Pressure ulcer: treatment

Authorship: The Brazilian Association of Physical Medicine and Rehabilitation
Final Elaboration: July 25, 2012

Participants: Talita Justino dos Santos Rosa, Lisley Keller Liidtke Cintra, Karla Barbosa de Freitas, Priscila Ferreira Dourado Laurindo de Alcântara, Fernando Spacassassi, Chenyfer Dobbins Paes da Rosa, Marta Imamura, Linamara Rizzo Battistella

DESCRIPTION OF THE EVIDENCE COLLECTION

METHODOLOGY:

We initiated the development of this guideline with the training of the authors, using the methodology employed by the Oxford Centre for Evidence Based Medicine, for the preparation of clinical guidelines for the Program Guidelines of the Brazilian Medical Association (BMA). We subsequently conducted seven meetings drafting the guideline, of these, three were conducted together with the BMA Program coordinators. We reviewed articles in the MedLine database, (via PubMed), the Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Controlled Trials (CENTRAL), through the Virtual Health Library, with no age limit. The search strategy used was based on structured questions in the P.I.C.O. format (from the initials: Patient, Intervention, Control and Outcome). The resulting search syntax for pressure ulcer was:

QUESTION 1: ((ulcer decubitus) OR (pressure ulcer)) AND ((saline hypertonic solution) OR (sodium chloride hypertonic solution) OR (saline solution))

QUESTION 2: ((ulcer decubitus) OR (bedsore) OR (bed sore) OR (pressure ulcer)) AND ((collagenase) OR (therapeutic use collagenase))

QUESTION 3: ((ulcer decubitus) OR (bedsore) OR (bed sore) OR (pressure ulcer)) AND (papain) AND (therapeutic use) OR (therapy) OR (toxicity)

QUESTION 4: ((ulcer decubitus) OR (bedsore) OR (bed sore) OR (pressure ulcers)) AND ((alginate) OR (agiderm) OR (kaltostat) OR (soybean) OR (calcium alginate) OR (coverages of calcium alginate))

QUESTION 5: ((ulcer decubitus) OR (pressure ulcer) OR (Bed sore) OR (Bed Sore)) AND ((Activated Charcoal) OR (Charcoal))

QUESTION 6: ((ulcer decubitus) OR (bedsore) OR (bed sore) OR (pressure ulcer)) AND ((Topical Negative Pressure Therapy) OR (negative-pressure dressing) OR (Negative Pressure Wound Therapy) OR (vacuum assisted closure))

QUESTION 7: ((ulcer decubitus) OR (bedsore) OR (bed sore) OR (pressure ulcer) OR (wounds)) AND ((extracorporeal shock wave therapy) OR (extracorporeal shock wave therapy)) NOT ((lepicondilits) OR (tendinopathy) OR (bone))

QUESTION 8: ((ulcer decubitus) OR (bedsore) OR (bed sore) OR (pressure ulcer)) AND ((essential fatty acids) OR (therapeutic use essential fatty acids))

QUESTION 9: (pressure ulcer) AND ((Dietary supplement) OR (nutritional supplement) OR (Dietary supplementation))

QUESTION 10: ((ulcer decubitus) OR (bedsore) OR (bed sore) OR (pressure ulcers)) AND ((hydrocolloid) OR (bandages hydrocolloid) OR (hydrocolloid dressing) OR (duoderm) OR (comfeel) OR (hydra gran) OR (replicate) OR (restore) OR (restore plus) OR (tegasorb))

QUESTION 11: ((ulcer decubitus) OR (bedsore) OR (bed sore) OR (pressure ulcers)) AND (“Debridement”)

QUESTION 12: ((ulcer decubitus) OR (bedsore) OR (bed sore) OR (Necrotic ulcer) OR (pressure ulcer) OR (Wound Healing)) AND ((hyperbaric chamber) OR (hyperbaric oxygen therapy) OR (hyperbaric oxygenations) OR (hyperbaric therapy oxygen))

For all searches we used Field: All Fields, Limits: no age limits; with the methodological filter for study types: narrow and broad. In this manner we retrieved 1,502 articles. On the basis of abstracts, we selected 109 works related to pressure ulcers and their treatment. We classified the strength of scientific evidence of these studies according to the standard of the Oxford Centre for Evidence Based Medicine. The randomized controlled trials were subjected to critical evaluation according to the Jadad scale, 1996. Finally, we selected 25 reference studies which, by their greater strength of scientific evidence, quality and clinical relevance, support the recommendations of this guideline.

