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THERAPEUTIC EFFICACY OF NANO BERBERINE GEL VERSUS 1% SILVER SULFADIAZINE IN PEDIATRIC THERMAL BURN INJURIES

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ABSTRACT

Objective: To evaluate the clinical efficacy, bacterial control ability, and the molecular mechanisms underlying the wound healing effects of Berberin nano gel compared with Silver Sulfadiazine 1% cream (SSD 1%) on superficial thermal burns in pediatric patients.

Methods: A prospective, controlled, within-patient (split-wound) study in 34 children with II-III degree burns treated at Le Huu Trac National Burn Hospital. Each child had two damaged zones that were equivalent: Zone A was treated with Berberine nano gel, and Zone B was treated with SSD 1%. Evaluation of complete healing time, time to 50% epithelialization, surface bacterial load (D0, D7, D14), and CHEOPS pain score.

Results: Time to complete healing was shortened with Berberine nano gel: superficial second-degree 8.26 ± 2.45 days vs. 9.71 ± 2.95 days; third-degree 14.85 ± 5.20 days vs. 18.41 ± 6.56 days ($p < 0.05$). The bacterial load was reduced in both zones over time. At D7, it was significantly lower in the Berberine nano gel group (43.22 ± 37.28 vs. 92.59 ± 81.14 CFU units; $p < 0.05$), whereas at D14 the difference was not significant. The drug was well tolerated, with a mean CHEOPS of 1.56 ± 1.56.

Conclusion: Berberine nano gel shortens wound healing time, improves early bacterial control, and is a potential alternative to 1% SSD for the treatment of superficial burns in children.

Keywords: Nano Berberine; Superficial burns in children; Antibacterial.

1. INTRODUCTION

Childhood burns remain a significant global health burden, associated with high morbidity, risk of infectious complications, scarring, and reduced quality of life. Children are particularly vulnerable; according to the World Health Organization, burns are among the leading causes of non-fatal trauma in young children [1]. Control of the bacterial load at the burn wound is key because when bacterial concentrations exceed a threshold of approximately 10 5 CFU/g tissue, wound healing can be significantly delayed [2].

In the treatment of superficial (second-degree) burns, 1% silver sulfadiazine (1% SSD) was once widely used as a topical antibacterial agent. However, a recent review of evidence suggests that the benefits of 1% SSD are limited; it may even delay epithelialization and is associated with an increased risk of infection compared with other options. Outpatient clinical guidelines also note that 1% SSD may inhibit epithelial and leukocyte proliferation and is therefore not a preferred choice for superficial burns [3].

Berberine, a natural alkaloid, exhibits broad-spectrum antibacterial, anti-inflammatory, and tissue regeneration-supporting activities. Nano-berberine/gel systems improve solubility, permeability, and wound retention, thereby increasing biological efficacy when applied topically. Several preclinical studies have shown that Berberine nano gel is safe, inhibits bacteria, and promotes wound healing in a skin-loss wound model, but comparative evidence comparing the treatment efficacy with 1% SSD in pediatric burn patients is limited [4]. To apply this preparation clinically, especially in pediatric patients, objective evidence of its efficacy and mechanism of action is needed. Therefore, this study was conducted to evaluate the level of pain and clinical efficacy in the local tissue of burn wounds in children treated with Berberine nano gel.

2. METHODS

2.1. Research objects and materials

- Patients in the research: Including 34 pediatric patients

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(under 18 years old) with superficial burns (II, III degree) due to heat (TBSA < 20%), treated at the Department of Pediatric Burn Treatment, Le Huu Trac National Burn Hospital.

- Selection criteria: Pediatric patients, superficial thermal burns, DTCT < 20%, no severe chronic diseases, and family consent to the study.

- Exclusion criteria: Patients with burns due to other causes, previous chronic/infectious diseases, or severe systemic conditions. Family members did not agree to participate in the study.

- the Pharmacy Department, Le Huu Trac National Burn Hospital, enterprise standards prepare Nano Berberin gel. Control drug: SSD Cream is produced by Hue Central Pharmaceutical Enterprise in accordance with enterprise standards.

2.2. Research methods

- Study design: Prospective, controlled study on the same patient (split-wound). Each patient had two equivalent burn zones treated in parallel: Zone A used Berberine nano gel and Zone B used 1% silver sulfadiazine (SSD 1%). The study was conducted at the Department of Pediatric Burn Treatment at Le Huu Trac National Burn Hospital from 01 to 05/2022.

