



Plastic Surgery

THE ROLE OF UNFRACTIONATED HEPARIN IN MANAGEMENT OF PARTIAL THICKNESS BURN WOUNDS

Brigadier Surajit Basu, SM

Mch (Plastic Surgery) Consultant Surgery & Reconstructive Surgery Command Hospital (Western Command), Chandimandir – 134107

ABSTRACT Burns is a preventable tragedy which is very painful to the victim especially if it happens to be superficial burns. 20 patients with bum injury were treated in a service hospital with unfractionated Heparin . There were 08 males and 12 females, with age varying between 01 and 50 years. We used Heparin in large doses both topically and parenterally in those cases with significant pain relief, reduction in resuscitation fluid requirement, early healing of wounds and reduction in total length of hospital stay.

KEYWORDS : Heparin ; Burns

INTRODUCTION

Pain and suffering in burn victims defy all description and treatment of bums is constantly evolving to improve the outcome. Heparin a commonly used anticoagulant is reported to have anti-inflammatory [1], neo-angiogenic [2] and neo-epithelialisation [3] potential by several authors. The beneficial effects of Heparin in treatment of bum patients when used topically and parenterally in large doses have been documented in several studies [4, 5, 6, 14]. Use of heparin causes significant relief of pain, reduction in requirement of resuscitation fluids, reduction of swelling and promotes bum wound healing. It is also documented that heparin causes decline in rate of bum wound infection. This study was carried out in 20 bum patients admitted in a referral service hospital to evaluate the effects of Heparin in bum casualties.

MATERIAL AND METHODS

This study is based on the experience in treating 20 patients of bums in the Bum Centre of a tertiary service hospital [Table 1]. Patients included in this study were those who had sustained burns injury involving 50% or less total body surface area and reported to this centre within 24 hours of injury. Patients were managed as per the protocol for study of use of Heparin in burns. On admission, a comprehensive history was taken with emphasis on time and type of burns, any history suggestive of inhalation bums, history of bleeding diathesis, history of medication with oral anticoagulants and associated conditions like pregnancy and systemic illnesses. A detailed examination was carried out with recording of weight ,size and depth of bums and presence of inhalation burns in the form of circumoral and nasal burns, nasal vibrissal burns and presence of soot in the oral cavity.

Patients were investigated for routine hematocrit and biochemical parameters and wound swabs, urine and blood samples were sent for bacterial culture and antibiotic sensitivity. Blood samples for PT (prothrombin time) and PTTK (partial thromboplastin time) were also taken. All investigations were repeated on Day 3, 7 and 14. Fluid resuscitation was carried out for all adults with more than 20% bums and children with more than 10% bums using the Parkland's formula. Strict monitoring of vital parameters, oxygen saturation and urinary output was done. Fluid requirement for first 24 hrs was calculated at

