

The Efficacy of Super-oxidised Hydrogel and Solution Compared to Potassium Permanganate Dressing for the Management of Cellulitis

Sabrina Ab Wahab¹, Tarita Taib¹, Rohna Ridzwan²

¹Dermatology Unit, Faculty of Medicine, Sungai Buloh Campus, Universiti Teknologi MARA, Sungai Buloh, Selangor, Malaysia

²Department of Dermatology, Selayang Hospital, Selayang, Malaysia

Keywords: super-oxidised hydrogel, super-oxidised solution, potassium permanganate dressing, cellulitis, local inflammation

Abstract: Cellulitis causes local residual inflammation which delays clinical resolution. Studies have shown that super-oxidised hydrogel and solution improves skin and soft tissue infection. This is a multicentre, prospective, open-label, comparative clinical study involving adults ≥ 18 years old, efficacy comparison between two methods of dressing; super-oxidised hydrogel and solution dressing compared to potassium permanganate dressing, assessment of reduction of local inflammation; erythema, oedema and cellulitis severity score. Thirty patients with 2 different sites of cellulitis received the super-oxidised hydrogel and solution dressing (SO Group) and potassium permanganate (KMnO₄ Group) wet wrap dressing at different sites of leg for 15 minutes, twice a day reviewed at end-of-treatment (day 3 and/or day 7). SO Group when compared to KMnO₄ Group showed difference in percentage of erythema reduction at Day 3 (50.05% vs 30.98%; $p=0.001$) and at Day 7 (71.10% vs 59.05%; $p=0.045$); with median reduction in limb circumference at Day 3 (1.90 cm vs 0.80 cm; $p=0.001$) and Day 7 (3.00 cm vs 1.80 cm; $p=0.021$). Both dressings showed reduction of cellulitis severity score (total score of 21); with median reduction of score at Day 3 (6.0 vs 5.5; $p=0.123$) and Day 7 (12.0 vs 11.0; $p=0.567$), and significant difference only in erythema scores ($p=0.029$). Diabetes mellitus, bullous type, and disease recurrence were significant associated factors. In conclusion, super-oxidised hydrogel and solution is more effective in improving local erythema and oedema compared to potassium permanganate dressing, in patients with cellulitis albeit no difference in the reduction of total cellulitis severity score.

1 INTRODUCTION

Cellulitis is a common acute bacterial infection affecting the tissues of the dermis and subcutaneous tissue (Halpern *et al.*, 2008). However, the residual local inflammations causes delay in resolution of clinical signs and furthermore may prolong hospitalization (Bruun *et al.*, 2016). Super-oxidised technology is a new concept of management in skin and soft tissue infections as a result of purified water and sodium chloride electrochemically processed solution with neutral pH and used primarily in wound infections and chronic inflammatory skin disease (Landa-Solis *et al.*, 2005). Its efficacy as an antiseptic was observed *in vitro* by destroying the functionality of the membrane-bound components of the

microorganism, hence providing anti-microbial properties (Armstrong *et al.*, 2015).

Subsequently, Medina-Tamayo *et al* studied on super-oxidised solution inhibition on mast cells degranulation, hence exploring its benefits in localized inflammatory reactions (Medina-Tamayo *et al.*, 2007). On the other hand, potassium permanganate dressing has been widely used as a reliable antiseptic. The most compelling evidence on cellulitic changes was supported by a randomized control trial by Jesús *et al* who reported statistically significant diminishing extent of cellulitis in diabetic foot ulcer; 80.9% of those treated with super-oxidised solution compared to 43.7% in those treated with conventional antiseptics with p value < 0.01 (Martínez-De Jesús *et al.*, 2007).

Therefore, this study aims to observe the efficacy of super-oxidised hydrogel and solution in reduction erythema, oedema and total cellulitis severity score when used as an adjunct to systemic antibiotics in cellulitis

2 METHODS

We conducted a multicentre, prospective, open-label, comparative clinical study between February 2017, and July 2017 at 2 centres, Pusat Pakar Perubatan Universiti Teknologi MARA and Hospital Selayang, Malaysia. After obtaining ethical approval, we enrolled adults aged 18 years or older with clinical diagnosis of Eron Class 1 and 2 limb cellulitis with presence of clinical signs of erythema, warmth and oedema and involving limbs must have a total surface area of erythema $\geq 75\text{cm}^2$.

