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The Effect of Polyurethane Film Versus *Apis Dorsata* Honey Spray for Wound Dressing Following Long Bone Fractures Osteosynthesis

Uzun Kemik Kırıklarında Osteosentez Sonrası Yara Pansumanında Poliüretan Film ve *Apis Dorsata* Bal Spreyinin Etkisi

Surianty Shafei[1,2], Mohd Ariff Sharifudin[1,3], Shaifuzain Ab Rahman[1], Abdul Nawfar Sadagatullah[1]

[1]Universiti Sains Malaysia School of Medical Sciences, Department of Orthopedics, Kubang Kerian, Malaysia
[2]Hospital Sultan Ismail Petra, Department of Orthopedics, Kuala Krai, Malaysia
[3]Universiti Sultan Zainal Abidin Faculty of Medicine, Department of Orthopedics, Kuala Terengganu, Malaysia

ABSTRACT

Objective: Surgical site infection (SSI) following implant-related fracture osteosynthesis remains a burden and challenging for orthopedic surgeons. Honey-based dressings can be used as prophylactic agents.

Methods: This prospective, randomized clinical study was designed to compare the effect of conventional polyurethane film and *Apis dorsata* honey spray as dressing materials after long bone fracture osteosynthesis.

Results: Forty participants with closed tibial or femoral diaphyseal fracture treated with open reduction and internal osteosynthesis with intramedullary implants or plates and screws were randomly divided into 3 groups: 16 were dressed with polyurethane film (group A), 13 with *Apis dorsata* honey spray (group B), and 11 as controls. Wounds of the two groups were dressed using a similar wound protocol immediately (D0) and three days (D3) after surgery. In the control group, wounds were treated with non-adhesive film only. All wounds were evaluated on day 14 (D14) and day 42 (D42) for local complications and the effects on skin commensals. On D42, wound dehiscence and scar formation were also evaluated. *Acinobacter* species were isolated from a control.

Conclusion: One patient from group A had superficial SSI. There was no significant association between wound healing and the dressing materials used. Honey dressing reduced the risk of hypertrophic scar formation. Other outcomes were comparable between groups A and B. *Apis dorsata* honey is a safe alternative dressing that is comparable to polyurethane film as a dressing material following long bone fracture osteosynthesis.

Keywords: Dressing material, fracture fixation, honey dressing, Tualang honey, wound healing

ÖZ

Amaç: İmplantla ilişkili kırık osteosentezini takip eden cerrahi alan enfeksiyonu (CAE), ortopedik cerrahlar için bir yük ve zorluk olmaya devam etmektedir. Bal bazlı pansumanlar profilaktik ajan olarak kullanılabilir.

Yöntemler: Bu prospektif, randomize klinik çalışma, uzun kemik kırığı osteosentezi sonrasında pansuman malzemesi olarak geleneksel poliüretan film ve *Apis dorsata* bal spreyinin etkisini karşılaştırmak için tasarlanmıştır.

Bulgular: Açık redüksiyon ve intramedüller implantlar veya plaklar ve vidalarla internal osteosentez ile tedavi edilen kapalı tibial veya femur diyafiz kırığı olan kırk katılımcı rastgele 3 gruba ayrıldı: 16'sına poliüretan film (grup A), 13'üne *Apis dorsata* bal spreyi (grup B) ve 11'ine kontrol grubu uygulandı. İki grubun yaraları ameliyattan hemen sonra (D0) ve ameliyattan üç gün sonra (D3) benzer bir yara protokolü kullanılarak pansuman yapıldı. Kontrol grubunda yaralar sadece yapışkan olmayan filmle tedavi edildi. Tüm yaralar, lokal komplikasyonlar ve deri komensalleri üzerindeki etkiler açısından 14. günde (D14) ve 42. günde (D42) değerlendirildi. D42'de yara açılması ve skar oluşumu da değerlendirildi. *Acinobacter* türleri bir kontrolden izole edildi.