QUALITY OF EVIDENCE AND STRENGTH OF RECOMMENDATIONS:

A: Experimental or observational studies of highest quality;
B: Experimental or observational studies of lower quality;
C: Case studies (uncontrolled studies);
D: Opinion with no critical evaluation, based on consensus; physiological studies, or animal models.

OBJECTIVE:
To provide information about which treatment is best indicated for pressure ulcers, according to which stage they present.

CONFLICT OF INTEREST:
The authors have no conflicts of interest to declare.

INTRODUCTION

A pressure ulcer (PU) is defined by the National Pressure Sore Advisory Panel (2007) as a localized injury to the skin and/or underlying tissue, usually over a bony prominence, as a result of pressure, or pressure in combination with shear. Prompt and effective treatment can minimize damage to the skin and speed up recovery.1

Pressure ulcers are associated with 41% of cardiovascular disease cases, 27% of neurological disease cases and 15% of orthopedic disease cases, with 62% of patients being over 70 years of age.2 The prevalence is higher in hospitalized patients and the chronically ill, who are debilitated and unable to perform essential care. Recurrent lesions result in hospital readmissions and increased medical costs.

According to the National Pressure Sore Advisory Panel Consensus Development Conference (2007), pressure ulcers can be classified as: Stage I - Intact skin, but with non-blanching hyperemia; Stage II - Partial-thickness loss of skin, reaching the dermis, presenting as a shallow open ulcer, without slough. May also present as an intact or ruptured serum-filled blister; Stage III - Full-thickness tissue loss, involving the subcutaneous layer without exposing tendon, bone or muscle. Slough may be present. Stage IV - Full-thickness tissue loss with exposed bone, tendon or muscle. Slough and/or necrotic tissue may be present in some parts of the wound bed; often includes undermining and tunneling.1 Pressure ulcers do not necessarily progress from stage I to stage IV, and do not heal from stage IV through to Stage I as the healing is generally by second intention.1

This guideline provides a comprehensive program for treatment of patients with ulcers in stages I, II, III and IV. The recommendations are intended to help professionals examine and treat patients with pressure ulcers.

1. WHEN SHOULD WE USE SALINE SOLUTION FOR PRESSURE ULCERS?
Moistened gauze with saline solution at a concentration of 0.9% applied to pressure ulcers at stage II for 35 weeks, with dressing change once per day, compared with the use of polyurethane foam showed no significant difference in the closing time of the ulcer (p = 0.817). Saline solution, when applied to the ulcer requires more frequent dressing changes than when compared to the control group (p < 0.001) (A).

The application of moist saline gauze for pressure ulcers in stages I and II for 10 weeks, with dressing change once per day, promotes complete healing of 63% of pressure ulcers, however with no significant difference when compared to the control group. (ARR = 0.93, CI 95% 0.16, 5.2) (B).

The use of saline solution for exudative pressure ulcers in stages II and III for 15 days, or until the ulcer is entirely covered with granulation tissue, with dressing change every 12 hours, promotes a 13% improvement, proving to be inferior when compared to the use of Dextranomer ointment (73%). Both showed differences greater than or equal to 25% in improvement from the beginning to the end of the study. (RR = 0.231 CI 95% -35% - 51%; RR 5% 5 - INF) (B).

Recommendation
The use of saline solution is recommended for pressure ulcers in stages II, III and IV to perform cleansing once per day, until healing is complete, as a preliminary procedure to other treatments (D).

No statistically significant changes were observed in healing when compared with other techniques and types of treatments. We do not recommend the use of saline solution as a treatment for pressure ulcers, because it proved ineffective when compared to other types of treatments (B).