We excluded patients diagnosed with necrotizing fasciitis, abscess or requiring surgical intervention, known allergy or intolerance to study medications, burn infections and deep vein thrombosis. Patients in sepsis with hypotension, with systolic blood pressure < 90 mmHg, acute confusion, tachycardia or tachypnoea were also excluded. Both methods of dressings were randomly allocated dressing to either proximal/anterior or distal/posterior area on the selected limb, in the same patient.

All patients received the super-oxidised hydrogel combined with solution dressing and potassium permanganate (KMnO₄) dilution 1:10000 wet wrap for 15 minutes twice a day. Standardized similar 2 pieces of gauze dressing equal to size of 3-inch length x 6-inch width at each intervention site. Similar plasters were used and was marked with a waterproof skin marker.

All measurements were performed with standardized similar flexible plastic measuring tape. Cellulitis severity score was used as a clinical assessment tool adapted from a previous clinical trial using a numerical value; none =0, mild =1, moderate =2, and severe =3; based on erythema, warmth, tenderness, oedema, ulceration, drainage and fluctuance at the affected area (Hepburn *et al.*, 2004).

Evaluation of the reduction of erythema and oedema performed by a single investigator, measured as percentage of reduction of total surface area erythema; and oedema reduction by reduction in limb circumference, at end-of-treatment (day 3 and/or day 7). Secondary endpoints include reduction of cellulitis severity score which measures erythema, warmth, tenderness, oedema, ulceration, drainage and fluctuance; at end-of-treatment (day 3 and/or day 7). Efficacy outcomes were presented as percentages, and

p values were from Mann-Whitney test; Chi square test compared severity scores; linear regression and analysis of variance identified potential associated factors.

3 RESULT

Thirty patients with 2 different sites of cellulitis area were enrolled and followed up to day 3, subsequently 15 patients received up to 7 days of both dressings. Baseline characteristics were similar as both dressings were applied in the same patient. Study showed that super-oxidised hydrogel and solution dressing (SO Group) was more effective in reducing erythema compared to potassium permanganate dressing (KMnO₄ Group), with significant difference in percentage of erythema reduction at Day 3 (50.05% vs 30.98%; *p*=0.001) and at Day 7 (71.10% vs 59.05%; *p*=0.045).

Super-oxidised hydrogel and solution was also more effective in reducing oedema compared to potassium permanganate dressing alone which was statistically significant, with median reduction in limb circumference at Day 3 (1.90 cm vs 0.80 cm; *p*=0.001) and Day 7 (3.00 cm vs 1.80 cm; *p*=0.021), respectively. There was no difference in both dressing in the reduction of cellulitis severity score (maximum total score of 21), with median reduction of score at Day 3 (6.0 vs 5.5; *p*=0.123) and Day 7 (12.0 vs 11.0; *p*=0.567) albeit erythema scores alone showed significant difference (*p*=0.029).

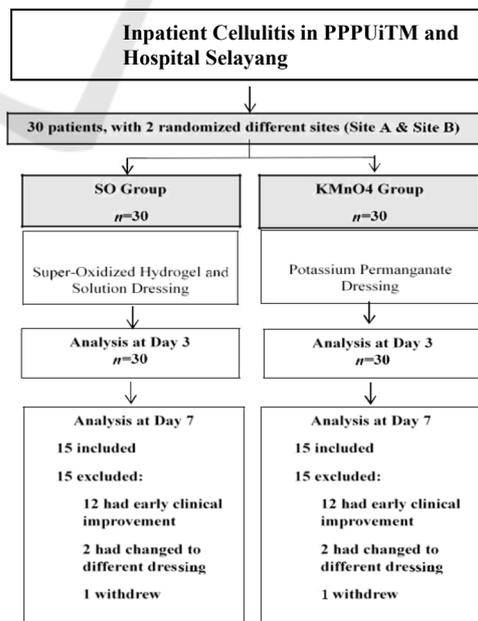


Figure 1 Study Flow Chart Figure

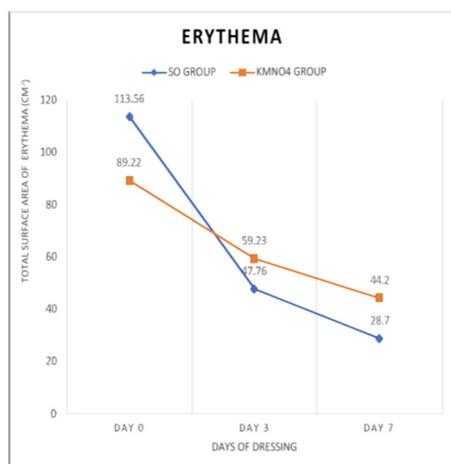
Variables that showed significant association identified were diabetes mellitus ($p=0.004$), recurrence of cellulitis ($p=0.035$), or who had bullous type cellulitis ($p<0.001$).