- Treatment process:

- Select and measure the study zone

+ On the same patient, choose two zones of similar size and depth (each zone is about 2-5% TBSA). Depth burn is divided into 5 degrees according to Le The Trung.

+ Estimate the general TBSA using the rule of 9 (Pulaski–Tennison/Wallace), palm (Blokhin and Glumov), or 1-3-6-9-18 (Le The Trung), depending on the location of the lesion.

+ Measure the wound area (cm^2) using sterile cellophane paper with 1 cm^2 grids: draw the border immediately before applying the medication (D0), and repeat at D5–7 and D10–14 on the same sheet using a different color ink to monitor contraction/ epithelialization.

- Standard intervention and care

+ Randomization: The assignment of treatments (A or B) to the two wound zones was randomized for each patient (Drawing random lots); record zone codes for all samples/laboratories.

+ Dressing change: Standard dressings were changed once daily, or every other day if the wound was clean and dry:

++ 1. Pain relief/anesthesia according to medical protocol; absolutely sterile operation.

++ 2. Wash surrounding healthy skin with 0.9% NaCl, disinfect with 70° alcohol; wash wound with 0.9% NaCl, remove pseudomembrane/necrosis, pat dry.

++ 3. Zone A: apply gauze soaked in Berberine nano gel (approximately 4–6 g/150 cm^2 of gauze). Zone B: gauze soaked in SSD 1% equivalent amount.

++ 4. Cover with 4–6 layers of sterile gauze, bandage tightly, and press lightly to secure. When the wound is clean and dry, allow it to be semi-exposed as directed.

2.3. Monitoring and evaluation indicators:

- General characteristics of the study subjects: age, gender, and characteristics of burns.

- Time to complete healing (days) – complete re-epithelialization.

- Time to reach 50% epithelialization (based on cm^2 zone from mesh paper and clinical assessment).

- Pain when changing bandage according to CHEOPS.

- Number of bacteria/cm 2 (CFU/cm^2) of wound surface at time: D0, D7, D14.

2.4. Data processing: Using SPSS 26.0 software. Within-patient pairwise analysis; distribution test by Shapiro–Wilk. Comparison of two regions: paired t-test (or Wilcoxon if non-normal distribution); repetition over time: two-factor RM-ANOVA or linear mixed model; CHE-OPS: Wilcoxon. Two-sided significance level $p < 0.05$.

2.5 Research ethics: The study was approved by the Biomedical Research Ethics Council of Le Huu Trac National Burn Hospital, Military Medical Academy.

3. RESEARCH RESULTS

3.1. Patient characteristics

Table 1. Some attributes of pediatric burn patients

Characteristic		Number (n= 34)	Percent (%)
Gender	Male	22	64.71
	Female	12	35.29
Age group	Under 1 year old	5	14.71
	1 – 5 years old	21	61.76
	6 – 10 years old	5	14.71
	10 – 18 years old	3	8.82
Etiology of burn	Flame/Contact	4	11.76
	Scald	30	88.24
Deep burns		10	29.41
Average length of stay ($\bar{X}$ ± SD)		22.09 ± 11.82 days 6-51 days	
TBSA ($\bar{X}$ ± SD)		8.35 ± 3.82 %	3-16%

The majority of pediatric patients were male (64.71%) and suffered from scald burn (88.24%). The 1-5-year age group had the highest rate (61.76%).

Table 2. Pain score assessment according to the CHEOPS scale (n=34)

Pain level	Number (n=34)	Rate (%)
Painless (0)	12	35.29
Mild pain (1-3)	19	55.88
Moderate pain (4-6)	3	8.82
Severe pain (7-10)	0	0
Total	34	100
Average score	1.56 ± 1.56	0-6

The majority of pediatric patients (90.6%) had low pain levels (no pain to mild pain) when applying the nano Berberin gel, indicating that the drug is suitable for pediatric patients.

3.2. Clinical and antibacterial efficacy

Table 3. Treatment time (days)

Indicators		Nano Berberine gel (n= 34)	SSD (n= 34)	p
50% epithelialization time		5.91 ± 1.93	6.76 ± 2.63	> 0.05
Treatment time (days)	Degree II	8.26 ± 2.45	9.71 ± 2.95	< 0.05
	Degree III	14.85 ± 5.20	18.41 ± 6.56	< 0.05

Berberine nano gel helps shorten the time to complete healing in both second- and third-degree burns compared with SSD 1%, achieving statistical significance ($p < 0.05$). It has significant clinical relevance, helping to reduce the risk of infection, pain, and hospital stay for pediatric patients.

