Debridement method optimisation for treatment of deep dermal burns of the forearm and hand

Ernest Zacharevskij[1,2,3]

Gytis Baranauskas[2,3]

Karolis Varkalys[2,3]

Darius Kubilius[2,3]

Rytis Rimdeika[1,2,3]

[1]Department of Plastic and Reconstructive Surgery, Lithuanian University of Health Sciences Hospital Kaunas Clinics

[2]Lithuanian University of Health Sciences, Medical Academy

[3]Lithuanian Wound Management Association, www.lzga.lt

Correspondence to: ernest.zacharevskij@gmail.com

Conflicts of interest: None

ABSTRACT

Introduction

Surgical debridement of marginal deep dermal burns of the forearm and hand frequently is too aggressive to residual healthy skin. Additional operation is needed - split thickness skin grafting. Donor site complications should be taken in consideration, also transplanted skin rejection and ulceration. Therefore, clinical trials should be targeted to assess effectiveness of alternative debridement methods.

Materials and Methods

Our team performed a randomised, controlled, parallel-group clinical trial designed to compare enzymatic, mechanical, and autolytic debridement methods for the treatment of deep dermal burns of the forearm and hand. Laser Doppler Imaging (LDI) performed on the third day post-burn, was used to predict burn wound healing time. Patients who LDI predicted burn wound healing time of no more than three weeks, were included in the study. For the first (control) group received standard treatment - dressings with 1% silver sulphadiazine cream. The second patient group was treated with hydrocolloid dressings to promote autolytic debridement. The third patient group received a combination treatment - dressings with silver sulphadiazine and mechanical debridement using special single-use monofilament polyester fibre pads. The fourth group was treated with application of enzymatic dressings. The treatment period for each patient was 3 weeks, which was followed by assessment at 6 months to evaluate post-burn scars.

Results

There were 82 patients with deep dermal burns of the forearm and hand included in the trial, with a minimum of 20 patients in each treatment group. The fastest burn wound healing was observed in the patient group treated with hydrocolloid dressings. Furthermore, the quality of scars according to the Vancouver Scare Scale (VSS) and return of function of the injured extremity according to Disabilities of the Arm, Shoulder and Hand Outcome Measure (DASH) also were the best for the hydrocolloid dressings group.

Conclusion

Accelerated autolytic debridement is an effective method for treatment of deep dermal burns of the forearm and hand and hypertrophic scar prevention in patients with LDI prediction of burn wound healing of less than 3 weeks.

INTRODUCTION

There is concrete scientific evidence that nonviable, necrotic cells and tissue debris should be removed from the surface of burn wounds to promote healing, because biochemical changes in the damaged tissues may affect the process of wound healing, leading to systemic complications, which in turn, can become chronic[1,2].

Timing of debridement is also very important in burn wound management. Several clinical trials demonstrated the advantage of early debridement after 3–5 days post-burn and grafting compared to conservative management after 2–3 weeks and final skin grafting[3-6]. Early debridement could reduce the average length of stay in the hospital and even the mortality rate of burn patients[4-7].

However, surgical excision of partial thickness burns should be performed qualitatively. If the wound bed has the potential for fast epitheliali-

sation, conservative wound management can reduce the overall need for skin grafting in selected patients and the associated hospital costs[8-11].

The acceptable time limit for burn wound self-epithelialisation is approximately 3 weeks. Several scientific reviews have reported that burn wounds that took longer than 21 days to heal posed a high risk of hypertrophic scar development of nearly 80%[12,13].

Traditional treatment of burns capable of healing within 2–3 weeks, such as superficial and partial thickness burns, is to manage the burn with non-operative local wound care including debridement and dressing changes, and aggressive range of motion exercises[14,15]. Partial thickness burns can be tangentially excised and covered with a temporary skin substitute[16,17]. However, there is no strong consensus on which topical antimicrobial agent or dressing is optimal for burn wound coverage to prevent or control infection [18-20]. If wound healing cannot be achieved within 21 days, additional necrectomy and skin grafting should be performed, especially in cases of burns of the forearm, hand, and face.