2. WHEN SHOULD COLLAGENASE BE USED FOR PRESSURE ULCERS?
Application of collagenase to pressure ulcers in stage II, III and IV with necrotic tissue, with dressing change twice daily benefits tissue debridement, presenting granulation tissue in approximately four weeks, and a 50% reduction in the necrotic area. In 61.7% (37) of the cases a there was a decrease of ≥ 50% in necrotic area with the use of collagenase, versus 57.4% (35) in the placebo group (p = 0.115) (RR = 8% IC 95% -35% - 51%; RRA 0.029 IC 95% 0.133 - 0.191, NNT = 34, CI 95% 5 - INF) (A). Collagenase continuously applied to stage IV pressure ulcers on the heel, after surgical debridement for removal of necrosis, with dressing change once daily for 6 to 12 weeks promotes complete healing in 91.6% of cases. This improvement was significant when compared to the control group, which showed an improvement of only 63.6%, with an average of 14 weeks of treatment (p < 0.005) (RR 75% CI 95% -18% - 100%; ARR 0.025 IC 95% 0.059 - 0.559, NNT = 4, CI 95% 2 - INF). Collagenase treatment leads to significant cost reduction, mainly due to the short treatment period, which results in reduced costs/personnel (B).

Recommendation
Collagenase treatment is recommended for pressure ulcers in stage II, III and IV with necrotic tissue, after debridement, with dressing change once or twice daily, for 4 to 12 weeks (A).

3. WHEN SHOULD WE USE PAPAIN IN THE TREATMENT OF PRESSURE ULCERS?
The continuous application of papain to stage III and IV pressure ulcers, clean, and with granulation tissue in the ischial, sacral, malleolus, trochanteric and calcaneus regions, with dressing change once or twice daily, after surgical debridement and strict bi-hourly rotation of decubital position, promotes 13% healing and reduction of ulcer volume in 42.1% (p 0.46) of patients after six weeks, compared with a control group undergoing vacuum-assisted closure (VAC), which showed 10% complete healing, and reduction in volume of 51.8% of ulcer size (ARR = 0.033 CI 95% -0.183 - 0.249, NNT = 30, CI 95% 4 - INF) (A).

Stage IV pressure ulcers diagnosed with osteomyelitis confirmed by bone biopsy or MRI, after receiving systemic antibiotic therapy for six weeks associated with continuous papain therapy, and dressing change one to two times per day showed no significant improvement, and had increased levels of inflammation. Vacuum-assisted closure (VAC) showed a reduction in lymphocytes 6.2/hpf, in comparison to
the treatment group with papain 45.0/hpf ($p = 0.41$), and increased the formation of new capillaries 5.1/hpf, ($p = 0.75$), suggesting that VAC therapy promotes the formation of granulation tissue in pressure ulcers to a greater degree than when treated with papain, promoting healing in 66.6% of pressure ulcers with osteomyelitis ($p = 0.25$)\(^{(A)}\).

Stage IV pressure ulcers in the sacral region with irregular areas of granulation tissue, little fibrinous exudate and light serosanguinous drainage, with an initial volume of 90 ml, after applying papain for 6 weeks, with dressing change once or twice daily, showed a reduction of 14 ml in volume and an increase of granulation tissue; with a total time to complete healing of ten weeks\(^{(A)}\).

**RECOMMENDATION**

Application of papain is recommended in stage III and IV pressure ulcers with granulation tissue, little exudate, and no signs of inflammation or osteomyelitis. Dressing change should be performed twice a day for 6 to 10 weeks to increase proliferation of granulation tissue and complete healing of the pressure ulcer. Vacuum-assisted closure has shown to be more effective, but is expensive, a reason why it is not widely used in public health services in Brazil \(^{(A)}\).

There was no scientific evidence found to support the use of papain in different concentrations for use with pressure ulcers in stages III and IV, with tissue necrosis and large amounts of slough. However, this technique is widely used in nursing practice, showing satisfactory results as an aid to healing \(^{(D)}\).

4. **WHAT IS THE EFFICACY OF CALCIUM ALGINATE FOR PRESSURE ULCER TREATMENT?**

Calcium alginate combined with hydrocolloid, applied to heavily exudating pressure ulcers, with dressing change once per day for 12 weeks promotes healing of 44% ($p < 0.46$). When compared to the control group there was no significant difference (RR = 17% CI 95% -60% - 94%, ARR = 0.060 CI 95% -0.206 - 0.326, NNT = 17, CI 95% 3 - INF)\(^{(A)}\).