Sonuç: Grup A'dan bir hastada yüzeysel CAE vardı. Yara iyileşmesi ile kullanılan pansuman malzemeleri arasında anlamlı bir ilişki yoktu. Ballı pansuman hipertrofik skar oluşumu riskini azalttı. Diğer sonuçlar Grup A ve B arasında benzerdi. *Apis dorsata* balı, uzun kemik kırığı osteosentezini takiben pansuman malzemesi olarak poliüretan filmle karşılaştırılabilecek güvenli bir alternatif pansumandır.

Anahtar Sözcükler: Pansuman malzemesi, kırık tespiti, ballı pansuman, Tualang balı, yara iyileşmesi

Address for Correspondence/Yazışma Adresi: Mohd Ariff Sharifudin/Abdul Nawfar Sadagatullah, MMed, Universiti Sains Malaysia School of Medical Sciences, Department of Orthopedics, Kubang Kerian, Malaysia
E-mail / E-posta: ariffsharifudin@unisza.edu.my/nawfar@usm.my
ORCID ID: orcid.org/0000-0002-6796-2904; **ORCID ID:** orcid.org/0003-0618-1562

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INTRODUCTION

Surgical site infection (SSI) carries potential devastating sequalities following implant-related fracture osteosynthesis. These complications remain a challenge, particularly in terms of costs, prolonged hospital stay, morbidity, and even mortality (1-3). Post-surgical wound dressing remains one of the contributing factors to the final wound outcome that needs special attention in reducing SSI (1,4,5). Other factors that may also influence the wound outcome include the severity of the injury, duration of the surgery, and the patient's co-morbidities (2,3,6-9). Wounds involving the lower limbs differ from those involving the trunk in terms of skin tension and involve wider exposed areas with a higher risk of infection. Furthermore, the presence of implants in the wound warrants extra attention in terms of dressing and wound care. Appropriate post-surgical dressing material is paramount in fracture osteosynthesis because any wound infection with an implant beneath may lead to osteomyelitis and result in chronic morbidities to the patient as well as a financial burden to the society (2,3,7,9,10).

Dressing materials are used on surgical wounds to provide a waterproof sealer and to prevent adhesion during wound dressing; hence, they may reduce pain as well. It may also provide a moist environment conducive to wound healing (5,11). Several dressing materials are commonly used, including polyurethane-based film dressing and paraffin-based materials. Polyurethane film spray, commonly known as Opsite* spray, is a convenient and innovative, quick-drying transparent film dressing spray for surface and surgical wounds. This product is widely used in local hospitals as a dressing material for post-surgical wounds. In orthopedic surgery, polyurethane film spray is a common dressing applied after long bone fracture osteosynthesis.

Honey is a semi-solid or saturated solution of natural sugars synthesized from flower nectar by honeybees (12,13). Although honey of various types shares the same general content and properties, each type has different potential and uses depending on the type, honeybee species, purity, and geographical origin (12-15). *Apis dorsata* or Asian rock bees produce honey in hives built high up in the Tualang tree (*Koompassia excelsa*), one of the tallest trees in Malaysia (12,13,15-17). Thus, the honey is also famously known as the Malaysian Tualang honey. It is one of the examples of local honey that can act as a potent anti-inflammatory agent with effective antimicrobial and antifungal effects, attributed to its high level of phenolic acids and flavonoids (13-15,18,19). Various studies have reported its effectiveness in treating diabetic wounds, burns, and other types of infected wounds (4,12,13,15,19,20).

To the best of our knowledge, there has been no study conducted on the potential of honey as a wound dressing post-osteosynthesis of fractures. Hence, the present study aimed to compare the effect of using a conventional polyurethane film (Opsite* spray) with *Apis dorsata* honey spray as a dressing material following internal osteosynthesis of long bone fractures.