Surgical debridement of burns of the forearm and hand is specific because important and delicate structures are encased within a relatively limited space in the dorsal aspect and covered by skin without a thick subcutaneous layer. The challenging shape of the hand and fingers and excellent blood supply of upper extremity tissues should also be taken into consideration[16]. Surgical debridement reduces the chance of burn wound self-epithelialisation but has a high probability of serious complications, such as massive bleeding, and microvascular and neurological damage[21]. Therefore, clinical trials should be targeted to alternative selective debridement methods for the treatment of deep dermal burns of the forearm and hand[22].

Laser Doppler Imaging

Proper initial burn treatment requires accurate burn degree evaluation and healing time prediction. Burn severity classifications are marked by characteristic changes in vasculature and blood flow[23]. A perfect instrument for burn severity evaluation is Laser Doppler Imaging (LDI), which produces a colour-coded image of dermal blood flow to quantify the inflamatory response in a burn and predict burn wound outcomes and healing times with high accuracy[23-25]. An LDI result is described by perfusion units (PU) and is defined by ranges for the three categories of healing potential (HP):

HP 14 days: colour-coded pink and red, >600 PU;
HP 14–21 days: green and yellow, 260–600 PU;
HP >21 days: blue and dark blue, <260 PU.

Several studies have compared LDI and clinical assessment to predict healing outcomes. These studies confirmed the utility of LDI for assessing burn wound depth and showed superior accuracy over clinical assessment[26-30]. The accuracy of LDI for the assessment of burn depth was 95% on the third day post-burn and 97% on the fifth day, compared to 60–80% for established clinical methods[28,30].

Materials and Methods

Our team performed a randomised, controlled, parallel-group clinical trial designed to compare enzymatic, mechanical, and autolytic debridement methods for the treatment of partial thickness deep dermal burns of the forearm and hand. The main inclusion criterion was LDI prediction[a] on the third day post-burn of no more than 3 weeks for burn wound healing *(Figure 1)*.

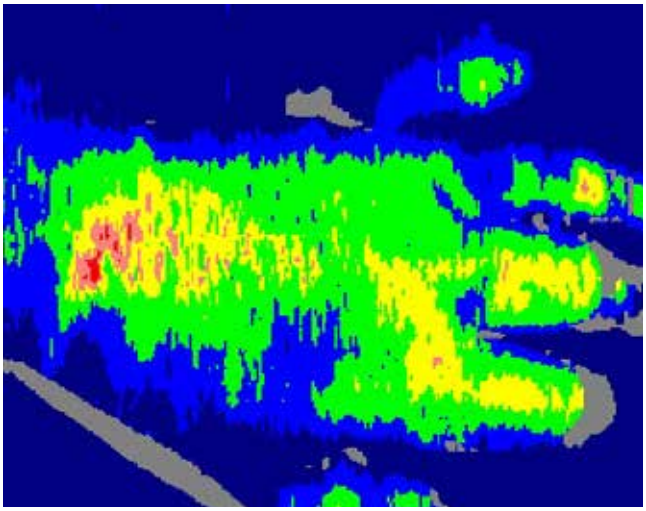

Figure 1: LDI color imaging hand on the third day post-burn, 378PU.

The study took place in the Department of Plastic and Reconstructive Surgery, Lithuanian University of Health Sciences Kaunas Clinics, Lithuania. The clinical trial was approved by the Lithuanianan Biomedical Studies Ethical Committee and Lithuanian State Data Protection Inspection. The trial was registered in the ISRCTN registry (ID: ISRCTN84005357).

There were four groups to which patients were randomly assigned. The first (control) group received standard treatment - dressings with 1% silver sulphadiazine cream[b] applied once daily.

The second patient group was treated with hydrocolloid dressings[c] changed every 3 days to promote autolytic debridement *(Figure 2-4)*.

The third patient group received a treatment combination - dressings with 1% silver sulphadiazine once daily and mechanical debridement with special single-use monofila-

Figure 2: Left hand 2B° burn, 94cm^2, 378 PU (hydrocolloid). 6 days post burn.

Figure 3: Left hand 2B° burn, 94cm^2, 378 PU (hydrocolloid) 6 days post burn.

Figure 4: Left hand 2B° burn, (hydrocolloid) 6 months post burn.

Figure 5: Mechanical debridement with single-use monofilament fiber pad: before after.

ment polyester fiber pads[d] for first 4–5 days once daily *(Figure 5)*.

