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MRSA에 감염된 흰쥐의 전층피부결손에 대한 은 함유 하이드로화이버 드레싱과 소수성 드레싱의 효과의 비교

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Comparison of Silver-containing Hydrofiber Dressing and Hydrophobic Dressing for Effects on MRSA-infected Full Thickness Skin Defect in the Rat

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Purpose: Aquacel Ag® is a hydrofiber wound dressing integrated with ionic silver. Sorbact® is a hydrophobic-coated dressing that uses the hydrophobic interaction with microbes. In this study, we compared the wound healing effects and the antibacterial effects of Medifoam®, Betadine soaked, Aquacel Ag® and Sorbact® dressings against MRSA-infected wounds.

Methods: Eighty rats were divided into four groups: Medifoam®; Betadine soaked; Aquacel Ag®; and Sorbact®. A 1.5 × 1.5 cm square full-thickness wound was made on the dorsum of each rat and infected with MRSA. Twenty-four hours thereafter, each dressing was applied to the wound and changed every other day. One, 3, 7, 11 and 15 days after the wound infection, swab culture grade, wound bed appearance score, and wound defect size change were evaluated, and 7 and 15 days after, histologic evaluation was compared between the groups.

Results: The bacteria load of wounds in the Sorbact® group decreased earlier than in the other groups. The wound bed appearance score of the Sorbact® group also increased quicker, compared with the other groups. However, the size of wounds of the Aquacel Ag® group decreased more rapidly, compared with other groups. From the histologic point of view, there was no significant difference between Betadine soaked, Aquacel Ag® and Sorbact® groups.

Conclusion: The hydrophobic dressing using Sorbact® showed a more rapid reduction in the MRSA load and an elevation in the wound bed appearance score, but a slower decrease in wound size change due to detachment of wound bed tissue when the dressing was eliminated in the low exudate wound. The silver-containing hydrofiber dressing using Aquacel Ag® was more effective in ultimate wound size reduction, but some debris was trapped in the wound tissue and induced foreign body reaction in the high exudate wound. Thus, ongoing selection process of treatment based on the evaluation of the infectious wound state will be very important.

Key Words: MRSA, Skin defect, Wound infection, Aquacel Ag, Sorbact

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I. INTRODUCTION

In plastic reconstructive surgery, the treatment of infectious wounds is a frequently occurring and difficult problem. The treatment consists of general antibiotics and local wound treatment. Usually, antibiotics are prescribed either for cellulitis or for bacteria invasion of the blood vessels. However, infections with antibiotic-resistant bacteria, such as methicillin-resistant-*Staphylococcus aureus* (MRSA), have become more common in the hospital,[1] therefore, the importance of local wound treatment has significantly increased.

There are several local wound treatment methods, such as the classic Betadine-soaked dressing, which is still frequently used in the clinic setting. This treatment is effective against bacteria, fungi, parasites, and viruses, and pathogenic resistance has not been reported yet.[2] Similarly, dressing materials containing silver have been developed and their efficacy has been also vertified.[3] Aquacel Ag® is an example of such dressing, it is an absorptive hydrofiber combined with silver ions.[3] Another kind of dressing, Sorbact® is a dressing material which removes bacteria by physical interaction using the cell-surface hydrophobicity of bacteria, rather than the intrinsic antibiotic activity of the dressing materials.[4] Thus, Sorbact® provides the benefit of reducing the bacterial burden without any side effects involving chemical

interactions with other materials. Each dressing method has been reported to be effective against *Staphylococcus aureus*,[4,5] but few studies that have compared their respective efficacies. In present study, we compared the efficacy of the following dressings: silver-containing hydrofiber dressing using Aquacel Ag®, hydrophobic dressing using Sorbact®, classic Betadine-soaked dressing and Medifoam®. Thus, a full thickness skin defect was experimentally produced on the dorsal area of rats, and MRSA was inoculated into the wound beds. Then, the reduction of the bacteria load, the wound healing, and the dressing properties after applying each material to the infected wounds were compared.

II. MATERIALS AND METHODS

A. Animals and Bacteria

Following one week adaptation period, eighty 180~200g Sprague-Dawley female rats (Koatech, Bucheon, Korea) were used in our experiments, according to the guidelines of the Associated Animal Study Ethics Committee.

We used the MRSA (American Type Culture Collection No. 33591) provided by the Korean culture center of microorganisms, Seoul, Korea. MRSA was prepared by culturing the bacteria on the Luria Bertani broth medium for 24 hours. Then the prepared bacteria suspension was swabbed on the Luria Bertani plates and the colony forming units (CFUs) were calculated. The amount of bacteria concentration in the suspension was adjusted to 2×10^9 CFU s/mL.

B. Materials

The following materials were used:

1) Betadine (povidone iodide; Sungkwang Pharm. Co. LTD., Bucheon, Korea);
2) Cutmed® Sorbact® (BSN Medical, Gothenburg, Sweden);
3) Aquacel Ag® (Convatec, Bristol-Myers Squibb Company, New York, USA);
4) Medifoam® (Ildong, Seoul, Korea).