MATERIALS AND METHODS

The study was designed as a prospective, randomized, unblinded, controlled study recruiting patients with closed tibial or femoral diaphyseal fracture treated with open reduction and internal osteosynthesis using intramedullary implants or plates and screws. The participants were selected among trauma patients aged between 15 and 45 years at the time of injury within a 12-month study period at a single tertiary center. Only patients who underwent primary closure of the surgical wound following the surgical procedures were included in the study. Patients who sustained any previous open fractures or osteomyelitis involving the ipsilateral bone were excluded from the study. Those with a history of allergic reactions to any honey-based products, a history of bronchial asthma, or a history of developing allergic reaction to any of the materials used in the study were also excluded. Other exclusion criteria were immunocompromised patients, prolonged use of corticosteroids, chemotherapy treatment, or a history of renal failure or diabetes mellitus.

The study was commenced after approval by the Human Research Ethics Committee USM (HREC) [approval number: USMKK/PPP/JEPeM/254.3(7.2)]. The participants were provided with complete information about the aims and the flow of the study. Written informed consent was required to participate in the study. The routine clinical assessment and treatment for which the participants came were conducted as usual, and none of the participants abandoned their right to receive the best possible consultation despite being part of the study.

The participants' basic demographics and detailed current and previous medical histories were recorded in a study proforma. This includes the severity of soft tissue injury sustained along with the long bone fracture. The severity of soft tissue injury associated with closed fractures was graded using the Tscherne and Oestern classification (21) (Table 1).

Randomization and Dressing Materials Used

Based on the dressing materials used following the intended internal osteosynthesis, the participants were divided randomly into 3 groups. In group A, the patients were subjected to wound dressing with polyurethane film (Opsite* spray), a moisture vapour permeable dressing spray that contains an acrylic copolymer, isopropyl alcohol, acetone, ethyl acetate, and propellants (dimethyl ether and butane 40), supplied by Smith & Nephew Malaysia. *Apis dorsata* honey spray was used for wound dressing in group B. Honey spray was supplied by the Federal Agricultural Marketing Authorities in a single batch in collaboration with the School of Pharmaceutical Sciences laboratory. The participants' wounds in the control group were dressed only with a breathable, self-adhesive, and absorbent film dressing (Mepore®) supplied by Molnlycke Health Care US. It is widely available in operation theatres as a standard dressing following Opsite* spray application.

Randomization was performed via elective operating theatre that available during working hours. The selection of dressing material for the patients was based on their operation day. The participants who were operated on Mondays and Thursdays were subjected to polyurethane film dressing. Honey spray dressing was used on the participants operated on Tuesdays and Fridays. Participants who were operated on Wednesdays were grouped as controls. The decisions on which operation day was chosen were based on the availability of the empty slot in the elective lists and the semi-emergency lists. The participants who were admitted earlier had priority to be listed in the operation lists.

All participants in group B were screened for allergy to the honey spray dressing one day before surgery. The dressing material was applied to the dorsum area of the participants' hands. Any form of allergic reactions, such as rashes, itchiness, or others, was observed and documented. This step was clearly stated in the written consent form and explained in detail to all participants. Participants who developed adverse reactions to the dressing material were excluded from the study.

Wound Closure and Dressing Technique Protocol

Following open reduction and internal osteosynthesis performed in the standard manner, all surgical wounds were primarily closed with Vicryl 2/0 and Dafilon 3/0 sutures (Figure 1A). The length of the surgical wounds was recorded in centimeter (cm) units (Figure 1B) and the operative time in hours and minutes. For the patients in groups A and B, a thin layer of the respective dressing materials was applied to the surgical wound immediately after wound closure (D0), followed by application of the non-adhesive film (Mepore®). The control group was treated with film (Mepore®) only.

Wound Assessment

The first wound inspection for all wounds was performed on D3 post-surgery, followed by the second assessment on D14 during surgical suture removal (Figure 2). Assessment included the presence of local changes such as redness around the wound, local oedema, and serous or purulent discharge. Signs of adverse reactions, such as itchiness and blister formations, were observed and documented, if any. After wound inspection on D3, a swab for culture and sensitivity was taken, and the wounds were re-applied with similar dressing materials used immediately after the surgery.