The fourth group was treated with application of a proteolytic enzyme complex[e] on gauze dressings once daily.

Patients were treated for 3 weeks and assessed at 6 months to evaluate the quality of post-burn scars according to the Vancouver Scar Scale (VSS) and functional recovery according to The Disabilities of the Arm, Shoulder and Hand Outcome Measure (DASH; official Lithuanian

[i] S042 NPWT; VivanoTec, Germany

translation). The VSS data for scar appearance and DASH data for hand functionality provided a complementary objective evaluation of post-burn scars.

We included in our study patients from 18 to 65 years with deep (2°) partial thickness burns of the forearms and hands. All participants agreed to participate in the trial protocol and signed the consent form. Patients with superficial and full thickness burns (according to clinical and LDI burn wound prediction), patients with known pregnancy (pregnancy test was performed for all female patients), and vulnerable persons (psychiatric diagnosis, confounding diseases) were excluded from the study.

Finally, 82 patients were selected and randomised into four trial groups, each including a minimum of 20 patients. Patients' clinical condition and burn wounds were evaluated after 3, 7, 14 and 21 days post-burn according to the study wound assessment protocol. Burn wound size was estimated by covering the wound with transparent film and using a ruler to measure square centimetres. Pain feeling was evaluated after 10 minutes according to the pain Visual Analog Scale (VAS) after dressings were changed. Clinical wound conditions, such as exudation, erythema, fluctuation, local heat in the wound, sensibility on palpation, swelling, necrosis persistence, amount of fibrin, appearance of granulation tissue, epithelialisation process, were evaluated for all wounds by the same physician according to the study protocol measurement parameters (percentage of whole wound area). During the first evaluation, patients also were asked to complete the DASH with the researcher's assistance, because this time was closer to the incident and it was easier for patients to remember how much hand function they had before the burn accident. Swabs were taken to identify wound contamination after 3, 7, and 14 days post-burn using the Levine method[31,32].

Autolytic debridement with hydrocolloid dressings

Autolytic debridement describes the biochemical process by which the wound naturally clears necrotic tissue in the presence of endogenous phagocyte cells and proteolytic enzymes. This process is promoted and strengthened by maintaining a moist wound environment[33,34]. Autolytic debridement is the most selective compared to other methods of wound debridement[35].

Hydrocolloid dressings are used mostly to treat partial thickness and full thickness skin wounds. They consist of a moulded gel agent and a waterproof outer layer. The gel layer forms an adhesion matrix that consists of an absorbent material like pectin, gelatine, or carboxymethylcellulose[36]. The inner layer of the dressing absorbs exudate and turns into a gel. When the dressing's moisture absorption increases, it becomes more permeable to water. This feature shows the moisture transfer ability of the dressing to control exudate in the wound[37].

The most important functions of hydrocolloid dressings are the maintenance of a natural environment for wound healing, promotion of autolytic debridement, control of exudate, insulation and a barrier against microorganisms, and pain control.

Hydrocolloid dressings should be changed every 3–5 days. The dressing may be kept on a maximum of 7 days for best results[38].

However, these bandages are not suitable for highly exudative or infected wounds because they are impermeable to oxygen, which could lead to development of an anaerobic infection in the wound. In addition, the adhesive component of the dressing can be allergenic[39].

Mechanical debridement with monofilament polyester fibre pads

Special single-use pads[c] are intended for the debridement of devitalised tissue, debris, and hyperkeratosis caused by chronic and acute wounds. There is no need for analgesia, and the process takes, on average, 2–4 minutes. The product's instructions recommend that emollients be washed from the skin before treatment with this device. A new pad is required for each separate area of skin being treated and for large areas, more than one pad may be required[40,41].

There is still need for more evidence, but a number of smaller, prospective, pilot, non-comparative studies and case studies have suggested that using the debridement pad on appropriate wounds will permit full debridement more quickly, compared to other debridement methods. In addition, the pad is convenient and easy to use, and is well tolerated by patients. This product is estimated to be a cost saving for complete debridement compared to other methods such as hydrogel, gauze, and bagged larvae[40,41], although some pain responses following debridement have been reported[42].