C. Methods

1) Wound preparation and bacteria inoculation

2,2,2 tribromoethanol (2.5 g) and 2-methyl-2-butanol (5 mL) was mixed with 200 mL of phosphate-buffered saline, then 1.25% tribromoethanol solution was injected intraperitoneally at the dose of 200 mg/kg. After anesthesia, we shaved the dorsal region, scrubbed it with Betadine solution, and made a 1.5 × 1.5 cm full thickness defect with scissors. MRSA (0.1 mL, 2×10^8/mL) was inoculated into the wound bed. A 3.0 × 3.0 cm Medifoam® (a foam dressing material) was fixed to the wound with Hypafix® (Smith & Nephew, London, UK) to facilitate bacteria inoculation and to inhibit desiccation of the wound bed.

2) Wound treatment

Twenty-four hours after wound preparation, 80 rats were divided into 4 groups of 20 rats each.

Dressings with different materials were performed as follows:

group 1, control;
group 2, 1.5 × 1.5 cm Betadine-soaked gauze;
group 3, 1.5 × 1.5 cm Aquacel Ag®; and
group 4, 1.5 × 1.5 cm Cutmed® Sorbact®.

As a second dressing material, the 2.5 × 2.5 cm Medifoam® was used and fixed with Hypafix®. Every other day, after washing the wound with saline, the dressing was changed. Prior to dressing removal, the dressing materials were soaked with normal saline, then detached carefully to prevent aggravation of the wound bed injury.

D. Evaluation

1) The swab culture

Swab cultures were done on the wound bed on days 1, 3, 7, 11 and 15 after wound infection. The surface of the center of the wound was scratched once with a sterile swab. Then, the swab was evenly smeared on a Luria Bertani plate and bacteria were cultivated at 37°C for 18 hours. The cultures were classified according to the area occupied by the bacterial colonies, as follows: grade 0, bacterial colonies did not appear on the culture dishes; grade 1, bacterial colonies were just a few and easily counted; grade 2, bacterial colonies were spread all over the culture dish; grade 3, the round shape of bacterial colonies could be detected, but there was a large number of bacteria and they could not be counted; and grade 4, the round shape of bacterial colonies could not be detected, and they were seen only as one opaque patch (Fig. 1).

2) Gross examination and wound bed appearance scoring

A gross examination was performed 24 hours after wound preparation and when the dressings were changed. The exudate absorbed into Medifoam® was inspected in the Medifoam®, Aquacel Ag®, and Sorbact® groups. If the exudate was absorbed into the full thickness of Medifoam®, so the Medifoam® was deformed, we defined the wound as 'high exudate wound', and

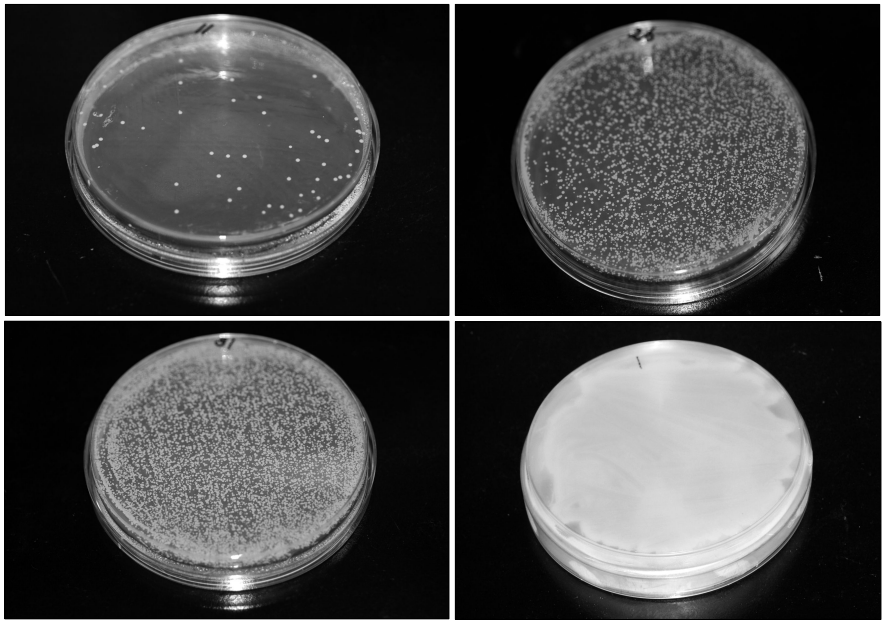

Fig. 1. Classification and demonstration of the amount of bacteria in the bacterial culture. We classified *the amount of bacteria* into five categories, as follows: grade 0, grade 1, grade 2, grade 3, and grade 4. Grade 0 indicates that bacterial colonies do not appear on culture dishes. (Above, left) Grade 1 indicates that bacterial colonies are just a few in number and can be easily counted, (Above, right) Grade 2 indicates that the bacterial colonies can be counted, but are spread over the entire culture dish. (Below, left) Grade 3 indicates that the round shape of bacterial colonies can be detected, but the amount is so large that the bacteria cannot be counted. (Below, right) Grade 4 indicates that the round shape of bacterial colonies cannot be detected, and they appear as one opaque patch.