The third and final assessment was performed during follow-up on D42 post-surgery. Any wound dehiscence or discharge was observed and recorded. The surgical scars were evaluated and documented as a normal scar appearance or a hypertrophic scar (protruding scar resembling a fibroma or collagen nevus).

RESULTS

A total of 42 participants fulfilled the study criteria. The following randomization, there were 16 participants in group A, 14 participants in group B, and 12 participants as controls. One participant from group B and the control group defaulted to follow-up and was excluded from the study. The remaining participants (n=40) consisted of 17 female and 23 male participants with a mean age of 19 years. None of the participants in group B developed an allergic reaction to the *Apis dorsata* honey dressing spray.

Femoral fractures were fixed in 33 participants (82%) and only 7 participants (18%) had tibial fractures. One participant from group A had bilateral femoral fractures. Thirty-eight participants had undergone open reduction and plating compared with intramedullary nailing in 2 participants. Associated injuries included fracture of the radius and scapula, avulsion fracture of the posterior cruciate ligaments, and concomitant fracture of the femur or tibia. There were 3 participants with polytrauma, one in each group. Only 3 participants (7.5%) had grade C2 soft tissue injury. The remaining participants either had grade C0 [19 (47.5%)] or C1 [18 (45%)]. None had grade C3 soft tissue injury. The mean operating time in all cases was 80 min. The mean length of the surgical wounds was 16.11 cm. The mean duration from the time of injury to the time of surgery was 5 days and 19 hours.

Wound Complications

None of the participants in all the 3 groups had clinical signs of

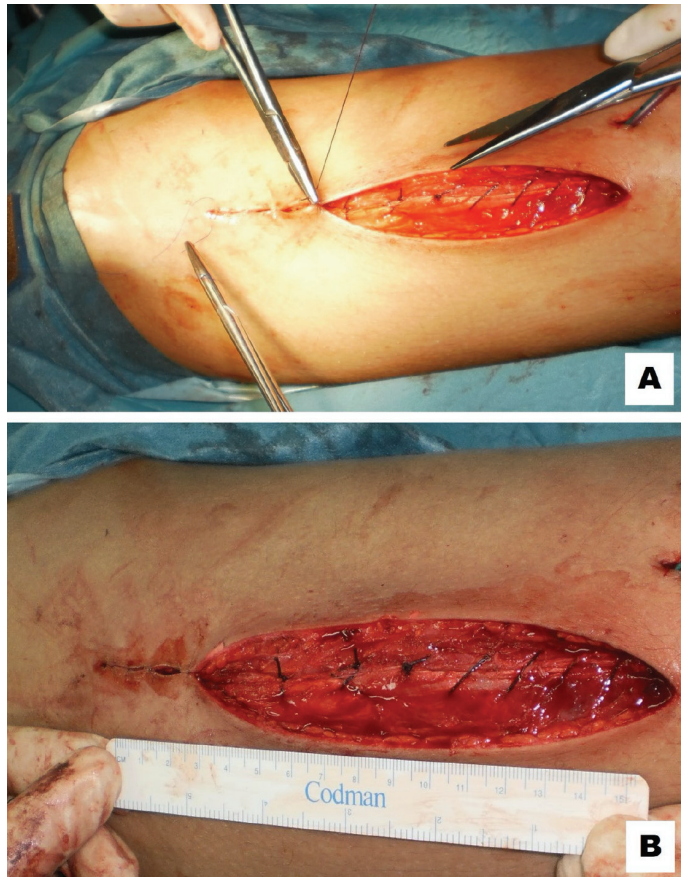

Figure 1. (A) Fascia closed with vicryl 2/0 and skin closure with dafilon 3/0 suture. (B) The surgical wound was measured using a sterile ruler in centimeter units.

