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Case Series

Heparin - hidden pillar in the management of burns

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ABSTRACT

Heparin has been used to treat burns for decades, but due to the lack of well-controlled clinical trials, this indication is little widespread and the calculation of dosage and application method becomes unclear. Its action on the burn is probably derived from its anti-inflammatory and angiogenic properties that do not depend on its known anticoagulant action, at the endothelial level, it reduces blood hyperviscosity, leukocyte count and acute phase reactants, and also reduces the need for escharotomies, fasciotomies and grafts. In the present study we confirmed that the use of topical heparin reduces healing time, epithelialization, as well as local discomfort, it can be used in second level hospitals not specialized in burns due to its easy systemic and topical application, being safe, which showed few complications despite being administered at high doses.

Keywords: Heparin, Burns

INTRODUCTION

The management of the burned patient has traditionally been used in second level hospital centers not specialized in burns, it consists of prophylaxis against infections, sequential debridement inside and outside the operation room, rehabilitation and management of skin loss. The patients most affected by burns are young patients, especially children, young people, mostly of reproductive age; with current treatments, thermal injuries continue to cause pain and significant consequences in healing, which is why it is necessary to find and use the treatment that reduces local discomfort, as well as having systemic effects and favoring the healing. Our research shows that heparin is a natural biochemical substance found in the body of humans and animals. It is a long chain compound of two highly sulfonated sugars. This highly reactive and acidic body substance is classified as glycosaminoglycan. It was first extracted from the liver (the hepatic organ) in 1916, isolated in pure form in 1935, and has since been used primarily as an anticoagulant medication.[1]

Since 1960, Saliba, his collaborators and other researchers have discovered and used other effects of heparin in studies with and without burns and in burn patients. Heparin is now known to have additional effects. The known effects of heparin are a therapeutic complement to the known pathology of burns. Research studies and clinical trials have validated that assumption. Glycosaminoglycans (GAGs) are a physiologically reactive class of highly acidic, negatively charged, structurally and functionally similar polysaccharides. They are long-chain compounds composed of repeating disaccharide units that have one carboxyl group and one or more sulfates, in which one sugar is N-acetylgalactosamine or N-acetylglucosamine. Endogenous GAGs are heparin, heparan sulfate, keratin sulfate, dermatan sulfate, chondroitin-4 sulfate, chondroitin-6

sulfate, and hyaluronic acid. Heparin is the most sulfated and acidic, Heparin is a highly sulfated polysaccharide composed of hexuronic acid and D-glucosamine residues linked by glycosidic bonds.[2]

Heparin has been used to treat burns for decades but due to the lack of well-controlled in clinical trials, this indication is little disseminated and the calculation of doses and method of treatment becomes unclear application. Its action on the burn is probably derived from its anti-inflammatory and angiogenic properties that do not depend on its known anticoagulant action. The anti-inflammatory action results from the deactivation of proinflammatory cytokines such as tumor necrosis factor (TNF)-alpha, selectins secreted by leukocytes such as CD11b, integrins such as ICAM-1 and the attenuation of complement activation. The angiogenic effect derives from the interaction with vascular endothelial growth factor (VEGF) and fibroblast growth factors. blood hyper viscosity, leukocyte count and acute phase reactants, and also reduces the need for escharotomies, fasciotomies and grafts. It is known that this medication helps reestablish the metabolic response associated with thermal trauma by inhibiting complement esterase C1, reducing oxygen free radicals and producing antagonism to histamine, bradykinin and prostaglandin E1.[3] In Ghana, the use of heparin for the treatment of burns has become popular, as reported in the original article by Agbenorku et al published in 2013. Although many burn studies, both in humans and animals, were reported to have tested large doses of heparin topical and parenteral producing significant therapeutic results, the intensive care units (ICUs) in Ghana had not been able to use it. Findings in heparin treatment included: pain relief, improved healing, and smooth skin. Less resuscitation fluids, fewer pulmonary and intestinal complications, and fewer infections were reported. These burn studies and additional ones revealed, and other non-burn studies confirmed, that heparin had anti-inflammatory, neo angiogenic, collagen-restoring, and epithelializing effects in addition to its anticoagulant effects.[3]

CASE SERIES

A prospective, descriptive and cross-sectional study was taken as a primary database; the universe was all patients with thermal trauma who arrived at the emergency department of the General Hospital of Queretaro.

The sample size was dependent on the number of thermal trauma cases that attended the emergency department during the study period and was 28 patients. Observation units were defined as patients who were admitted to the emergency department with a diagnosis of thermal trauma and who presented criteria for in-hospital management.

Precautions on the use of heparin: big doses (>50,000 IU/day) were not used after the 3rd day of the burn; it was never injected under burned, wounded or bleeding tissue; parenteral administration of heparin was withdrawn after 24 hours, before performing any surgical procedure.

Preparation of heparin for topical use

A standard 10 ml syringe was filled. With 5000 IU/ml heparin and sprayed on the burned surface with a #30 needle until it was completely covered, this procedure was performed 5 times a day with a time interval of 5 hours after bathing in the shower. Topical treatment was only applied to the bloody areas and the duration in days of the treatment was given based on the epithelialization of the wounds and was suspended when this was completed. The amount of heparin used by this route did not enter into the calculation of parenteral heparin, since it lacks absorption and its only effect is at a local level. Calculation of heparin for parenteral administration: The formula to calculate the parenteral dose is as follows: 400 IU of heparin multiplied by the patient's weight in kg, multiplied by the percentage of body surface burned (2nd and 3rd degree) and divided by 15.

$$Total\ parenteral\ dose = 400\ IU \times Weight\ (kg) \times \%SC$$

Figure 1: 22-year-old male with 40% total body surface area burned on (a) and (b) 9 day of hospital stay and (c) and (d) 45 days post-burn with the use of heparin.