Table I. Modified Wound Bed Appearance Score

Appearance score	Granulation tissue	Fibrinous tissue	Slough	Eschar or crust
3	100%	-	-	-
2	50~99%	+	-	-
1	< 50%	+	±	-
0	±	±	±	+

Modified from Falanga 2000.[6]

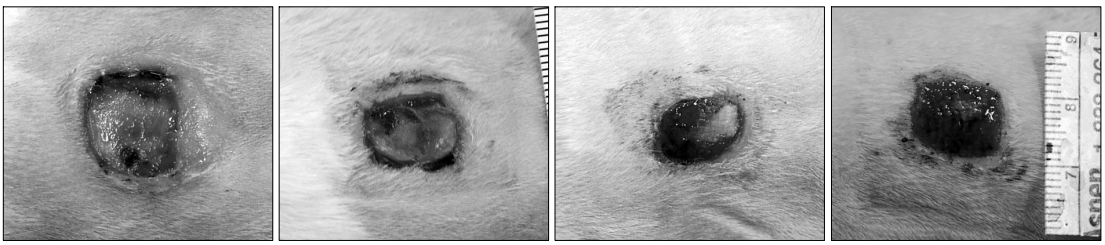

Fig. 2. Modified wound bed appearance score. We classified the appearance of the wound bed into four categories; (Left) appearance score=0, (Left, center) appearance score=1, (Right, center) appearance score=2, and (Right) appearance score=3.

if the exudate was partially absorbed into the Medifoam® or the Medifoam® was just stained, we described the wound as 'low exudate wound'. We referred to MEASURE evaluation as reported by Keast,[6] on days 1, 3, 7, 11, and 15 after wound preparation, we compared the wound healing effect in time by evaluating the wound bed appearance score, based on the modified Falanga's wound bed appearance grading method[7] (Fig. 2, Table I).

3) Calculation of the wound size

A photograph of the wound was taken with a digital camera (D80; Nikon, Tokyo, Japan) on days 1, 3, 7, 11, and 15 days after wound preparation. A ruler was placed near the wound for the purpose of calibration when the size of the wound was measured with an image analysis program (Uthscsa, Image Tool for Windows, version 3.00, The University of Texas Health Science Center, San Antonio, Texas. USA).

4) Histologic examination

Seven and 15 days after wound infection, respectively, 10 rats from each group were euthanized and each wound, together with the surrounding marginal skin, was excised and fixed in 10% buffered formalin solution.

The fixed tissue was embedded with paraffin, then cut at 3 μm thickness and stained with hematoxylin and eosin stain. We inspected the degree of inflammation, re-epithelization, and granulation tissue formation with a light microscope (Olympus BX 51) (× 40, × 100). The results were classified into five scores, summed and compared between the groups (Table II).

5) Statistical analysis

Statistical analysis was performed using the personal computer program PASW statistics 18 (SPSS, Inc, Chicago, IL, USA), and all data are presented as the mean ± standard deviation. For results comparison, i.e. the swab culture, wound bed score, and wound defect size, the ANOVA test was used. For comparison of the results of histologic score, we used the Kruskal-Wallis test and Mann-Whitney U tests. A p-value < 0.05 was considered as statistically significant.

III. RESULTS

A. Swab cultures

Twenty-four hours after the inoculation of bacteria, all wound swab culture results were grade 4. On day 3, There was no statistically significant difference between the investigated groups, although, Sorbact® showed as the greatest reduction (3.65 ± 0.58). On day 7, the Sorbact® group still showed the greatest reduction (3.15 ± 0.59), and there were statistically significant differences compared to the Medifoam® (3.75 ± 0.47), Betadine-soaked gauze (3.60 ± 0.50) and Aquacel Ag® (3.65 ± 0.49) groups

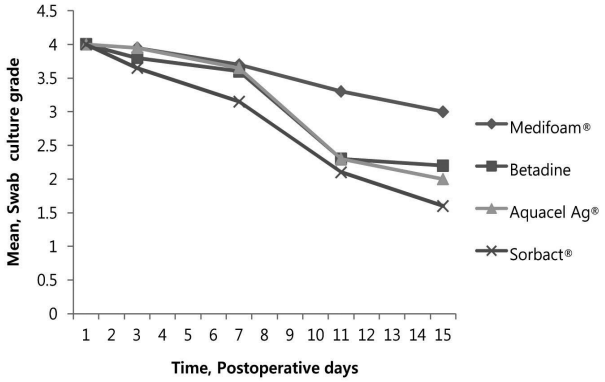

Fig. 3. Changes in swab culture grades.