Table 4. Bacterial load on the burn wound surface (x5x103 CFU/cm^2)

Time	Number of bacteria		p
	Berberine nano gel	SSD	
D_0 (n=34)	50.79 ± 71.70	69.56 ± 80.48	> 0.05
D_7 (n=32)	43.22 ± 37.28	92.59 ± 81.14	< 0.05
D_{14} (n=25)	9.44 ± 14.32	19.00 ± 23.18	> 0.05

At D_0 (n=34), the average number of bacteria in the berberin nano gel zone and the SSD zone was 50.79 ± 71.70 and 69.56 ± 80.48, respectively, with no statistically significant difference ($p > 0.05$). By D_7 (n=32), the corresponding values were 43.22 ± 37.28 and 92.59 ± 81.14, with a statistically significant difference ($p < 0.05$). At D_{14} (n=25), the number of bacteria decreased in both zones (berberin nano gel 9.44 ± 14.32; SSD 19.00 ± 23.18), and there was no significant difference ($p > 0.05$).

4. DISCUSS

The study provides the first clinical evidence on the use of Berberine nano gel for the treatment of superficial burns in children, demonstrating high safety and superior treatment efficacy compared to SSD 1%. The results showed that, in the same patient, nano berberine gel shortened the time to complete wound healing in both second- and third-degree burns compared with silver sulfadiazine 1% (SSD 1%); the difference was statistically significant at both burn levels. The bacterial load on the wound surface decreased in both zones over time, but at D7, the zone where nano berberine gel was applied had a significantly lower bacterial count than SSD; by D14, the difference was no longer significant. At the same time, the pain level was low during dressing changes, and no allergic reactions were recorded. These findings align with the primary objectives of our study, which demonstrated the effectiveness of berberine nano gel in treating thermal burns in children.

Compared with the literature on the effects of 1% SSD, recent reviews and guidelines suggest that 1% SSD is no longer the preferred choice for superficial burns: The Storm-Versloot VM study concluded that the evidence does not support the use of silver preparations to promote healing or prevent infection, and that SSD may even delay epithelialization [5]. Another clinical review also found that SSD may inhibit leukocytes and epithelial proliferation, which is associated with a higher risk of scarring [6]. These researchers are consistent with our results, which show that SSD had a delayed healing time.

Bacterial loads decreased over time in both zones, reflecting the effectiveness of standardized dressing procedures, debridement, nutritional care, and uniform pain control. The leading difference at D7 suggested the advantage of earlier bacterial control with berberine nanogel; by D14, both sites had achieved similar reductions. In practice, a load threshold of approximately 10 5 CFU/g tissue is often considered indicative of impaired wound healing; therefore, early reduction of the bacterial burden may create a favorable "window" for epithelialization [2], [7].

Pharmacologically, berberine has broad-spectrum antibacterial activity, inhibits biofilm formation, exhibits anti-inflammatory effects, and modulates signaling pathways involved in wound healing. Studies on nanocarrier/liposome-in-gel systems have shown that nanoformulations increase permeability, prolong retention at the site of injury, improve control of inflammation and infection, and accelerate epithelialization, including in a Staphylococcus aureus infection model. Our observations of early bacterial reduction are consistent with the described mechanism [8], [9].

In the context of children being a group susceptible to thermal burns and at high risk of complications, the trend of limiting the use of 1% SSD for superficial burns is increasingly emphasized in practice. Our results show that the Berberine nano gel is a viable alternative in terms

of wound-healing efficacy and early bacterial control. These findings add practical evidence to the efforts to innovate herbal-based topical preparations, mainly when supported by nanocarrier systems [5], [6].

5. CONCLUDE

In this prospective, randomized, controlled study of 34 pediatric patients with second- and third-degree thermal burns, Berberine nano gel improved clinical outcomes compared with 1% silver sulfadiazine. Berberine nano gel shortened the time to complete healing: second-degree, 8.26 ± 2.45 days vs. 9.71 ± 2.95 days, and third-degree, 14.85 ± 5.20 days vs. 18.41 ± 6.56 days ($p < 0.05$). At D7, the surface bacterial load was significantly lower (43.22 ± 37.28 vs. 92.59 ± 81.14; $p < 0.05$). The gel was well tolerated, with a low mean pain score (1.56 ± 1.56).

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