**RECOMMENDATION**

Application of calcium alginate combined with hydrocolloid is recommended for pressure ulcers in stage III and IV, with large amounts of exudate, once daily for 12 weeks \(^{(A)}\).

We suggest further studies to support the use of calcium alginate alone as a primary curative \(^{(D)}\).

5. **OF WHAT BENEFIT IS THE USE OF ACTIVATED CHARCOAL IN PRESSURE ULCER TREATMENT?**

The application of activated charcoal to pressure ulcers at stage II, III and IV with tissue necrosis, slough, large amounts of exudate, after debridement and cleansing with saline solution, and dressing change two or three times a week for four weeks promotes reduction of 26.9% of the surface of the ulcers. When associated with outpatient debridement, activated charcoal also promotes complete debridement of necrotic tissue and slough in 37.9% of pressure ulcers, a significant result when compared to the use of hydrocolloid (16.1%) ($p = 0.056$)\(^{(A)}\) (RR = 58% CI 95% 0% - 100% ARR = 0.218 CI 95% -0.001 - 0.437, NNT = 5, CI 95% 2 - INF) \(^{(A)}\).

**RECOMMENDATION**

Activated charcoal should be applied after outpatient debridement and cleansing with sterile saline solution, for pressure ulcers in stages II, III and IV with necrotic tissue and extensive slough, whether or not draining exudate, for a period of four weeks, with dressing change two or three times per week.

6. **WHAT IS THE EFFICACY OF VACUUM-ASSISTED CLOSURE IN PRESSURE ULCER TREATMENT?**

Vacuum-assisted closure promotes 50% reduction of the volume of stage IV ulcers in an average of two weeks when applied after surgical debridement, with continuous subatmospheric pressure of 125 mmHg and dressing change three times per week ($p = 0.001$)\(^{(A)}\) (RRR = 22%, CI 95% -209% - 100%, ARR = 0.032 CI 95% -0.299 - 0.363, NNT = 31, CI 95% -3 - INF) \(^{(B)}\).

The application of vacuum dressing promotes 50% reduction in the volume of stage III and IV pressure ulcers in the pelvic area, after surgical debridement, when treatment averages 27 days with continuous sub-atmospheric pressure of 125 mmHg, and dressing change every 2-7 days, in patients with spinal cord injury ($p = 0.9$)\(^{(B)}\).

Vacuum dressing promotes a 51.8% reduction in the volume of stage III and IV ulcers in the pelvic, malleolar and calcaneal regions, after debridement, when treated for six weeks with dressing change performed three times per week ($p = 0.46$). It can promote complete healing in 10% of cases (RR = 5%, CI 95% -177% - 100%, ARR = 0.005 CI 95% -0.177 -0.187, NNT = 200, CI 95% 5 - INF) \(^{(A)}\).

**RECOMMENDATION**

Vacuum-assisted closure is recommended in the treatment of stage III and IV pressure ulcers, with continuous subatmospheric pressure of 125 mmHg and dressing change three times per week \(^{(B)}\).

In comparison with conventional techniques, this therapy showed no significant difference in the results and is more expensive. We suggest further pharmaceutical-economic studies on the vacuum-assisted closure technique in Brazil \(^{(D)}\).

7. **WHAT IS THE EFFECTIVENESS OF SHOCK WAVE THERAPY IN PRESSURE ULCER TREATMENT?**

Shock wave therapy, when applied to pressure ulcers with three months or longer duration, given for 6-8 weeks in two four-week periods, with a two-week washout period, decreases the extent of the lesion in 100% of ulcers and promotes wound healing in 55.6%\(^{(A)}\).

Acute or chronic pressure ulcers undergoing shock wave therapy of 100-1000 shocks/cm\(^2\) 0.1 ml/mm\(^2\), once a week or every 15 days, with a total of three sessions, show epithelialization and complete healing of 71.4%. However, with ulcers of > 10cm in diameter and > 1 month duration, there is no beneficial result ($p < 0.005$)\(^{(A)}\).

The use of shock wave therapy does not have a statistically significant result in the treatment of pressure ulcers when compared to other types of treatment, despite the results showing good response to the treatment. There is a need for larger, high-quality studies before this treatment method can be recommended \(^{(D)}\).
8. What is the efficacy of essential fatty acid treatment for pressure ulcers?