Table II. The Histologic Score

	Inflammation	Epithelization	Granulation
	Accumulation of inflammatory infiltrates	The length of new epithelization compared to that of the whole defect area	The thickness of the granulation tissue compared to that of the normal dermis
0	Dense accumulation of inflammatory infiltrates in the whole defect area	No epithelization	No granulation tissue
1	Large accumulation groups of inflammatory infiltrates	0 < Epithelization ≤ 1 / 3	Thin, immature granulation tissue with few fibroblasts, capillaries
2	Small accumulation groups of inflammatory infiltrates	1 / 3 < Epithelization ≤ 2 / 3	Moderately thick granulation tissue with more fibroblasts and extensive neo-vascularization
3	Minimal inflammatory cell accumulation was observed	2 / 3 < Epithelization < 1	Thick granulation tissue, with many fibroblasts and extensive collagen deposit
4	No difference with the normal tissue	Completely covering the wound	Thick, vascular granulation tissue(as thick as the normal dermis)

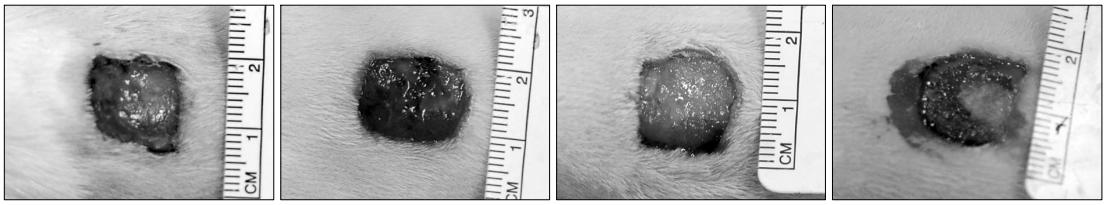

Fig. 4. Wound bed appearance on post-operative day 3; (Left) Medifoam® group, appearance score=0, (Left, center) Betadine-soaked group, appearance score=1. (Right, center) Aquacel Ag® group, appearance score=1. Note the wound bed appearance with debris in the Aquacel Ag® group. (Right) Sorbact® group, appearance score=2; mild bleeding was seen.

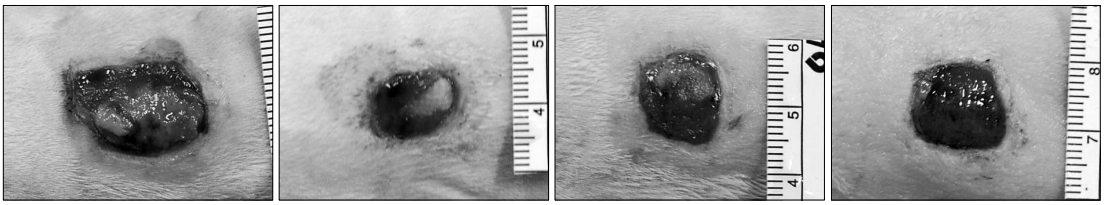

Fig. 5. Wound bed appearance on post-operative day 7; (Left) Medifoam® group, appearance score=1, (Left, center) Betadine-soaked group, appearance score=2, (Right, center) Aquacel Ag® group, appearance score=2, (Right) Sorbact® group, appearance score=3.

(p=0.006, p=0.035, and p=0.015 respectively). On day 11, the bacteria burden of the Betadine-soaked gauze (2.30 ± 0.94) and Aquacel Ag® (2.30 ± 0.94) groups was sharply reduced. There was a statistically significant difference between the Sorbact® (2.10 ± 1.10) and Medifoam® (3.30 ± 0.48) groups (p=0.006). On day 15, There were statistically significant differences between the Sorbact® (1.60 ± 0.69) and Medifoam® (3.00 ± 0.81) groups and between the Aquacel Ag® (2.00 ± 0.66) and Medifoam® groups (p=0.001 and p=0.024, respectively) (Fig. 3).

B. Gross findings

On day 1, every wound showed changes suggestive of infection, such as crust or biofilm formation and a large sanguine-purulent exudate. On day 3, the wounds in the Medifoam®, Aquacel Ag®, and Sorbact® groups were high exudate wounds. After day 7, all the wounds in the three groups changed to low exudate wounds. Through the whole experiment period, the exudate in the Medifoam® group decreased slower than in the other groups, but the difference (in Medifoam® changes) between the Aquacel Ag® and Sorbact® groups was not definite on gross examination.

On day 3, the signs of infection in the Medifoam® group were similar or more severe than on day 1, but they were reduced from day 5. Compared to other groups, the signs of infection regressed slower. The Betadine-soaked group showed bleeding because of desquamation at the surface of the wound bed when the dressing was removed. In contrast, the Aquacel Ag® group showed no bleeding when the dressing was removed. Nevertheless, in high exudate wounds, the gel formed dressing-derived debris was not removed completely from the wound surface until day 5, and more slough was noted in this group than others (Fig. 4). After 7 days, as the signs of inflammation and exudate were reduced, removal of the dressing material was easier. The gross signs of infection rapidly decreased in the Sorbact® group. However, in the low exudate wounds, 7 days after infection, the newly generated epithelium and the granulation tissue easily detached when the dressing was removed due to adherence of the dressing materials (Fig. 5).

On day 1, the wound bed appearance score was 0 in all groups. On day 3, the wound bed appearance score increased in the following order: Sorbact® (0.70 ± 0.66), Betadine (0.30 ± 0.47), Aquacel Ag® (0.25 ± 0.44), and Medifoam® (0.15 ± 0.36) groups. There were statistically significant differences between the Sorbact® and Medifoam® groups, and between the Sorbact® and Aquacel Ag® groups (p=0.004 and p=0.027, respectively). On day 7, the wound bed appearance score was increased in the following order: Sorbact® (2.55 ± 0.60), Aquacel Ag® (1.80 ± 0.77), and Betadine (1.45 ± 0.75) and Medifoam® (1.45 ± 0.82) groups. There were statistically significant differences between the Sorbact® and the other groups, i.e. Medifoam®, Betadine and Aquacel Ag® groups (p < 0.001, p < 0.001 and p=0.011 respectively). However, on day 11, there was no statistically significant difference between the groups, and on day 15, each group scored 3 for this measure (Fig. 6).