Burn wound treatment with silver sulphadiazine leads to pseudoeschar formation, mostly during first week post-burn; thus, the combination of silver sulphadiazine with mechanical debridement can improve the ability to examine the wound surface, remove debris more quickly, and promote epithelialisation.

Enzymatic debridement

During process of enzymatic debridement proteolytic enzymes hydrolyse peptide conjoins of collagen molecules

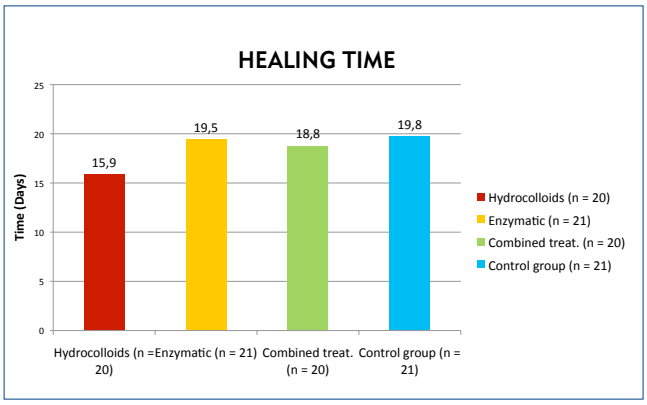

Figure 6

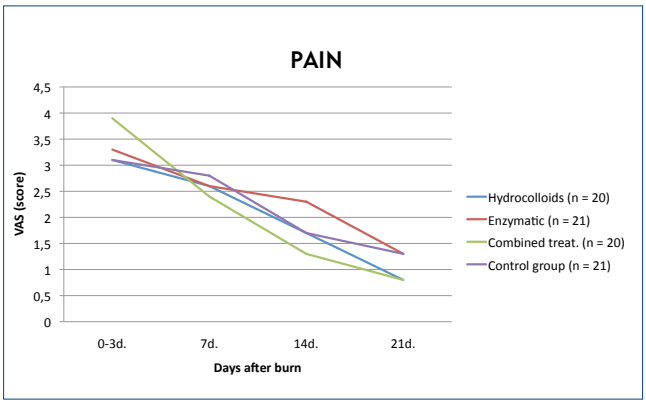

Figure 7

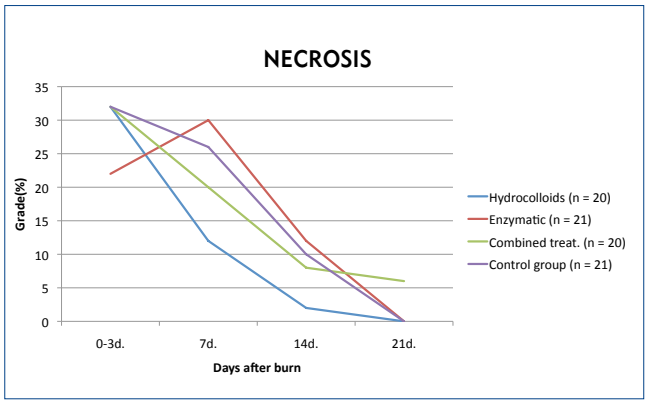

Figure 8

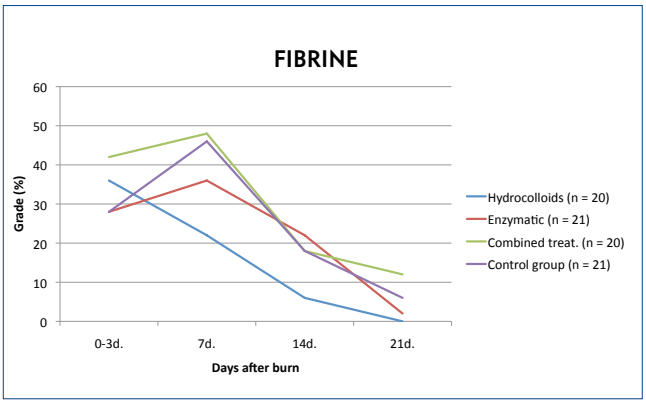

Figure 9

and other proteins; therefore, dead tissue loses attachment to the wound and is removed from the wound environment. Enzymatic debridement has a highly-selective mode of action, is quite safe for the surrounding healthy tissues, and therefore can be used in long-term care facilities and even in outpatient departments[43,44].