The fatty acid Mepentol, a basic hyperoxygenated fatty acid, when applied twice daily for 30 days to Stage I pressure ulcers in the pelvic region (sacrum and trochanter) and the calcaneal region, with frequent nightly repositioning (RR = 0.68) and application of barrier products, is effective in reducing the incidence of development of new pressure ulcers by 7.32% (12 of 164) (p < 0.006), and reduces the risk of developing ulcers by 58% compared to patients who received placebo - of every ten patients one is prevented from acquiring pressure ulcers (RR = 0.42, CI 95% = 0.22-0.80; NNT = 9.95). After 20 days the Mepentol has a protective effect on pressure zones, making them less prone to develop pressure ulcers (p = 0.0054)^16 (A).

When a 20 ml solution of essential fatty acids (EFA) is applied all over the body (1.6 gr. EFA with linoleic acid extracted from sunflower oil, 112 IU vitamin A, and 5 IU Vitamin E), with priority given to regions with potential to acquire pressure ulcers (locations of bony prominences), every 8 hours for 21 days, associated with protein-rich food supplementation or parenteral nutrition diet, as contrasted with the control group who were given enteral macronutrient nutrition (p < 0.05). When compared, the healing time for these pressure ulcers showed no significant difference between groups (p < 0.05)14 (A).

9. Which nutritional supplements are indicated for the improvement of pressure ulcers?

Critically ill ICU patients with acute lung injury with pressure ulcer (15.2%), whose enteral macronutrient diets were supplemented with essential fatty acids such as eicosapentaenoic acid (EPA), gamma linolenic acid (GLA) and vitamins A, C and E, which were provided in accordance with 75% of Resting Energy Expenditure within 48 hours of admission, for seven days, showed a 32.6% increase in the number of patients with a new pressure ulcer (Stage I = 32.6%, Stage II = 46.7%, and stage III = 40%), while the control group jumped to 49% of patients who acquired new pressure ulcers (Stage I = 25%, Stage II = 37.5%, Stage III = 33.3%, and Stage IV = 4.2%) (p < 0.05). There is a significant difference in the incidence of new pressure ulcers in patients who received the fatty acids and vitamins in their diet, as contrasted with the control group who were given enteral macronutrient nutrition (p < 0.05). When compared, the healing time for these pressure ulcers showed no significant difference between groups (p < 0.05)14 (A).

10. When is hydrocolloid used in pressure ulcer treatment?

Hydrocolloid is used on Stage I and II ulcers, in dressings applied after cleaning the wound, with dressing change twice per week. In eight weeks, it promotes healing of 85% (p < 0.05) of Stage I ulcers, 67% of stage II ulcers (p < 0.005) in the ischial, sacral and gluteal regions in patients with medullary lesions10 (RR = 57% CI 95% = 18% - 96%, ARR = 0.342 CI 95% = 0.109 - 0.575, NNT = 3 CI 95% = 2 - INF) (A).

When used in Stage II and III ulcers after cleaning with sterile saline, with dressing change every four days, this treatment promotes healing of 50% of ulcers (p = 0.893) when continued for eight weeks. The results, however, show no significant difference in relation to the comparison group11 (RRR = 3% CI 95% = -45% - 50%, ARR = 0.014 CI 95% = -0.230 - 0.258, NNT = 71, CI 95% = 4 - INF) (A).

Use hydrocolloid dressings on Stage II and III pressure ulcers provided they are shallow. Stage IV ulcers or deep ulcers can be filled with hydrogel or hydrofiber dressing, with replacement every three days on average depending on the amount of exudate produced. This treatment promotes healing of 35% (α = 0.04) and reduction in ulcer surface of 60% (α = 0.01) after five dressing changes12 (RRR = 46%, CI 95% = -85% - -7%, ARR = -0.297 CI 95% = -0.548 - -0.046, NNH = 3, CI 95% = -22 - INF) (A).