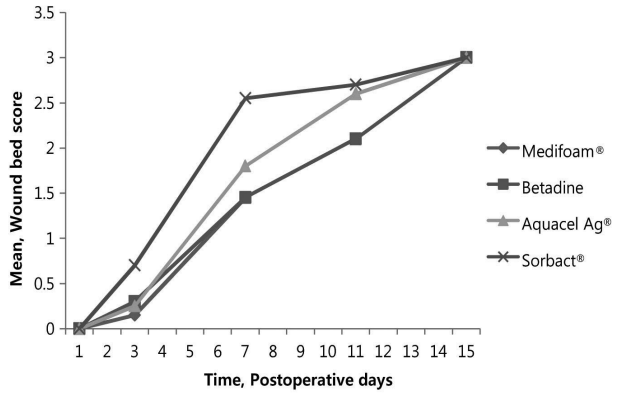

Fig. 6. Changes in wound bed appearance score.

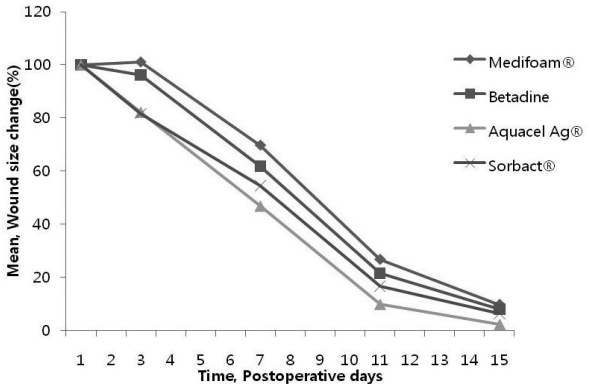

Fig. 7. Wound size change (%) curves in each investigated group (%).

C. Changes in the wound size

On day 3, the wound sizes were decreased in the following order: Sorbact® (81.67 ± 10.24%), Aquacel Ag® (82.17 ± 8.86%), Betadine (96.13 ± 15.19%), and Medifoam® (101.08 ± 21.8%). There were statistically significant differences between the Medifoam® and Aquacel Ag® groups, the Betadine and Aquacel Ag® groups, the Medifoam® and Sorbact® groups, as well as the Betadine and Sorbact® groups (p=0.001, p=0.021, p=0.001 and p=0.016 respectively). On day 7, the wound size decreased in the following order: Aquacel Ag® (46.84 ± 9.14%), Sorbact® (54.58 ± 12.30%), Betadine (61.89 ± 10.31%), and Medifoam® (69.72 ± 25.14%). There were statistically significant differences between the Betadine and Aquacel Ag® groups, the Medifoam® and Aquacel Ag® groups, as well as the Medifoam® and Sorbact® groups (p < 0.001, p=0.016, and p=0.015 respectively). On day 11, there were statistically significant differences between the Medifoam® (26.68 ± 8.49%) and Aquacel Ag® (9.90 ± 2.26%) groups, the Betadine (21.58 ± 4.23%) and Aquacel Ag® groups, and the Medifoam® and Sorbact® (16.68 ± 7.75%) groups (p < 0.001, p=0.001 and p=0.005, respectively). On day 15, the wounds in the Aquacel Ag® (2.35 ± 2.76%) group re-epithelized and healed statistically significantly more than in the Medifoam® (9.70 ± 4.55%) groups and Betadine soaked (8.06 ± 3.72%) groups (Medifoam®, p=0.004; Betadine, p=0.031) (Fig. 7).

D. Histologic inspection

On day 7, the wounds in every group showed inflammation, granulation formation and partial re-epithelization, but there was no statistically significant difference between groups. On day 15, all groups showed more epithelization and less inflammation, but the Medifoam® (6.30 ± 0.94) group showed a histologic score which was statistically significantly lower than the score in the

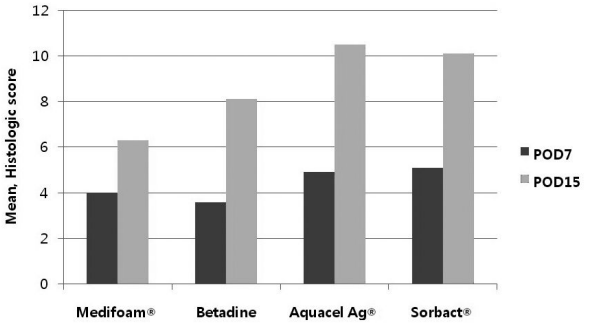

Fig. 8. Histologic score results.

Betadine (8.10 ± 1.72), Aquacel Ag® (10.50 ± 3.34) and Sorbact® (10.10 ± 2.51) groups (p=0.021, p=0.005, and p < 0.001, respectively). In several wounds treated with Aquacel Ag®, the dressing materials were trapped inside the wound tissue, triggering inflammation and foreign body reaction (Fig. 8~11).