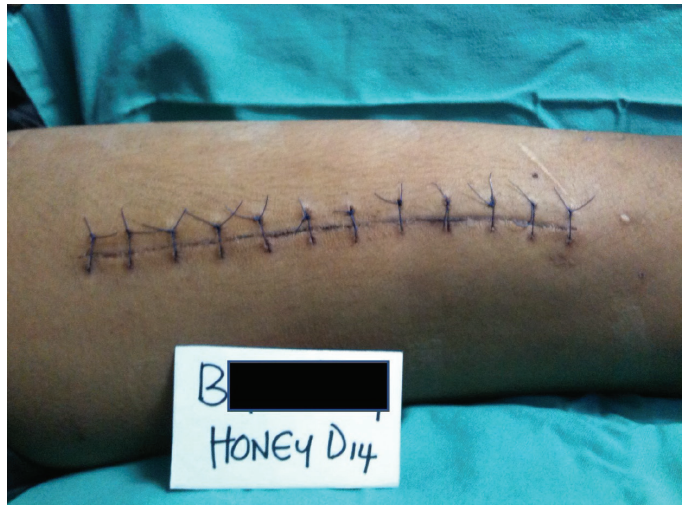

Figure 2. Wound appearance of a patient from group B.

infection on D3 post-surgery. However, a participant from group A had a 2 cm superficial wound dehiscence with serous discharge identified during surgical suture removal. The wound healed well following dressing with normal saline and sterile strip application. No further antibiotics or debridement was required. Analysis using Fisher's exact test found no significant correlation between wound complications and the dressing materials used ($p>0.950$).

Wound Commensal Microorganisms

Acinobacter species was isolated via swab culture from the surgical wound of a participant from the control group on D3 post-surgeryday 3. However, Fisher's exact test analysis also found no significant correlation between the dressing materials used and their effect on wound commensal microorganisms ($p>0.275$).

Wound Assessment on D42

All wounds healed without any clinical signs of infection or dehiscence on D42 post-surgery. Only 3 out of 13 patients (23.1%) in group B had a hypertrophic scar compared with group A (43.8%) and the control group (72.7%) (Figure 3). Table 2 summarizes the association between the dressing material used and wound healing.

Factors Influencing Wound Healing

Simple logistic regression showed that none of the factors analyzed except for the dressing material used was significant in influencing wound healing in all patients. Multiple logistic regression analysis showed that the use of honey dressing spray had a significant influence on wound healing. These are summarized in Tables 3, 4.

DISCUSSION

The majority of participants (82%) in the present study had femoral fractures, although the tibia is the most common long bone fracture of the lower limbs (6,7,21). One of the criteria of patients who were recruited for this study was any fracture of the femoral or tibial shaft that required open reduction and was internally fixed with an implant device. Thus, the smaller number of participants with tibial fracture included in the study was because this type of fracture may be treated conservatively with a full-length cast or intramedullary device with a close reduction method. Compared with femoral fractures in adults, it is rarely indicated for conservative treatment with closed reduction method and casting. Almost all participants were treated with plating of the fractures compared with intramedullary fixation. This finding corresponds with the standard technique of surgery that ordinary compression plates generally need an open reduction method compared with intramedullary fixation, which can be performed using the closed method or indirect reduction (7,21). The recommended fixation of closed diaphyseal femoral and tibial fractures generally involves either intramedullary nailing or plating. However, plating usually has a narrow indication of usage, for example in diaphyseal fracture with concurrent neck of femur fracture.

Most participants (80%) had other associated injuries, which may contribute to the mean duration before surgery. It will influence the urgency of the surgery compared with elective surgery in a stable trauma case. The severity of soft tissue injury contributes to the risk of wound infection and the healing process (6,7,21). There was an equal distribution of participants in the groups with regard to the severity of soft tissue injuries. Thus, each group of participants had a similar risk of infection and outcome.