4ml / kg / % TBSA bums in adults and at 4ml/ kg / % TBSA burns plus an additional requirement of 100ml / kg for first 10 kg, 50 ml / kg for next 10 kg and 20ml / kg for third 10 kg in children. The fluid used was Inj Ringers' Lactate. In the second 24 hrs, Inj 5% Dextrose in water at 2ml / kg / % TBSA burns plus colloids in form of Fresh Frozen Plasma at 0.2 ml / kg / % TBSA burns was administered in adults. In children in second 24 hrs instead of Inj 5% Dextrose in water, Inj 5% Dextrose in 0.45 % saline was used. The requirement of the fluid in each case was titrated to maintain the urine output between 0.5ml – 1ml/kg/hour. Inj Morphine in a dose of 0.1 mg/Kg body weight IV was given in all cases at admission for pain relief except in case No. 5 who was pregnant and thus Inj Morphine was avoided in this case. Thereafter patients received Inj Morphine as per requirement if needed. Pain relief was graded using the Visual Analogue Scale (VAS). Inj Heparin (5000 IU/ml) was administered as IV infusion 5000 IU 6 hrly in all cases except case No 5 with pregnancy and case No 4, 8, 9, 13, 15, 16, 19 who sustained minor bums. All patients received topical Heparin in dosage of 25000 IU every 4 hrs. Topical Heparin application was done by spraying solution consisting of 5ml of Inj Heparin (5000 IU / ml) diluted in 500ml of normal saline over the entire burnt area with a syringe and also by injecting small amounts of the solution into the blisters. The burn wounds of all patients were evaluated on day 4 and those with deep bums were taken up for tangential excision. In all these cases Heparin administration was stopped from the fourth day (cases 5, 11, 12 and 14). In rest of the 16 cases both IV infusion and topical application of heparin was continued till day 7. Heparin use was monitored by clinical signs of edema, healing of wounds, and reepithelialisation . Parenteral dosage were monitored by PTTK measurements which was maintained at 1-3 times the normal value. Exposure method of wound management was carried out for first 7 days in all cases except those taken up for tangential excision. Thereafter closed dressings with Ung Silver sulphadiazine 1 % was done till the wounds healed. For each patient wounds were evaluated on day 1, 4, 14 and 21. All our patients received Inj Cefotaxime 50-100 mg/kg iv 8th hourly and Inj Gentamicin 3mg/kg /day. Rest of the patients after 7 days received antibiotics based on wound swab and blood culture sensitivity reports. All patients were followed up to study the following parameters: pain relief, resuscitation fluid requirement, bum wound healing and presence of sepsis.

Table 1 Master chart of patients treated with Heparin

| S No | Age (yrs) | Sex (M/F) | Weight (kgs) | Burn surface area (%) | Depth | Unfractionated inj heparin administration | | I/V fluid (ml) requirement estimated | | Actual I/V fluid infused (ml) | | Inj Morphine 0.1mg/kg single dose | Remarks |
|------|-----------|-----------|--------------|-----------------------|----------------------------|---|--------------------------------|--------------------------------------|-------|-------------------------------|--------|-----------------------------------|----------|
| | | | | | | I/V 5000 IU hrly day 1-7 | Topical 25000IU 4 hrly day 1-7 | Day 1 | Day 2 | Day 1 | Day 2 | | |
| 1 | 27 | F | 55 | 25% | II ^o Sup | Yes | Yes | 5500 | 3025 | 2950 | 2150 | Yes | |
| 2 | 21 | F | 50 | 25% | II ^o Sup | Yes | Yes | 5000 | 2750 | 3300 | 2200 | Yes | |
| 3 | 36 | M | 70 | 20% | II ^o Sup | Yes | Yes | 5600 | 3080 | 2000 | 2000 | Yes | |
| 4 | 20 | M | 48 | 12% | II ^o Sup | No | Yes | Started | on | oral | fluids | Yes | |
| 5 | 24 | F | 50 | 50% | II ^o Sup & Deep | No | Yes | 10000 | 5500 | 9000 | 2800 | Not given | Pregnant |
| 6 | 40 | F | 50 | 25% | II ^o Sup | Yes | Yes | 5000 | 2750 | 3000 | 2100 | Yes | |
| 7 | 43 | M | 50 | 30% | II ^o Sup | Yes | Yes | 6000 | 3300 | 3200 | 2000 | Yes | |
| 8 | 01 | F | 08 | 10% | II ^o Sup | No | Yes | Started | on | oral | fluids | Yes | |