IV. DISCUSSION

Wound infection shows the imbalance between the host homeostasis and proliferation of bacteria. If the wound infection occurs, the healing process is disturbed by several mechanisms. Infection lowers the partial pressure of oxygen in the affected tissues, and lengthens the inflammatory phase. Severe infection impairs the chemotaxis, movement, and phagocytosis of leukocytes. Colonies of bacteria delay neo-angiogenesis and epithelization. The inflammatory infiltrates slow fibroblast proliferation, and thus, slow the extracellular matrix synthesis and deposition. Collagenase from bacteria breaks down the collagen of the wound, and thus impairs the tension and contracture of the wound.[8] Therefore, in the wound healing process, the control of wound infections is a very

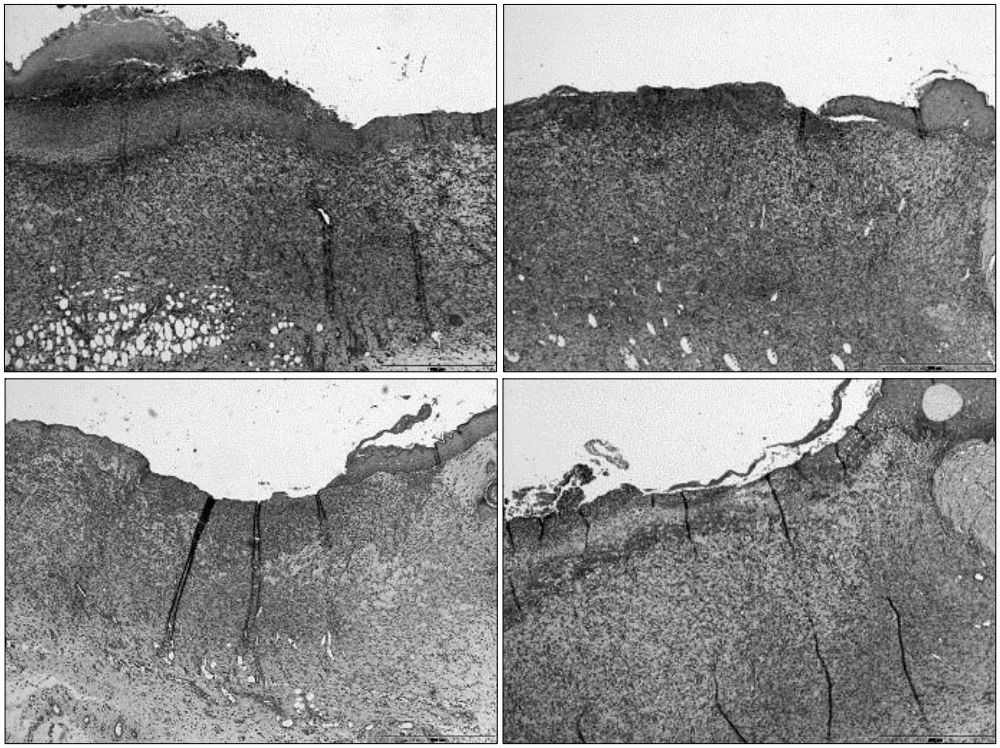

Fig. 9. Histologic findings of the wound after 7 days (hematoxylin and eosin stain, × 40). (Above, left) Medifoam® group. (Above, right) Betadine-soaked group. (Below, left) Aquacel Ag® group. (Below, right) Sorbact® group.