In our study of burn wound debridement methods, we used a local enzymatic product[e]. This proteolytic enzyme complex was applied using gauze dressings to cover the wound, and was performed once daily.

The enzyme complex is obtained from Streptomyces flavus. Characteristics of the enzyme complex included: proteolytic activity, no less than 5 u/cm^3 and collagenase activity, no less than 1500 u/cm^3. The preparation was stabilised with glycerine (ratio 1:1). Streptomyces flavus is a non-pathogenic microorganism, assigned to Biosafety Risk Group I. There is no evidence of illness in humans from using this preparation[45]. Upon contact with healthy skin, the enzymatic collagenase preparation does not produce any irritation[46].

Results

We included 82 patients with deep dermal burns of the distal forearm and hand in the trial, with a minimum of 20 patients in each of the four groups to permit statistical analysis.

Patient demographics were similar between groups with respect to the patients' age, total burn wound area, spread of burn cause, burn size, LDI burn depth evaluation, and primary DASH score($p>0.05$) .

The fastest rate of burn wound healing was observed in the patient group treated with hydrocolloid dressings (n=20) 15.9 ± 2.6 days compared to the control group (n=21) 19.8 ± 2.9 days, the treatment combination group (n=20) 19.3 ± 2.5 days, and the enzymatic dressings group (n=21) 19.5 ± 2.3 days ($p<0.05$) *(Figure 6)*.

No difference was detected in pain VAS between groups at 10 minutes after the dressing change procedure during evaluations at 3, 7, 14, and 21 days post-burn [Figure 7]. Burn wound contamination was more common in the hydrocolloid dressings group, but no significant difference was found between groups and none of the patients was excluded from the study because of burn wound infection. The most common microorganism, detected by swabs, was Staphylococcus aureus (methicillin-sensitive strains). Necrotic tissue and wound debris were significantly reduced in the hydrocolloid dressings group because of the induced autolytic debridement process ($p<0.05$) *(Figure 8-9)*.

The amount of fibrin in burn wounds during evaluation after 7 days post-burn was statistically higher in the