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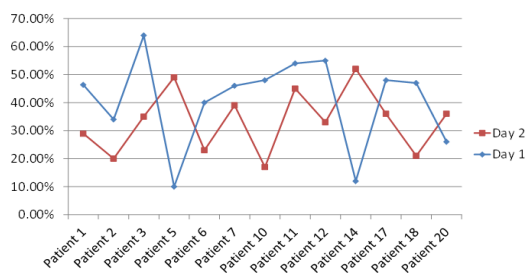
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|----|----|---|----|-----|----------------|-----|-----|---------|------|------|--------|-----|--|
| 9 | 03 | F | 18 | 9% | II° Sup | No | Yes | Started | on | oral | fluids | Yes | |
| 10 | 01 | M | 09 | 25% | II° Sup | Yes | Yes | 1800 | 495 | 936 | 410 | Yes | |
| 11 | 31 | F | 48 | 35% | II° Sup & Deep | Yes | Yes | 6720 | 3696 | 3110 | 2045 | Yes | |
| 12 | 29 | F | 52 | 35% | II° Sup & Deep | Yes | Yes | 7280 | 4004 | 3300 | 2700 | Yes | |
| 13 | 50 | M | 68 | 5% | II° Sup | No | Yes | Started | on | oral | fluids | Yes | |
| 14 | 45 | F | 48 | 45% | II° Deep | Yes | Yes | 8640 | 4752 | 7600 | 2300 | Yes | |
| 15 | 02 | M | 11 | 10% | II° Sup | No | Yes | Started | on | oral | fluids | Yes | |
| 16 | 15 | F | 32 | 15% | II° Sup | No | Yes | Started | on | oral | fluids | Yes | |
| 17 | 30 | M | 45 | 30% | II° Sup | Yes | Yes | 5400 | 2970 | 2800 | 1900 | Yes | |
| 18 | 18 | M | 40 | 25% | II° Sup& Deep | Yes | Yes | 4000 | 2200 | 2100 | 1720 | Yes | |
| 19 | 06 | F | 22 | 12% | II° Sup | No | Yes | Started | on | oral | fluids | Yes | |
| 20 | 15 | F | 30 | 25% | II° Sup | Yes | Yes | 3000 | 1650 | 2200 | 1050 | Yes | |

Table 2 Results of burn patients treated with heparin

| S No | Age (Yrs) | Sex (M/F) | Weight (kgs) | Burn surface area (%) | Depth | Percent reduction in resuscitation fluid requirement | | Pain relief by VAS | Wound healing time (days) |
|------|-----------|-----------|--------------|-----------------------|----------------|--|--------|--------------------|--|
| | | | | | | Day 1 | Day 2 | | |
| 1 | 27 | F | 55 | 25% | II° Sup | 46.36% | 28.92% | 0 | Epithelisation in 14 days |
| 2 | 21 | F | 50 | 25% | II° Sup | 34% | 20% | 0 | Epithelisation in 16 days |
| 3 | 36 | M | 70 | 20% | II° Sup | 64% | 35% | 0 | Epithelisation in 14 days |
| 4 | 20 | M | 48 | 12% | II° Sup | On oral fluids | | 0 | Epithelisation in 14 days |
| 5 | 24 | F | 50 | 50% | II° Sup & Deep | 10% | 49% | 5 | Tangential excision done and wound healed in 24 days |
| 6 | 40 | F | 50 | 25% | II° Sup | 40% | 23% | 0 | Epithelisation in 16 days |
| 7 | 43 | M | 50 | 30% | II° Sup | 46% | 39% | 0 | Epithelisation in 15 days |
| 8 | 01 | F | 08 | 10% | II° Sup | On oral fluids | | 0 | Epithelisation in 07 days |
| 9 | 03 | F | 18 | 9% | II° Sup | On oral fluids | | 0 | Epithelisation in 10 days |
| 10 | 01 | M | 09 | 25% | II° Sup | 48% | 17% | 0 | Epithelisation in 14 days |
| 11 | 31 | F | 48 | 35% | II° Sup & Deep | 54% | 45% | 0 | Tangential excision done and wound healed in 18 days |
| 12 | 29 | F | 52 | 35% | II° Sup & Deep | 55% | 33% | 0 | Tangential excision done and wound healed in 14 days |
| 13 | 50 | M | 68 | 5% | II° Sup | On oral fluids | | 0 | Epithelisation in 10 days |
| 14 | 45 | F | 48 | 45% | II° Deep | 12% | 52% | 0 | Tangential excision done and wound healed in 24 days |
| 15 | 02 | M | 11 | 10% | II° Sup | On oral fluids | | 0 | Epithelisation in 06 days |
| 16 | 15 | F | 32 | 15% | II° Sup | On oral fluids | | 0 | Epithelisation in 12days |
| 17 | 30 | M | 45 | 30% | II° Sup | 48% | 36% | 0 | Epithelisation in 14 days |
| 18 | 18 | M | 40 | 25% | II° Sup& Deep | 47% | 21% | 0 | Epithelisation in 14 days |
| 19 | 06 | F | 22 | 12% | II° Sup | On oral fluids | | 0 | Epithelisation in 09 days |
| 20 | 15 | F | 30 | 25% | II° Sup | 26% | 36% | 0 | Epithelisation in 14 days |