The duration of the wound exposed to the environment and the length of the wound will influence the rate of SSI (2,7,9). The entire cohort of participants had a mean operating time of 2 h and a mean wound length of 16.11 cm. The complexity and difficulty in the internal osteosynthesis method were also determined by the types of fracture, availability of an appropriate implant, and surgeon's experience. There is a standard surgical exposure for open reduction and osteosynthesis of femoral and tibial diaphyseal fractures, but no standard wound length is recommended in the literature. Adequate exposure for assisting in the surgical procedure is generally quoted (7,22).

There was an isolated case of superficial wound infection in group A, as evident by the presence of wound dehiscence and serous discharge at D14 post-surgery. No intervention was needed as the wound healed well until the final assessment on D42. The participant underwent open reduction with intramedullary femoral osteosynthesis at 3 weeks after trauma because of a limited slot for elective operation. The decision to use the open reduction method was made due to the difficulty in fracture reduction as soft callus had already formed. The surgery was completed within 130 min. No other associated injuries were noted. The longer operating time with difficult reduction were the possible factors that influenced wound healing in the patient.

One of the aims of wound assessment was to identify local adverse reactions to honey spray. None was detected in all participants in group B. Although the participants in group B had yellowish skin staining surrounding the wound from the honey dressing, it did not affect wound healing, and the stain was easily resolved with normal saline irrigation. There was no significant correlation between the dressing materials used and wound complications. These results may be due to the strict selection of participants and the small sample size. Young and fit individuals, mild to moderate soft tissue injuries, and simple fracture patterns also have a good prognosis in wound healing (21). Thus, the dressing method is not the only factor that affects the wound healing process.

The thin film formed on the wounds in groups A and B acted as a barrier to the external environment. Limited studies are available to prove whether the film may reduce the number of commensals on the skin. In a study by Wille and Blussé van Oud Alblas (23), polyurethane

Table 1. Tscherne and Oestern classification for closed fractures (24)

Grade	Energy	Typical fracture pattern	Typical soft tissue damage
C0	Low	Spiral	None to minimal
C1	Mild to moderate	Rotational ankle fractures and dislocations	Superficial abrasion/ contusion
C2	High	Transverse segmental complex	Deep abrasions
C3	High	Complex	Extensive skin contusion

Figure 3. Example of hypertrophic scar formation in a patient in group A.

film with chlorohexidine possessed the most antimicrobial activity with regard to the microflora of the skin. However, this study showed no significant correlation between the dressings used and their effects on wound commensals. The only microorganism that was isolated from one of the participants' wounds (from the control group) was *Acinobacter* species. *Acinetobacter* species is a Gram-negative *Coccobacillus* that is found within environmental soils, water, sewage, and foodstuffs (as spoilage organisms) such as milk products, meat, poultry, and fish. Microorganisms also present as commensals in human skin. In immunocompromised patients, it may become virulence and responsible for SSI and other healthcare-associated infections in intensive care units (8,9). In the case of a control in this study, the participant remained asymptomatic because he was a healthy and fit individual. His wound also healed without any complications.

Table 2. Association between dressing materials and wound healing

Group	Wound assessment on D42		c^2 stat (df)	p-value*
	Healed with a normal scar	Healed with a hypertrophic scar		
Group A	9	7	5.951 (2)	0.051
Group B	10	3		
Control group	3	8		

*Chi-square test.

Table 3. Clinical factors influencing wound healing analyzed using simple logistic regression

Clinical Factors		Crude OR (95% CI)	p-value
Age		1.020 (0.923; 1.127)	0.702
Gender			
	Male	0.865 (0.246; 3.050)	0.822
	Female	1	
Type of dressing material			
	Polyurethane film (group A)	0.292 (0.056; 1.525)	0.144
	Honey spray dressing (group B)	0.133 (0.018; 0.716)	0.021
	Control group	1	
Site of the fracture			
	Diaphysis of the right tibia	0.000 (0.000; 0.000)	0.950
	Diaphysis of the right femur	0.675 (0.168; 2.709)	0.579
	Diaphysis of the left tibia	0.250 (0.021; 3.041)	0.277
	Diaphysis of the left femur	1	
Type of implant			
	Intramedullary nails	1.235 (0.072; 21.241)	0.884
	Plates and screws	1	
Associated injuries			
	No	0.680 (0.139; 3.337)	0.635
	Yes	1	
Soft tissue injury			
	Grade C2	4.333 (0.326; 57.649)	0.267
	Grade C1	2.708 (0.708; 10.360)	0.146
	Grade C0	1	