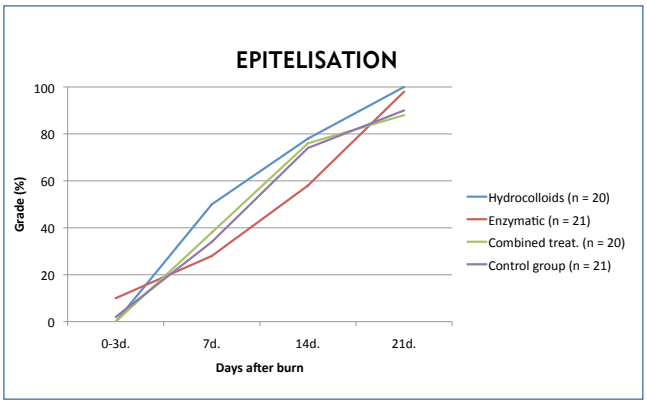

Figure 10

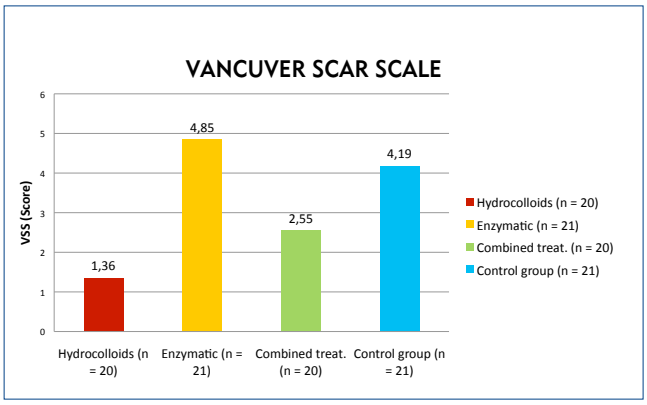

Figure 11

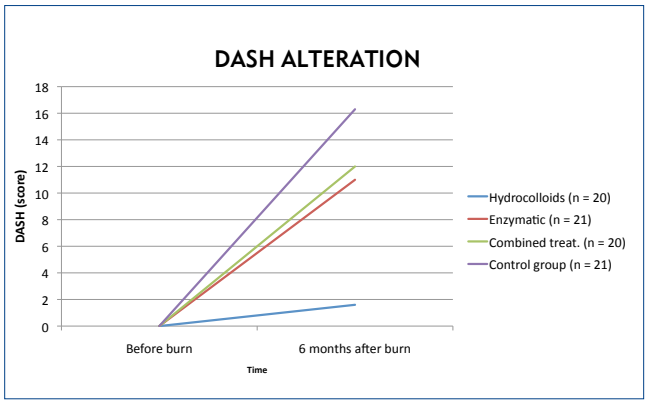

Figure 12

control and treatment combination groups, most likely due to silver sulphadiazine-induced pseudoeschar formation ($p<0.05$) *(Figure 9)*. Mechanical debridement with monofilament polyester fibre pads did not have a good fibrin layer clearance effect, as we had prognosticated in our study.

The epithelialisation process was statistically slower at 14 days for the enzymatic group ($p<0.05$); however, all wounds had healed by 21 days *(Figure 10)*.

The quality of scars evaluated at 6 months post-burn according to the VSS and extremity function according to the DASH mean scores were lowest (best scar outcome and least disability, respectively) for the hydrocolloid dressings group (1.36 and 1.6, respectively) compared to the control group (4.19 and 16.3, respectively), the treatment combination group (3.0 and 9.8, respectively), and the enzymatic dressing group (4.85 and 11.0, respectively) *(Figure 11-12)*.

The difference in means of wound healing speed and VSS between groups was statistically significant as determined by ANOVA $p<0.05$. Moderate correlations were found between fastest wound healing time and best VSS values ($R=0.51$; $p<0.01$) and fastest wound healing time and change in DASH at 6 months post-burn ($R=0.5$; $p<0.01$).

Conclusion

Comparison of enzymatic, mechanical, and autolytic debridement in our clinical trial revealed that burn wound healing was significantly faster, and scarring and limb functional recovery were better in the hydrocolloid dressing group.

Accelerated autolytic debridement with hydrocolloid dressings was the most effective method for the treatment of deep dermal burns of the distal forearm and hand and prevention of hypertrophic scarring in patients with an LDI healing prediction of less than 3 weeks.

All debridement methods we evaluated in our study had positive effect on necrosis elimination from the wound surface and promotion of burn wound epithelialisation. During ordinary burn treatment, it is useful to change debridement methods, if clinical examination shows that debridement efficacy is insufficient or even harmful for burn wound epithelialisation.

FOOTNOTES

a. All Laser Doppler images were captured with the MoorLDLS2 Laser Doppler Line Scanner (Moor Instruments, Devon, UK)