4 DISCUSSION

The primary outcome was the significant reduction of erythema. Our study showed statistically significant improvement of erythema with super-oxidised hydrogel and solution dressing compared to potassium permanganate dressing. After 3 days of skin dressing, there was significant reduction in percentage of erythema, SO group vs KMnO4 group; $p=0.001$ and those deemed indicated to extend up to 7 days of skin dressing had also significant reduction in percentage of erythema; $p=0.045$.

Our findings were supported by previous clinical trials that had proven the efficacy of super-oxidised solution. To the best of our knowledge, a randomized controlled trial by Jesús et al reported diminishing extent of cellulitis in diabetic foot infections treated with super-oxidised solution when compared to conventional disinfectant ($p<0.01$)(6). Previously, this novel hydrogel and solution was mainly studied on wounds, where Pandey et al found statistically significant decrease in surface area of surgical wounds when compared to povidone iodine ($p=0.001$) (Pandey *et al.*, 2011). This supports the premise that the super-oxidised hydrogel and solution dressing is beneficial in cellulitis, and other SSTIs.

Figure 2 Comparison of Erythema Reduction Between SO Group vs KMnO4 Group



Further evidence demonstrated in our study was the greater difference in limb circumference between SO group vs KMnO4 group with median (1.90 cm (IQR 1.43) vs 0.80 cm (IQR 1.65); $p<0.001$) at day 3 and day 7 (3.00 cm (IQR 2.30) vs 1.80 cm (IQR 1.90); $p <0.05$). We measured the reduction in limb circumference and noted similar modality previously used in several studies as an indicator of reduction of oedem (Caban, 2002; Beasley, 2011; Brindle *et al.*, 2017). The positive outcome from our study in cellulitis was the greater reduction in oedema with super-oxidised hydrogel and solution compared to potassium permanganate dressing. One study described greater reduction of wound size and periwound oedema in the super-oxidised solution group (70%) when compared to povidone iodine treated group (50%) (Kapur & Marwaha, 2011) .

We relate that improving oedema will contribute to resolution of signs. Our findings support the evidence that super-oxidised hydrogel and solution reduces oedema as a sign of local inflammation in SSTIs. Previous literature did advocate compression dressings to improve oedema in cellulitis (Gunderson, 2011). From our study, both methods of dressing showed improvement in severity of oedema. These findings support the benefits of skin dressing in cellulitis, but more study data is required.

Particular of interest is the similar treatment response in both methods of dressings by evaluating the cellulitis scoring. Our data did not show any significant difference in the reduction of cellulitis severity score between the two methods of dressing. Although no statistical differences were noted in the reduction of score between the groups, the two study treatments differed in terms of their anti-inflammatory properties. The possible reason for comparable cellulitis severity score in both groups may be due to the difficulty in measuring progressive overall inflammatory outcomes by clinical signs. Our findings showed statistically significant improvement in erythema severity scoring in SO group compared to KMnO4 group at day 7 with p value 0.029. In determining the efficacy, based on this finding, it can be demonstrated that super-oxidised hydrogel and solution has better control in erythema.

We acknowledge the limitation of open label study and blinding was impossible due to the different colour of both dressings. We also took measures to avoid carryover effect with both intervention and comparison dressing requiring at least a 2 cm gap ,considered based on Baranoski et al who discussed on healing ridge (Baranoski & Ayello, 2012). Most major factors affecting the outcome were controlled through the exclusion criteria. However, important

confounding factors that were unable to be controlled were diabetes mellitus, bullous type cellulitis, and disease recurrence that were significantly associated.

5 CONCLUSION

Super-oxidised hydrogel and solution is more effective in improving local erythema and oedema, as compared to potassium permanganate dressing, in patients with cellulitis albeit no difference in the reduction of total cellulitis severity score. There was improvement of the overall local inflammation with intervention by both methods of dressing in this study.

ACKNOWLEDGEMENT

This study was sponsored by both the investigator and Dyamed Biotech Sdn Bhd who supplied the study products. We would like to thank our Head of Department, Dr Mohd Arif bin Mohd Zim for his support of this investigator-initiated clinical research.

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