Table 3. Continued

Clinical factors	Crude OR (95% CI)	p-value
Duration of injury to surgery	0.999 (0.996; 1.003)	0.707
Duration of surgery	1.003 (0.982; 1.026)	0.757
Surgical wound length	1.183 (0.888; 1.577)	0.251

OR: Odds ratio, CI: Confidence interval.

Table 4. Clinical factors influencing wound healing analyzed using multiple logistic regression

Clinical factors	B	Adjusted OR (95% CI)	p-value
Type of dressing material			
Polyurethane film (group A)	-1.232	0.292 (0.056, 1.525)	0.144
Honey spray dressing (group B)	-2.185	0.133 (0.018, 0.716)	0.021
Control group		1	

Backward LR method applied. Hosmer and Lemeshow test, p=0.866. Classification table 67.5% correctly classified. The area under the receiver operating characteristic curve was 0.708. OR: Odds ratio, CI: Confidence interval.

None of the participants had wound dehiscence at the end of the study period. The rate of SSI in a clean surgery is 1 to 2% (2,3,24). The possible reason for no case of wound infection in the current study was the strict study criteria of healthy individuals without co-morbidities. Surgical prophylactic antibiotic usage also plays a role in reducing wound infection (1-3,8-10). All patients in this study were administered intravenous cefuroxime 1.5 g as a prophylactic antibiotic before surgery.

Another finding that was recorded during the final wound assessment was the presence of a hypertrophic scar. The current study showed not significant association between the type of dressing used and healing. Although in group B, most patients' wounds healed with a normal healthy scar compared with the wounds of the other two groups, this cannot reflect the advantages of honey dressing as the result was not statistically significant (Table 2). The possible reasons were limited sample size and crude assessment of the scars at D2 post-surgery.

Study Limitations

A better scar assessment should involve an expert plastic surgeon or team with more objective scar evaluation, which was one of the limitations of the study. Nevertheless, multiple logistic regression analysis revealed that patients dressed with honey spray dressing had a lower risk of developing hypertrophic scars compared with the other groups (Table 4). This result was attributed to the anti-inflammatory and antimicrobial potential of honey, and its effects on reducing wound contracture (13,16,25). Mohamad Shah et al. (26) reported that apart from the antimicrobial effects, the active components of *Apis dorsata* honey also demonstrated an antiproliferative effect on human keloid fibroblasts, with the potential to be used for keloid treatment.

CONCLUSION

Apis dorsata honey spray has comparable effects with the widely used polyurethane film for wound dressing following long bone osteosynthesis. Apart from promoting healing and preventing SSI, the risk of hypertrophic scar formation was lower.

Acknowledgments: The findings of the present study were presented at the Medical Research Symposium 2021 organized by the Kulliyyah Faculty of Medicine of International Islamic University Malaysia on December 14th, 2021 and received the second best clinical oral presentation award.

Ethics

Ethics Committee Approval: The study was commenced after approval by the Human Research Ethics Committee USM (HREC) [approval number: USMKK/PPP/JEPeM/254.3(7.2)].

Informed Consent: Written informed consent was required to participate in the study.

Authorship Contributions

Concept: S.S., M.A.S., S.A.R., A.N.S., Design: S.S., M.A.S., S.A.R., A.N.S., Data Collection or Processing: S.S., M.A.S., S.A.R., A.N.S., Analysis or Interpretation: S.S., M.A.S., S.A.R., A.N.S., Literature Search: S.S., M.A.S., S.A.R., A.N.S., Writing: S.S., M.A.S., S.A.R., A.N.S.

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