b. "Sulfargin", Grindeks AS, Riga, Latvia

c. GranuFlex®, ConvaTec, Greensboro, NC, USA

d. "Debrisoft" Lohmann&Rauscher GmbH & Co, Vienna, Austria

e. "Streptomyces flavus 197 Ferment", Biocentras, LTU, Vilnius, Lithuania

REFERENCES

1. Steed DL, Donohoe D, Webster MW, Lindsley L. Effect of extensive debridement and treatment on the healing of diabetic foot ulcers. Diabetic Ulcer Study Group. J Am Coll Surg 1996 Jul; 183(1):61–64.
2. Hansbrough JF, Zapata-Sirvent RL, Peterson VM, Bender E, Claman H, Boswick JA. Characterization of the immunosuppressive effect of burned tissue in an animal model. J Surg Res 1984 Nov; 37(5):383–393.
3. Janzekovic Z. A new concept in the early excision and immediate grafting of burns. J Trauma 1970 Dec; 10(12):1103–1108.
4. Herndon DN, Barrow RE, Rutan RL, Rutan TC, Desai MH, Abston S. A comparison of conservative versus early excision. Therapies in severely burned patients. Ann Surg 1989 May; 209(5):547–552.
5. Sorensen B, Fisker NP, Steensen JP, Kalaja E. Acute excision or exposure treatment? Scand J Plast Reconstr Surg 1984; 18:87–93
6. Maslauskas K, Rimdeika R, Saladžinskas Z, Ramanauskas T. The epidemiology and treatment of adult patients with hand burns in Kaunas University of Medicine Hospital in 1985, 1995, 2001 and 2002. Medicina 2004; 40(7):620-626.
7. Thompson P, Herndon DN, Abston S, Rutan T. Effect of early excision on patients with major thermal injury. J Trauma 1987 Feb; 27(2):205–207.
8. Palmieri TL, Greenhalgh DG. Topical treatment of pediatric patients with burns: a practical Guide. Am J Clin Dermatol 2002; 3(8):529–534.
9. Cuttle L, Naidu S, Mill J, Hoskins W, Das K, Kimble R. A retrospective cohort study of Acticoat® versus Silvazine in pediatric population. Burns 2007 Sep; 33(6):701–707.
10. Jeffrey SLA. Debridement of pediatric burns. In: Granick MS, Gamelli RL. Surgical wound healing and management. Informa Health Care, USA, 2007; 53–56.
11. VenclauskienėA, Baseviêus A, Zacharevskij E, Vaièekauskas V, Lukoševiêus S, Rimdeika R. Lazerinės doplerografijos vertêvertinat nudegimo žaizdė savaiminės epitelizacijos tikimybė Lietuvos bendrosios praktikos gydytojas; Kaunas: Vitae Litera. 2013; 17(6):374-378.
12. Davis SC, Mertz PM, Bilevich ED, Cazzaniga AL, Eaglstein WH. Early debridement of second degree burn wounds enhances the rate of reepithelialization – an animal model to evaluate burn wound therapies. J Burn Care Rehabil 1996 Nov-Dec; 17(6 Pt 1):558–561.
13. Deitch EA, Wheelahan TM, Rose MP, Clothier J, Cotter J. Hypertrophic burn scars: analysis of variables. J Trauma 1983 Oct; 23(10):895–898.
14. Samuel P Mandell, Matthew B Klein. Primary operative management of hand burns. In: UpToDate, Marc G Jeschke & Kathryn A Collins (Eds.), UpToDate; 2016.
15. Goodwin CW, Maguire MS, McManus WF, Pruitt BA Jr. Prospective study of burn wound excision of the hands. J Trauma 1983 Jun; 23(6):510-7.
16. Hyakusoku H, Orgill PD, Teot L, Pribaz JJ, Ogawa R. Color Atlas of Burn Reconstructive Surgery. ISBN: 978-3-642-05069-5. Springer-Verlag Berlin Heidelberg 2010. p. 22-25.
17. Uhlig C, Rapp M, Hartmann B, Hierlemann H, Planck H, Dittel KK. Suprathel – an innovative, resorbable skin substitute for the treatment of burn victims. Burns 2007 Mar; 33(2):221-9.
18. Mayer Tenenhaus, Hans-Oliver Rennekampff. Local treatment of burns: Topical antimicrobial agents and dressings. In: UpToDate, Marc G Jeschke & Kathryn A Collins (Eds.), UpToDate, 2016.
19. Hoogewerf CJ, Van Baar ME, Hop MJ, et al. Topical treatment for facial burns. Cochrane Database Syst Rev 2013.
20. Wasiak J, Cleland H, Campbell F, Spinks A. Dressings for superficial and partial thickness burns. Cochrane Database Syst Rev 2013.
21. Singer AJ, McClain SA, Taira BR. Rapid and selective enzymatic debridement of porcine comb-burns with bromelain derived Debrase: acute phase preservation of non-injured tissue and zone of stasis. J Burn Care Res 2010 Mar-Apr; 31(2):304–309.