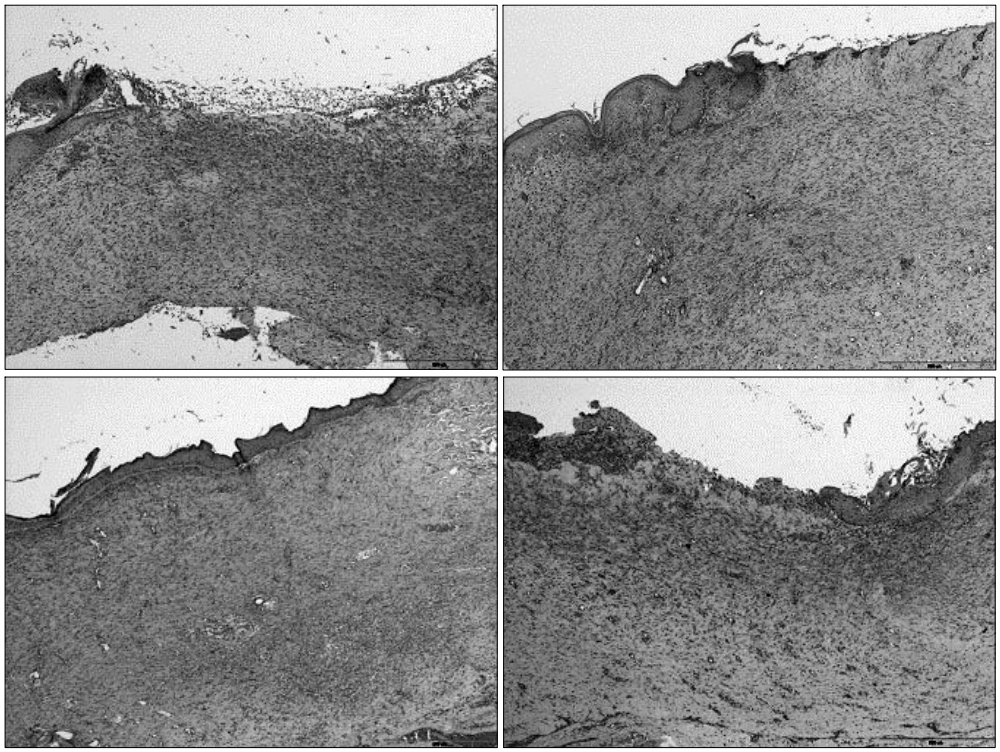

Fig. 10. Histologic findings of the wound after 15 days (hematoxylin and eosin stain, × 40). (Above, left) Medifoam® group. (Above, right) Betadine-soaked group. (Below, left) Aquacel Ag® group. (Below, right) Sorbact® group. Note the full area of epithelization in the Aquacel Ag® group.

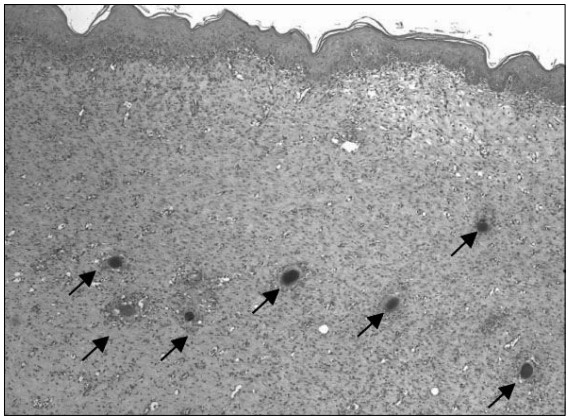

Fig. 11. Aquacel Ag® group, Postoperative 15 days after wound infection (hematoxylin and eosin stain, × 40). Dressing material debris (arrow) was trapped in the wound tissue and foreign body reaction was observed in the adjacent area.

important.

MRSA is one of the most common antibiotic-resistant bacteria, responsible for hospital-acquired infections.[1] When the infection occurs in patients with chronic wounds, such as pressure sores, diabetic feet, and ischemic leg ulcers, wound healing is very difficult, and can induce sepsis in patients with poor general health and impaired immune system, leading increased mortality. Some antibiotics known to be effective against the MRSA infection, have significant side effects (e.g. nephropathy and hepatopathy), therefore consistent decisions regarding their use are difficult. Therefore, when infection is localized to the wound, effective local treatment with debridement might be more important.

Silver ions are highly reactive substance which binds negatively charged proteins, RNA, DNA, and chloride ions. The antimicrobial activity of silver ions consists of inhibiting the bacterial DNA replication and electron transport elements, and preventing the respiratory chain of cytochromes, thus eventually suppressing bacteria.[5] Silver has been used in various forms (i.e. metallic, liquid, and cream), and extended antibacterial properties have been reported against several pathogen types including anaerobic, aerobic, gram-positive, gram-negative bacteria, and fungi.[5] Aquacel® consists of hydrofibers made of 100% sodium carboxymethylcellulose, and it absorbs the exudate directly into the fiber structure by capillary action. It retains the exudate in the fiber, and spreads the exudate within the entire dressing.[9] After absorbing the exudate, Aquacel® is transformed into a soft, cohesive, and transparent gel sheet, so that it can be modified to fit the curvature of the wound surface, providing a moist environment.[9]

Aquacel Ag® is a dressing material which combines Aquacel® and 1.2% silver, thus presenting the advantages of both products. The silver ions show their antimicrobial action when they are slowly released into the wound. The hydrofiber structure provides the moist environment and restrains bacteria in the fibers. *In vitro*, Bowler et al.[10] showed that Aquacel Ag® was effective in various antibiotic-resistant bacteria, such as MRSA, vancomycin-resistant *enterococci* (VRE), *Pseudomonas aeruginosa* (PA), and *Serratia marcescens* (SM). The therapeutic effect was sustained for 14 days. Another study reported the efficacy of Aquacel Ag® on the wound healing rate and decreased pain when the dressing was changed.[5]

Sorbact® is a dressing material using hydrophobic interactions between bacteria. The proteins expressed on the surface of microorganisms induce hydrophobic properties on the surface of the cells; if the microorganisms are close to the hydrophobic solid form of the Sorbact® material, they expel water molecules and attach to the Sorbact® to reduce the increased entropy. *In vitro*, the hydrophobic dressing was able to bind $> 10^8$ *S. aureus* and $> 10^{6,7}$ *Enterococcus faecalis*.[4] Thus, the wound healing was accelerated by reducing the amount of bacteria. This action is halved when the wound is washed with disinfectants or antiseptics before applying the dressing.[4] Therefore, in this experiment, wounds were washed with saline only, when the dressing was changed.

