**TREATMENT OF PARTIAL THICKNESS BURNS WITH ZN-HYALURONAN: LESSONS OF A CLINICAL PILOT STUDY**

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**SUMMARY.** A clinical investigation to determine the effectiveness of Zn-hyaluronan gel for the treatment of partial thickness burns was carried out. 60 patients were enrolled in the study with an average of 3% TBSA burn. Exudation lasted 3 days, no infectious complications were observed. By day 14 the wounds of 52 patients have healed, average complete healing time was 10.5 days. An overall 93.3% healing rate was achieved within the planned observation period. Reduction of spontaneous and movement-related pain was reduced to less than half of the initial values by day 5.5 and 6.3 respectively. Development of a thin, elastic, well tolerable and protective membrane-like layer was noted. This kept the wounds moist while clean during wound-healing, and was spontaneously shed as epithelisation proceeded. Zn-hyaluronan gel is a novel topical wound care product that has proven to be suitable for the treatment of partial thickness burns.

**Keywords:** partial thickness burn, zinc, hyaluronic acid, conservative treatment, multi-center prospective clinical trial

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*Curiosa®* gel (Richter Gedeon Ltd. Budapest, Hungary) is available as a medical device since 2004 for the treatment of inflammatory conditions as acne vulgaris, minor abrasions and chronic wounds (3, 4). Its hyaluronan content is derived from natural cockscomb. Besides Hungary, it is available in different markets under various trade names: Cicactiv Uleugel®, Curiosin®, Face-It®, Hyaluzinc® for the treatment of acute and chronic wounds (5, 6).

In order to document the previously described, bene-
ficial effect of Znhyg in the treatment of burns, an open label, prospective multi-center pilot study (67561/HU, 2008-2009) was conducted involving 3 Hungarian burn departments. Primary goal of the study was limited to the acquisition of information about the effect of Znhyg on burn wound healing in adult patients.

**Materials and methods**

Patients (N=60) who had predominantly superficial second degree burns, occasionally mixed with first and deep second degree burns (1—2A—2B), were enrolled as volunteers into the study. These patients were judged upon enrollment as expectedly requiring no surgery for healing. Goals of the study were to closely monitor the changes in the wound condition, together with therapeutic outcomes of Znhyg topical application, and to judge the easy and

![Graph showing reduction in wound size over time](image)

**Fig. 1** - Reduction in the wounds’ size over time. Wound size on a given day is expressed as a percentage of initial wound size, and mean values calculated. All but 4 patients’ wound area was reduced to 0 by day 21. Average healing time of patients treated with **Cu- riosa® gel**, was 10.5 days (n=56).

![Images of wound healing process](images)

**Fig. 2** - 19 year old male, scald injury caused by hot water, affecting 10% body surface (only a portion of the original wound is shown). (a) On day 0 blisters and semibullous areas are present. (b) These transform into a painless, well tolerable elastic membrane-like layer by day 3. (c) Membrane peels off mostly by day 7. (d) No detectable trace of the injury is seen 180 days post burn.
safe use of the product as well as patients’ compliance. There was no control group assigned to this study. From the anticipated results, effectiveness of Znhyg therapy in partial thickness burn wounds could be determined. Znhyg was applied once daily in a thin layer either as open treatment (face, genitals) or under vaseline-impregnated gauze + cotton gauze multi-layer bandaging (torso and extremities). Wound dressing changes were performed until full epithelisation or a maximum of 21 days. Based on clinical experience, burns not requiring surgical therapy to heal, will do so within 3 weeks. Burn wounds not being able to re-epithelize with conservative treatment in 3 weeks will require surgical excision and grafting mostly with autologous split thickness skin. Cosmetic outcome and scar quality were recorded on follow up at 1, 3 and 6 months after healing.

Parameters of wound healing recorded at evaluation intervals included extent of wound area, wound base quality, parameters of surrounding skin and treatment related pain. Collected data was statistically analyzed with SAS for Windows 8.2 program. Healing times were subjected to survival analysis and Kaplan-Meier diagrams were generated. Changes of the burn wound parameters, treatment tolerability, and ease of use were all recorded. Global judgment of both therapist and patient about safety and effectivity of therapy were compared and evaluated. Possible complications and serious adverse events were monitored as well.

**Results**

In the study population hot water scalds (n=28/60) were the dominant cause of burn injury; other causes included hot oil (n=11), flame (n=11), contact (n=5), and other types of burns (n=5). Wound size was 3% TBSA on average, in 21 cases skin over joints was also involved. Burns were seen on all body parts; in 13 cases burns were noted in more than one area. The first two observations were carried out at standard time-points, while further evaluations were timed individually (at 3-4 day intervals). Re-epithelisation was assessed by mechanical (grid) planimetry and its progress was calculated by linear interpolation. End of observations were determined according to wound healing; there was obvious variability in their timing.