**CHART 1
PERCENT REDUCTION IN REQUIREMENT OF RESUSCITATION FLUIDS IN PATIENTS TREATED WITH HEPARIN**



RESULTS

We managed 20 patients with second degree burns including 8 males and 12 females. Age of these patients ranged from 01 yr to 50 yrs and size of burns wound varied from 5% to 50% TBSA. Case No.5 was found to have twin gestation of 18 wks duration on admission. During the course of Heparin therapy none of our patients suffered from any bleeding episode. The results of the study are summarized in **Table 2**. All 20 patients were evaluated for the following parameters:

1. Pain relief: A single dose of injection morphine given to each patient except case No 5 who was pregnant on admission provided adequate pain relief in all cases and in no case repeat administration of injection morphine was necessary during their stay in the hospital. Subjectively the extent of pain relief was graded to be excellent by self assessment in every case [Fig 1].

2. Resuscitation fluid requirement: All adult patients with more than 20% burns and children with more than 10% were resuscitated with IV fluids during the first 48 hrs. The fluid requirement for resuscitation was calculated as per the Parkland formula. In the 13 cases who underwent fluid resuscitation it was found that there was a significant reduction in actual requirement of resuscitation fluid compared to the estimated fluid volume requirement in both first and second 24 hours. A 10% to 64% reduction in resuscitation fluid volume requirement was seen for the first 24 hrs and 17% to 52% reduction in fluid requirement in the second 24 hrs. (**Chart 1**).

3. Burn wound: Burn wounds in all cases were evaluated on Day 1, 4, 14, 21 for amount of soakage, edema, epithelization, healing and presence of infection. In all our cases considerable reduction in soakage from wound, tissue swelling and edema was seen by Day 4 [Fig 2]. After evaluation on Day 4, 4 cases underwent tangential excision for their deep burns. In these patients the wounds healed after 18 to 24 days [Fig 3]. In rest of 16 cases in whom heparin administration was continued till Day 7 early healing of wounds was observed and in them the time taken for healing varied from 6 to 16 days [Fig 4].

4. Sepsis: Wound swab and blood cultures were carried out for all cases on Day 1, 3, 7, 14. In all cases the wound swab & blood culture reports were negative. Clinically also none of the patients showed evidence of burn wound sepsis or septicemia.

DISCUSSION

During the last two decades, great strides have been made in treatment of burns with a view to alleviate pain and suffering. Several studies have demonstrated the beneficial effects of commonly available anticoagulant Unfractionated Heparin in large doses both topically and

parenterally in treatment of burns. It is known to cause significant relief of pain, reduction in requirement of resuscitation fluids, reduction in local swelling, promote neoangiogenesis, repithelisation and early burn wound healing [4, 5, 6, 7, 14]. At molecular level, several studies have demonstrated the anti histaminic and anti inflammatory properties of Heparin [1]. Heparin also promotes neoangiogenesis as demonstrated by several studies [2]. In the present study we found that all our patients had significant pain relief. It is interesting to note that **the pain relief** was significant irrespective of **the burn size**. Other authors have also reported similar findings [8]. In our series, we found that there was a reduction in actual requirement of resuscitation fluid as compared to the estimated fluid volume in both first and second 24 hours which compared very well with other studies [4, 5, 6, 7, 8].

