (in lakhs) administered and the average cost (in rupees) of the heparin used in treating H patients increased progressively with the increase in TBSA. An amount of one lakh is equivalent to 100,000 IU of heparin.

None of the C patients and none of the H patients had a bleeding problem. Except for mortality, there were no other serious complications. Topical use of heparin was safe in this study.

## Discussion

Heparin administered topically for a limited time in these burn patients clearly improved treatment. This ethics-committee-approved study was conducted in a uniformly controlled manner without any bias in the initial selection of patients and without any deviation in performance. The duration of the study was half a year. The same doctors, nurses, and ancillary staff treated all the C and H patients in the same burns unit, using the same facilities. During the test period a total number of 226 patients were admitted to the unit. The subjects in the study were the first 100 consecutively admitted burn patients out of the 226 patients who had the same parameters and characteristics as regards age (<15 yr) and presentation of scald or fire mode burns in less than 50% TBSA, as in the previous three years 60% of burn mortality occurred in this age group; second-degree superficial and deep was chosen as the degree of severity because historically survival rates were higher in this group [14-16]. The 100 patients with these parameters were prospectively randomized without bias into two similar 50-patient cohorts, a control group labelled C and a test-variable group labeled H.

There were benefits to doctors, nurses, and ancillary therapists with heparin use. In H patients, the benefits of relieved pain, along with the fewer water baths and dressings and the non-use of hard-to-manage antibiotic topical creams rendered the treatment of H patients easier and more pleasant than that of C patients for these therapists. Also, the burns unit environment was notably quieter, calmer, and more pleasant.

With heparin, the burn blisters, which were not removed and rarely became infected, functioned as natural skin grafts that required no further care [17,18]. Smooth new skin was evident beneath the dried thin blister when it flaked off, usually in 7-14 days [19].

Clinically, without determination of quantity, there was a reduction in burn surface infections in H patients compared with C. One explanation may be that orally administered antibiotics were able to reach the burns from within the body via the increase in blood flow mediated by the enhanced neoangiogenic-revascularization of the ischaemic burns [20], which was consistently evident in H patients, and at earlier times in H than in C, as also reported in previous studies.

## Conclusions

Clearly, in similarly treated equal numbers of statistically similar children patients with similar burns, the addition of heparin administered only topically in the initial week significantly reduced the amount of IV fluids ($p<0.04$), days in hospital ($p<0.0001$), and the time before healing ($p<0.0006$) in patients treated with heparin compared with a control group of patients not treated with heparin. Equally clearly, patients treated with heparin suffered less pain and required less pain medicine and fewer antibiotics, dressings, and procedures; costs were also lower than in the control cohorts. The lower mortality and the fewer grafts in heparin-treated patients than in non-heparin-treated patients observed in this study were not clearly found to be heparin-related. Further studies are planned.

### References

1. Saliba MJ Jr (2001) Heparin in the treatment of burns: A review. Burns 27: 349-358.
2. Reyes AE, Astiazaran JA, Chavez CC, Jaramilla F, Saliba MJ (2001) Burns treated with and without heparin: Controlled use in a thermal disaster. Annals of Burns and Fire Disasters 14: 183-191.
3. Saliba MJ Jr (1997) The effects and uses of heparin in the care of burns that improves treatment and enhances the quality of life. Acta Chir Plast 39: 13-16
4. Ramakrishnan KM (2002) Recent concepts in burn wound healing. National CME in Burns and Plastic Surgery, 2002, Session on Burns, Kanchi Kamakoti Child Trust Hospital, Chennai, India. Sponsored by National Academy of Medical Sciences (India), New Delhi.
5. Saliba MJ (2002) The role of heparin in the management of burns. National CME in Burns and Plastic Surgery, 2002, Session on Burns, March 2002, Kanchi Kamakoti Child Trust Hospital, Chennai, India. Sponsored by National Academy of Medical Sciences (India), New Delhi 1: 5-12.
6. Babu M (2002) Pharmacological modulation of burn wound healing. National CME in Burns and Plastic Surgery, 2002, Session on Burns, March 2002, Kanchi Kamakoti Child Trust Hospital, Chennai, India. Sponsored by National Academy of Medical Sciences (India), New Delhi 1: 13-16.
7. Presentations by Saliba MJ, Escamillo AR, Ramakrishnan KM, Jayaraman V, Zhao-fan Xia, Xu Lin Chen (2003) International Burn Conference, Shanghai and Hefei City, China.
8. Presentations by Saliba MJ, Escamillo AR, Ramakrishnan KM, Jayaraman V, Zhao-fan Xia, et al. (2004) Syllabus of Proceedings, Fifth International Heparin in Burns Symposium held during Twelfth International Society of Burn Injuries Congress, Yokohama, Japan.
9. Presentations by Saliba MJ, Escamillo AR, Ramakrishnan KM, Jayaraman V, Zhao-fan Xia, et al. (2005) Syllabus of Proceedings, Sixth International Heparin Therapy In Burns, Fifth Asian Pacific Burns Congress, Shanghai, China.
10. Troshvia K, Dimitrov R (2001) Application of heparin in the local treatment of burns. Acta Chir Plast 43: 143-144.
11. Bonilla MA, Saravia M, Zayas G (2000) Introduction of heparin treatment by parenteral and topical administration in burned children in El Salvador. Proceedings, Heparin Effects In Burns International Symposium, Las Vegas, Nevada, USA.
12. Saliba MJ, Dempsey WC, Kruggel JL (1973) Large burns in humans, treatment with heparin. JAMA 225: 261-269.
13. Saliba MJ Jr, Saliba RJ (1975) Heparin in burns: Dose-related and dose-dependent effects. Thrombos Diath Haemorrh 33: 113-123.
14. Azizkhan RG, Azizkhan JC, Zetter BR, Folkman J (1980) Mast cell heparin

stimulates migration of capillary endothelial cells in vitro. J Exp Med 152: 931-944.

15. Macaig T, Mehlman T, Friesel R, Schreiber AB (1984) Heparin binds endothelial cell growth factor, the principal endothelial cell mitogen in bovine brain. Science 225: 932-925.
16. Folkman J, Shing Y (1992) Control of angiogenesis by heparin and other sulphated polysaccharides. Adv Exp Med Biol 313: 355-364.
17. Zapat-Sirvant RL, Hansbrough JF, Greenleaf GE, Grayson LS, Wolf P ( 1994) Reduction of bacterial translocation and intestinal structural alterations by heparin in a murine burn injury model. J Trauma 36: 1-6.
18. Ehrlich HR, Griswold TR, Rajaratanam JB (1986) Studies on vascular smooth muscle cells and dermal fibroblast in collagen matrices: Effect of heparin. Exp Cell Res 164: 154-162.
19. Ferrao AV, Mason RM (1993) The effect of heparin on cell proliferation and type-I collagen synthesis by adult human dermal fibroblasts. Biochem Biophys Acta 1180: 225-230.
20. McCarthy DW, Downing MT, Brigstock DR, Luquette MH, Brown KD, et al. (1996) Production of heparin-binding epidermal growth factor-like growth factor (HB-EGF) at sites of thermal injury in paediatric patients. J Invest Dermatol 106: 49-56.