In this study, we compared the above-mentioned dressing materials with the clinically widely used Betadine and Medifoam® dressings. Betadine has a wide range of antibacterial effects, the great advantage of low-cost, and virtually no resistance, so it is a generalized infection wound dressing method.[2] Medifoam® is one of the foam dressing materials, and maintains a wet environment on the wound surface; it absorbs the exudate, accelerates re-epithelization, and does not adhere to the wound bed. Due to these properties, Medifoam® promotes wound healing, however, when used on infected wounds, it can create a good environment for bacterial proliferation, so it may have adverse effects on infected wound healing.

The Aquacel Ag® dressing showed the highest wound healing rate, however, in the early stages of infective wounds with excessive exudate, the dressing formulations failed to maintain the original form and some residues attached to the slough on wounds on removal of the dressing, thus scoring low in both wound bed appearance measurements and swab culture grades. Nevertheless, after 7 days, in the low exudate wounds,

the dressing material was easy to remove and showed rapid improvement in both wound bed state and wound swab culture. In several cases, in the high exudate wounds, the Aquacel Ag® debris was trapped inside the wound tissue and induced a foreign body reaction. These findings were consistent with results from the previous study conducted by Bell.[11] However, the dressing material which did not damage the surface of the wound produced the most rapid wound healing.

In the initial high exudate wound, Sorbact® showed significantly faster improvement in the wound appearance score compared with the other groups, as well as significantly reduced amount of bacteria in the wound swab culture. These effects may be due to removal of bacteria by hydrophobic interactions, as well as to mechanical removal of crust and biofilm when the dressing was changed. After 7 days in the low exudate wound, the decrease in wound size was slower than Aquacel Ag® group. As the wound exudate diminished, Sorbact® detached the newly formed epithelium and granulation tissue when the dressing was changed. Although Sorbact® was soaked with enough saline when the dressing was eliminated, it was not fully wet due to its hydrophobic surface; thus, it was difficult to prevent the desquamation of the wound surface in the Sorbact® group.

The wound size of 1.5 × 1.5 cm, used in other previous studies about the infectious wound healing in rat,[12,13] was considered that the effect of contraction on wound healing was not completely excluded. However, we used this wound defect size without any manipulation, keeping in mind that wound infection effects not only epithelization but also wound contraction, as previously demonstrated.[8,13]

Akiyama et al.[14] reported *Staphylococcus aureus* made biofilm by producing glycoclyx at 4 hours after inoculation on the damaged skin of mice. Ueda et al.[15] reported that critical colonization wound could be made by inoculating *Pseudomonas aeruginosa* in full thickness defect on the back of healthy rat 24 hours after bacterial inoculation. The wound healing in the critical colonization wound group was delayed compared with the control group. In our study, every wound definitely showed the locally infected appearance, covered in biofilm or crust with excessive exudate 24 hours after inoculation.

By testing the cultures with sterile cotton swabs, we investigate the changes in the number of bacteria, and the results were graded for semi-quantification. Measuring the exact number of bacteria in wounds has limitation, but in the clinic, it is the major non-invasive way to evaluate wound infections in patients; thus, it is considered to reflect the antibacterial effects of different dressing materials. In assessing the state of the wound, we referred to the MEASURE Evaluation, which was reported by Keast[6] (M: measure, E: exudate, A: appearance, S: suffering, U: undermining, R: re-evaluate, E: edge). Because we experimented on rats, and used an acute wound infection model, among the multiple assessment items, the wound bed appearance scoring system was applied by a slight modification. It was considered to be useful as a semiquantitative assessment of wound infections with bacterial test. However, as this evaluation does not include the exudate or the adhesion of the dressing material that could lead to wound surface desquamation, it is considered insufficient to predict the rate of the wound size reduction, which is the ultimate goal of wound care.

The Aquacel Ag® and Sorbact® dressings surely seem more expansive than the Betadine soaked dressing. Furthermore, because both dressings need a secondary dressing, the burden on the patient is heavier. Therefore, in terms of cost efficiency, the reasonable choice of the dressing material for wound infection evaluation is very important.

Although Aquacel Ag® and Sorbact® are not representatives for the silver-containing and hydrophobic dressings, this study objectively evaluated the efficacy of the respective dressing formulations. The antimicrobial efficacy of the dressing material, as well as creating appropriate environment for wound healing, must be considered for the ultimate goal of rapid wound healing. Periodic evaluation of the changes in the wound status is important, and the ongoing process of treatment selection should be based on that evaluation.

V. CONCLUSION

Infectious wound healing is best, when the removal of bacteria is effective, and at the same time, the property of the topical dressing material is suitable for it. In this study, Aquacel Ag® and Sorbact® were applied to MRSA-infected wounds and their effects were compared to control groups using Betadine and Medifoam®. Aquacel Ag® showed significantly better effects on wound size reduction, however, in the high exudate wounds, Aquacel Ag® was incompletely removed and remained the dressing debris with slough. Initially, Sorbact® showed significantly faster improvement in the wound bed state and reduction of the bacterial burden. However, in the

low exudate wounds, there was no significant difference compared to the Betadine soaked group in wound size change, because of mechanical loss of the wound surface produced by the Sorbact® dressing material. In conclusion, to accomplish optimal wound healing, the wound states should be evaluated often and the active process of choosing the appropriate dressing materials should be addressed accordingly.

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