22. Gong C, Lyu K, Wang G, Wang G, Zhu S, Xia Z. Debridement of burn wounds using a hydrosurgery system. Zhonghua Shao Shang Za Zhi 2015 Dec; 31(6):470-2.
23. Droog EJ, Steenbergen W, Sjoberg F. Measurement of depth of burns by laser Doppler perfusion imaging. Burns 2001 Sep; 27(6):561–8.
24. Pape SA, Baker RD, Wilson D, Hoeksema H, Jeng JC, Spence RJ, Monstrey S. Burn wound healing time assessed by laser Doppler imaging (LDI). Part 1: Derivation of a dedicated colour code for image interpretation. Burns 2012 Mar; 38(2):187-194.
25. Hoeksema H, Van de Sijpe K, Tondu T, Hamdi M, Van Landuyt K, Blondeel P et al. Accuracy of early burn depth assessment by laser Doppler imaging on different days post burn. Burns 2009 Feb; 35(1):36–45.
26. Holland AJ, Martin HC, Cass DT. Laser Doppler imaging prediction of burn wound outcome in children. Burns 2002 Feb; 28(1):11–7.
27. Jeng JC, Bridgeman A, Shivnan L, Thornton PM, Alam H, Clarke TJ et al. Laser Doppler imaging determines need for excision and grafting in advance of clinical judgment: a prospective blinded trial. Burns 2003 Nov; 29(7):665–70.
28. La Hei ER, Holland AJ, Martin HC. Laser Doppler imaging of paediatric burns: burn wound outcome can be predicted independent of clinical examination. Burns 2006 Aug; 32(5): 550–3.
29. Nguyen K, Ward D, Lam L, Holland AJ. Laser Doppler Imaging prediction of burn wound outcome in children: is it possible before 48 h? Burns 2010 Sep; 36(6):793–8.
30. Pape SA, Skouras CA, Byrne PO. An audit of the use of laser Doppler imaging (LDI) in the assessment of burns of intermediate depth. Burns 2001 May; 27(3):233–9.
31. Bonham PA. Swab cultures for diagnosing wound infections. J Wound Ostomy Continence nurs. 2009 Jul-Aug; 36(4):389-95.
32. Gardner SE, Frantz rA. Wound bioburden. In: Baranoski S, Ayello EA, editors. Wound Care Essentials Practice Principles. New York, NY: Lippincott, Williams & Wilkins; 2004, p. 91-116.
33. Dissemond J, Goos M. Optionen des Debridements in der Therapie chronischer Wunden. J Dtsch Dermatol Ges 2004; 2(9):743–751.
34. Eaglstein WH. Moist wound healing with occlusive dress¬ings: a clinical focus. Dermatol Surg 2001 Feb; 27(2):175–181.
35. Kramera A, Lademannb J, Bendera C, Sckellc A. Suit¬ability of tissue tolerable plasmas (TTP) for the management of chronic wounds. Clinical Plasma Medicine 2013.
36. Fletcher J, Moore Z, Anderson I, Matsuzaki K. Hydrocol¬loids and pressure ulcers Made Easy. Wounds International 2011; 2:1-5.
37. Kannon GA, Garrett AB. Moist wound healing with occlusive dressings. A clinical review. Dermatol Surg 1995; 21(7):583–590.
38. Ousey K, Cook L, Young T, Fowler A. Hydrocolloids in practice. Wounds UK 2012.
39. Arnold TE, Stanley JC, Fellows EP, Fellows EP, Moncada GA, Allen R et al. Prospective, multicenter study of managing lower extremity venous ulcers. Ann Vasc Surg 1994 Jul; 8(4):356–362.
40. Meads C, Lovato E, Longworth L. The Debrisoft monofilament debridement pad for use in acute or chronic wounds. Appl Health Econ Health Policy 2015 Dec; 13(6):583–594.
41. Haemmerle G, Duelli H, Abel M., Strohal R. The wound debrider: a new monofilament fibre technology. Br J Nurs 2011 Mar 24 – Apr 14; 20(6):S35-6, S38, S40-2.
42. Bahr S, Mustafi N, Hättig P, Piatkowski A, Mosti G, Reimann K et al. Clinical efficacy of a new monofilament fibre-containing wound debridement product. J Wound Care. 2011 May; 20(5):242–248.
43. Strohal R, Dissemond J, Jordan O'Brien J, Piaggesi A, Rimdeika R, Young T et al. EWMA Document: Debridement. J Wound Care 2013; 22 (Suppl. 1): S1–S52
44. Dissemond J. Modern wound dressings for the therapy of chronic wounds. Hautarzt. 2006 Oct; 57(10):881–887.
45. "Regulations for worker protection from the influence of biological agents in the", "National news" No. 56-1999, 2001.
46. Medical methodic M 2.1: 1995 "Determination methodic of acute skin irritation (erosion) for chemical agents and preparations".