Heparin was administered both parenterally and topically for 4 days to all our patients. A marked reduction in soakage from the wound, swelling and oedema were noted in all cases. Four of our cases were found to have deep burns when evaluated on the 4th day and they were subjected to tangential excision. Burn wounds healed faster in those patients in whom Heparin was administered till Day 7. Reduced healing time in burns with Heparin therapy has been reported by other authors [7, 8, 14]. An interesting feature of our study was that none of our patients showed any evidence of burn wound infection or sepsis. The burn wound swab and blood cultures were found to be negative in all patients under study. Fewer infections with Heparin therapy have been reported by other authors [5, 6]. None of our patients suffered from any bleeding episode which compares favourably with studies carried out by Saliba et al [7, 9, 14].

CONCLUSION

We conclude that use of Heparin in large doses both topically and parenterally facilitates the management of partial thickness burns by causing reduction in resuscitation fluid requirement, significant pain relief, reduction of edema, swelling, and promotes faster healing.

Fig 1 Photograph of Case 9 showing the child smiling on day 2 free of pain



Fig2 Photograph of Case 8 showing significant reduction in local swelling, oedema and soakage at day 4 with use of heparin DAY 1



DAY 4



Fig 3 Photograph of Case 11 who underwent tangential excision of burns wound and split skin grafting on day 18



Fig 4 Photograph of Case 4 showing complete epithelisation by day 14 DAY 1



DAY 14



REFERENCES

- Marcos Guilherme Praxedes Barretto, Maria da Graça Nascimento Figueira Costa, Maria Cristina do Valle Freitas Serra et al. Comparative study of conventional and topical heparin treatments for burns analgesia. Rev Assoc Med Bras 2010; 56(1): 51-5.
- Tyrell DJ, Horne AP, Preuss JMH, et al. Heparin in inflammation: potential therapeutic applications beyond anticoagulation. Adv Pharmacol 1999;46:151-208.
- Azizkhan R.G., Azizkhan J.C., Zetter B.R., Folkman J.: Mast cell heparin stimulates migration of capillary endothelial cells in vitro. J. Exp. Med., 152:931-44, 1980.
- Folkman J., Shing Y.: Control of angiogenesis by heparin and other sulfated polysaccharides. Advances in Experimental Medicine and Biology, 313: 355-64, 1992.
- Macaig T. et al.: Heparin binds endothelial cell growth factor, the principal endothelial cell mitogen in bovine brain. Science, 225: 932, 1984.
- Saliba M.J., jr: Heparin in the treatment of burns. JAMA, 200: 650, 1967.
- Saliba M.J., jr, Griner L.A.: Heparin efficacy in burns. I. Significant early modification of experimental third degree guinea pig thermal burn. Aerospace Med, 41: 179-87, 1970.
- Saliba M.J., jr: Heparin efficacy in burns. II. Human thermal burn treatment with large doses of topical and parenteral heparin. Aerospace Medicine, 41: 1302-6, 1970.
- Saliba M.J., jr, Dempsey W.C., Kruggel J.L.: Large burns in humans, treatment with heparin. JAMA, 225: 261-9, 1973.
- Saliba M.J., jr: Heparin, nature's own burn remedy? Emergency Medicine Medicine, 106: 111, 1973.
- Saliba M.J., jr, Saliba J.R.: Heparin in burns: dose related and dose dependent effects. Thrombos. Diasthes. Haemorrh. (Stuttg), 33: 113-23, 1974.
- Mangus D.J., Falces E., Gilchrist D.R.: Heparinization and the use of culture-specific antibiotic liquids in the treatment of large burns. In: Proceedings, Reference 8, p. 127 + 19 p. Suppl.
- Saliba M.J., jr: Heparin in the treatment of burns: a review. Burns, 27: 349-58, 2001.
- Venakatachalapathy T.S., Mohan Kumar S., Saliba M.J.: A comparative study of burns treated with topical Heparin and without Heparin. Ann Burns Fire Disasters, Dec 31, 2007; 20(4): 189-198