With Stage III and IV ulcers, following cleaning with saline solution, the dressing can be applied with or without calcium alginate (depending on the amount of exudate produced by the ulcer) in the ischial, coccyx and trochanteric regions. This treatment promotes healing in 44% of stage III ulcers within 12 weeks. This result was not significant compared to the control group (p = 0.46).12 (RRR = 8% CI 95% = -69% - 85%, ARR = 0.031 CI 95% = -0.264 - 0.326, NNT = 32, CI 95% = 3 - INF) (A).

Hydrocolloid may be applied to Stage III or IV ulcers after cleaning with sterile saline solution, for eight weeks, noting that in deep ulcers hydrocolloid paste should be used, with dressing change every three days or more, according to the amount of exudate produced by the ulcer. This treatment promotes a reduction of 43% of the ulcer area in the calcaneal, sacral and trochanteric regions without any debridging prior to treatment. However, these results were significantly lower compared to the study group (p < 0.001)13 (A).

Recommendation

Hydrocolloid dressings are recommended for Stage I and II pressure ulcers, with dressing change every 5 days, after
cleaning with saline, for a period of 8 weeks (A). Application of hydrocolloid dressings to Stage III and IV ulcers is recommended, for 8 weeks, noting that ulcers which present with cavity should be filled with hydrogel bandage or hydrofiber dressing, with replacement every three days on average if there is a large amount of exudate (A).

11. WHEN SHOULD THE SURGICAL DEBRIDEMENT PROCEDURE BE USED FOR PRESSURE ULCER?

Surgical debridement is indicated for ulcers in Stages III and IV when there is tissue necrosis and slough, after cleaning with sterile saline 0.9%. When combined with activated charcoal, it promotes full debridement of necrotic tissue and slough in 37.9% of ulcers treated, this being a significant result when compared to the use of hydrocolloid (16.1%) (p = 0.056).11 (RR = 58% CI 95% 0% - 100% AR = 0.218 CI 95% -0.001 - 0.437, NNT = 5, CI 95% 2 - INF) (A).

The application of surgical debridement in necrotic pressure ulcers in Stages II to IV, treated with hyperbaric oxygen for between 4-16 weeks, in the sacral, ischium, trochanter, calcaneus, foot and other (leg, elbow and back) regions, promotes healing within 16 weeks (A) [ARR = 0.677 CI 95% 0.518 -0.836, NNT = 1, CI 95% 1 - 2] (A).

Surgical debridement is used in clean Stage III and IV pressure ulcers, with little granulation tissue, in the ischial, sacral, malleolus, trochanteric, and calcaneal regions as a technique prior to the start of treatment to achieve better absorption and results in the application of topical substances (A).

Surgical debridement in Stage IV pressure ulcers with necrotic tissue on the heel is performed to remove the necrosis as a technique prior to the application of continuous collagenase, with dressing change once per day, for 6 to 12 weeks with an average of 10 weeks, promoting complete healing of 91.6%, (p < 0.005) (RR = 75% CI 95% -18% - 100%; ARR = 0.025 CI 95% -0.059 - 0.559, NNT = 4, CI 95% 2 - INF) (B).

RECOMMENDATION

Surgical debridement is recommended for ulcers in Stages III and IV with tissue necrosis, a large amount of slough and little granulation tissue, after cleansing with sterile 0.9% saline solution, in the ischial, sacral, malleolus, trochanteric and calcaneal regions, as a technique prior to other types of treatment (A).

12. WHAT IS THE EFFICACY OF HYPERBARIC CHAMBER TREATMENT IN PATIENTS WITH PRESSURE ULCER?

The application of topical hyperbaric oxygen (1.004-1.013 atmospheres) to necrotic pressure ulcers in stages II to IV, after surgical debridement, treated between 4 to 16 weeks, four hours a day, four days a week, in the sacrum, ischium, trochanter, calcaneus, foot and other (leg, elbow and back) regions promotes healing within 16 weeks (A) [ARR = 0.677 CI 95% 0.518 - 0.836, NNT = 1, CI 95% 1 - 2] (A).

Treatment with topical hyperbaric oxygen presented lower financial costs for pressure ulcers: 81.3% stage II, 37.9% stage III and 36.1% stage IV (A).

RECOMMENDATION

Topical Hyperbaric Oxygen therapy is indicated for the treatment of necrotic ulcers in Stages II to IV, after surgical debridement, for a period of 4 to 16 weeks, 4 hours per day, 4 days a week.