Only in the first three days, 40% of the total heparin was administered subcutaneously and the rest intravenously divided into three doses, one every 8 hours. Coagulation times were always maintained in ranges no more than 2 to 3 times above the normal value. After the third day of the burn, the intravenous route was suspended to continue with the subcutaneous and topical route, determining the doses based on clotting times.

Patients diagnosed and registered with thermal trauma were subject to the following inclusion criteria to

participate in our study: second degree deep burns affecting 15% in adults, third degree burns of any extent, burns in special areas (hand, feet, genitals, flexural folds), and socioeconomic incompetence for outpatient management.

The exclusion criteria were: patients with non-recent thermal trauma, patients with coagulation disorders, patients on anticoagulant treatment, patients with allergy to heparin, patients with active bleeding, and patients with suspected perforated peptic ulcers.

Figure 2: 54-year-old male with 20% total body surface area burned on (a) and (b) 5 day of hospital stay and (c) and (d) 42 post-burn with the use of heparin.

28 patients with a diagnosis of burn classified with criteria that warranted in-hospital management were studied, 17 men (60%) and 11 women (39%) were treated, the age ranges were: less than 18 years old, 1 (3.5%), from 19 to 28 years old, 11 (39%), from 29 to 38, 8 (28.5%) from 39 to 49 years old, 5 (17%) from 50 or more 3 (10.71%) (Figure 1). The most frequent etiology of thermal trauma found in descending order was: scald in 12 (42.5%) patients, direct fire in 8 (28.5%) patients, electrical burn in 5 (17.85%) and burns. mixed in 3 (10.81%) patients, in the latter they included electrical in combination with the other two main causes. Regarding severity based on the affected body surface, patients were classified as mild in 1 (3.57%) cases, moderate in 11 (39.5%) and severe in 10 (35.71%) and critical in 6 (21.42%) patients. Subsequent to the calculation of the burned body surface and the resuscitation measures, the administration of heparin was initiated; an analysis of the amount administered to the patient was performed, finding that 3 (10.71%) patients required up to 29,0000 IU, 10 (35.71%) patients from 30,000 to 39,000 IU, 9 patients (32.1%) from 40,000 to 49,000 IU and in 5 patients (17.81%) more than 50,000 IU were administered (Figure 2). Regarding the estimation of pain evaluated with the visual analogue scale (VAS), it was found that 12 (42%) patients were located in intensity numbers 4 and 5, that is, almost half of the patients had adequate pain control, 9 (32.4%) patients placed the symptom between numbers 6 to 8, having poor pain control, and 7 (25%) patients reported it in numbers 1 to 3, having excellent pain control. pain control, no patient had numbers 9 and 10 with poor pain control. Only one patient presented complications and it was due to bleeding which was reversed by suspending the administration of heparin and performing hemostasis through compression. In 2 patients (7.14%) the clotting times were prolonged more than 3 times the nasal time, there were 3 (10.71%) who presented infection in the burned area. There was no mortality in the patients included in the study. Intrahospitalary stay: 11 (39%.28) patients remained hospitalized from 6 to 10 days, 8 (28.5%) patients remained hospitalized from 11 to 15 days, 3 (10.71%) patients stayed for 16 to 20 days. 3 patients (10.71%) from 1 to 5 days and 3 (10.71%) patients with more than 20 days of hospital stay.

DISCUSSION

Current treatment of second- and third-degree burns is complex, uncomfortable for the patient, and costly for health systems. The consequences of burns affect the quality of life and produce emotional and social impacts on patients. Multidisciplinary participation by general surgeons, intensive care physicians, plastic and reconstructive surgeons is important, since various interventions may be necessary.

Heparin and its hidden pillar in the management of burn patients could change this situation. It is worth mentioning that not all hospitals are equipped to treat patients with thermal trauma, so this treatment could be started in any second level hospital. In 2014, in Tijuana, Mexico, Escamilla et al, treated 31 burn patients who received intravenous, subcutaneous and topical heparin, their work was published as the first report on electrical burns and their effects in Mexico, in conjunction with the La Jolla Burn Institute of San Diego and the General Hospital of Tijuana, in which the results showed the favorable effect that heparin has on second degree burns as an analgesic and reducer of erythema and the inflammatory phenomenon in its entirety. In addition to promoting healing and reducing microthrombi, the average hospital stay was 18.6 days, which resulted in a decrease in infection, resulting in smoother, scar-free, and significantly fewer contractures.[4]

In our present study, the results are encouraging: systemic and topical application of heparin is easy to use, safe when used at the recommended doses, and showed few complications despite being administered at high doses. Good pain control was achieved, as well as adequate healing at 45 days, a low infection rate, and we observed a short hospital stay, on average 6 days in our patients. Heparin is affordable and can be economically advantageous for the health system and more convenient

for the patient. Finally, due to the characteristics of the topical and intravenous heparin treatment system (simplicity and convenience), its incorporation into the routine of secondary level hospitals and burn centers could be advantageous for the patient.[5]

CONCLUSION

This publication demonstrates how easy the systemic and topical application of heparin is, being safe in recommended doses, which showed few complications despite being administered at high doses. Low molecular weight heparin could become a key pillar in the management of burns, since the current management of these injuries is usually painful for the patient, and costly for institutions. This drug has shown to have promising results, being easy to access, a simple method of application and with excellent results in favor of the prognosis of the burn patient.

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