Minimal wound exudation was observed the first 3.03 days (median 1 day). Clinical signs of infection, evidenced temporarily by mild redness and swelling were recorded in the surrounding skin in only 2 patients (1.2%). No obvious infectious complications or adverse events, however, were observed during the whole study. Wound size was reduced to 50% of starting values by the 5th day in average. By day 14, 52 patients had their wounds healed. Burn wounds of all 56 patients healed in a mean 10.5 days. All but 4 patients had full epithelisation at day 21 as anticipated (Fig 1.) This resulted in 93.3% healing within the planned observation period. Two cases out of these 4 patients fully healed on day 24. General condition of the remaining two patients did not allow surgical intervention, and according to the decision of the investigator, further Znhyg therapy was carried out. 100% epithelisation was observed at day 29 and 58. Their case demonstrated that even when the ideal surgical intervention cannot be carried out, this therapy would result in healing of the wound.

During the study both spontaneous and movement-related burn pain was observed and evaluated on a 1-10 visual analog scale. All but two patients had some degree of pain initially. The scores very soon decreased significantly to less than half of the initial values. Spontaneous pain was observed until day 5.5 (median=4 days, interk-vartile range: 2-6.25 days). Only 8% of patients (n=5) recorded spontaneous pain after 10 days. Movement-related pain lasted until day 6.35 days on average. Only nine patients (15%) indicated pain at movement after day 10.

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**Fig. 3** - Close-up photograph of a burn wound on day 0 (a), day 6 (b) and day 10 (c) with Zn-hyaluronan therapy. Gel forms a protective membrane that peels off as epithelisation progresses.
Discussion

Both patients and health-care providers involved in the study judged the immediate soothing and pain relieving effect of Znhyg to be excellent or good. During conservative treatment of burns, the most widely used local remedy, silver-sulfadiazine ointment creates a heavy, oozing fatty layer that is difficult to tolerate. This adherent thick layer also makes proper determination of the burn depth very difficult. On the contrary, patients receiving Znhyg topical treatment developed a thin, transparent and well-tolerable membrane-like film on their wounds. Compliance during treatment with the substance was judged to be excellent. A major advantage of this treatment option is the development of a protective elastic membrane on the treated surface. This builds up as a new layer of the gel is applied on top of the previous layer each day. The membrane subsequently is shed as healing progresses over time.

Based on the effective healing process and favorable outcome, Curiosa® gel was judged as a valid and safe topical therapeutic alternative for partial thickness burns.

In summary, Znhyg therapy is suitable for effective treatment of minor burns. It is advised for topical treatment of 1° degree and superficial 2° degree burns, and even of the mixed 2°A/2°B subtype. Its use in purely deep partial thickness (2°B) burns is not recommended, since most of these wounds as well as full-thickness burns require surgical treatment.

Conclusions

For effective treatment of the burned wound, daily use of the Znhyg is suggested either with or without the use of a dressing. Wound treatment can be performed by lay personnel even at home, but due to the dynamic nature of burns, continuous medical evaluation is advised. Partial thickness wounds treated with the product are expected to heal fast and without adverse events. As a bonus, this medical device does not stain clothing, unlike other widely used antiseptic topical medications. Curiosa®, Zn-hyaluronan containing gel is a novel wound care product, suitable for the treatment of small household injuries, bruises and mild, typically superficial burns. It can be a practical component of any household medicine cabinet.

RéSUMÉ. Les Auteurs ont effectué une étude clinique dans le but de déterminer l’efficacité du gel Zn-hyaluronan dans le traitement des brulures d’épaisseur variable (60 patients ; surface brulée moyenne, 3% ; période de l’exsudation, 3 jours ; aucun cas de complications infectieuses). Ils ont obtenu la guérison des lésions de 52 patients après 14 jours (temps moyen de la guérison complète, 10,5 jours). Un pourcentage total de guérison de 93,3 a été obtenu à la conclusion de la période projetée d’observation. La douleur spontanée et la douleur provoquée par le mouvement ont manifesté une réduction à moins de la moitié des valeurs précédentes respectivement après 5,5 et 6,3 jours. On a noté le développement d’une strate mince, élastique et bien tolérée, semblable à une membrane, qui maintenait l’humidité et la propreté des lésions pendant les phases successives de la guérison. Cette strate disparaissait graduellement avec le développement de l’épithélialisation. Le gel Zn-hyaluronan est donc un nouveau produit dans le traitement topique des lésions qui s’est démontré approprié aussi dans le traitement des brulures à épaississement variable.

Mots-clés: brûlures à épaisseur variable, zinc, acide hyaluronique, traitement conservatif, épreuve clinique prospective multicentrique

BIBLIOGRAPHY


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