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Efficacy and Safety of PL-5 (Peceleganan) Spray for Wound Infections

A Phase IIb Randomized Clinical Trial

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Objective: To assess the safety and efficacy of antimicrobial peptide PL-5 (Peceleganan) spray in the treatment of wound infections.

Background: Antimicrobial peptide PL-5 spray is a novel topical antimicrobial agent.

Methods: We conducted a multicenter, open-label, randomized, controlled phase IIb clinical trial to evaluate the efficacy and safety of PL-5 spray, as compared with silver sulfadiazine, in patients with skin wound infections. The primary efficacy outcome was the clinical efficacy rate on the first day after ending the treatment (D8). The secondary efficacy outcome was the clinical efficacy rate on the fifth day posttreatment (D5), the bacteria clearance rate, and the overall efficacy rate at the mentioned 2 time points. The safety outcomes included adverse reactions and pharmacokinetic analysis posttreatment.

Results: A total of 220 patients from 27 hospitals in China were randomly assigned to 4 groups. On D8, the efficacy rate was 100.0%, 96.7%, 96.7% for the 1‰ PL-5, 2‰ PL-5, 4‰ PL-5 groups, respectively, as compared with 87.5% for the control group. The efficacy rate among the 4 groups was significantly different ($P < 0.05$). On D5, the efficacy rate was 100.0%, 93.4%, 98.3% for the 1‰ PL-5, 2‰ PL-5, 4‰ PL-5 groups, respectively, as compared with 82.5% for the control group. The efficacy rate among the 4 groups was significantly different ($P < 0.05$). The blood concentration of PL-5 was not detectable in pharmacokinetic analysis. No severe adverse event related to the application of PL-5 was reported.

Conclusions: Antimicrobial peptide PL-5 spray is safe and effective for the treatment of skin wound infections.

Trial Registration: ChiCTR2000033334.

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Wound infections due to various causes has been considered as the most devastating complications of the wound healing process.1,2 Topical antimicrobial agents are frequently used to treat infected skin wounds in addition to intravenous or oral antibiotics, however, the choices of conventional topical antimicrobial agents are limited. As antibiotic resistance has become a worldwide concern due to the fast bacterial mutations and adaptations,2,3 quite a number of researchers have turned their attention to antimicrobial peptides (AMPs),4,5 a numerous and diversified group of small peptides endowed with potent antibacterial, antiviral, and antifungal activities.6–8 AMPs cause bacteria disruptions through nonspecific interactions with the surface membrane of pathogens, a mechanism that is less likely to induce resistance.3 Therefore, AMPs are recognized as a potential source of pharmaceuticals targeting antibiotic-resistant bacterial infections.6 Nowadays, >4000 AMPs with antimicrobial activity have been identified.2,4 Unfortunately, a large number of them have failed to reach the clinical trial stage due to in vivo ineffectiveness, toxicity, and other economic issues.2,3,9

PL-5 (Peceleganan) is one of the AMPs screened from hundreds of candidates in our rationally designed AMP library,4,10,11 which is a chemically synthesized α-helical AMP containing 26 amino acid residues. PL-5 spray is the first topical AMP spray agent specifically developed for skin wound infections. In the preclinical studies, as compared with conventional antibiotics, PL-5 showed a stronger and broader spectrum of antibacterial activities against both Gram-positive and Gram-negative bacteria,12 advantageously for drug-resistant bacteria (Supplementary Appendix p.3–14, Supplemental Digital Content 1, http://links.lww.com/SLA/D862). Pharmacodynamics tests, toxicity tests, allergy, and irritation tests, phase I and phase IIa clinical trials were all successfully accomplished with encouraging results (Supplementary Appendix p.15–24, Supplemental Digital Content 1, http://links.lww.com/SLA/D862).

The primary objectives of this phase IIb clinical trial were evaluating the safety and efficacy of PL-5 spray in the treatment of wound infections as compared with active control drug silver sulfadiazine (SSD) cream. The secondary objectives were confirming the optimal dosage of PL-5 spray for clinical application, and evaluating the pharmacokinetic (PK) characteristics of the PL-5 absorbed through the wound bed.

METHODS

The study was conducted in China involving 27 hospitals. A full list of principal investigators is given in the appendix (Supplementary Appendix p.1–2, Supplemental Digital Content 1, http://links.lww.com/SLA/D862). The study was designed and reported in accordance with The CONSORT statement,13 and conducted in accordance with the ethical principles of the Declaration of Helsinki,14 and the Good Clinical Practice guidelines of the International Council for Harmonisation.15 Ethical approvals from each independent ethics committee were obtained. The study protocol and the statistical analysis plan is included in the Supplementary Appendix (Supplemental Digital Content 1, http://links.lww.com/SLA/D862).

Study Design

The trial was divided into 2 parts. Part 1 was a multicenter, open-label, randomized, controlled phase IIb clinical trial designed to evaluate the efficacy and safety of PL-5 spray, as compared with an active control drug, the SSD cream (a widely used conventional topical antibiotic agent which has a broad antibiotic spectrum and rarely causes drug resistance),16 for the treatment of skin wound infections. Also, the optimal effective dosage of PL-5 spray was explored. Part 2 of the trial evaluated whether PL-5 spray may enter the bloodstream by absorption through the wound bed. For part 1 of the trial, patients with skin wound infections were recruited and randomly assigned to 4 groups, receiving 1‰ PL-5 or 2‰ PL-5 or 4‰ PL-5 or 1% SSD treatment, respectively. For part 2 of the trial, patients who consented to blood sample collection were all given 4‰ PL-5 for the treatment of skin wound infections. Blood samples from these patients were collected at designated time points according to the PK analysis protocols.

Patients

Eligible patients were between 18 and 75 years of age, diagnosed with secondary open wound infections caused by burns, abrasions, scratches, lacerations, stitched wounds, trauma ulcers, pressure ulcers, venous ulcers, or Wagner grade 2 diabetic foot ulcers, etc. The Skin Infection Rating Scales (SIRS) (Table S1, Supplemental Digital Content 1, http://links.lww.com/SLA/D862) scores of the infected wounds were no <8, and the patients met the clinical indications for topical antibiotic treatment. A positive microscopic bacteria examination was needed before the onset of the study. Table S2 (Supplemental Digital Content 1, http://links.lww.com/SLA/D862) details the inclusion and exclusion criteria adopted. Investigators from each center would supply information about the trial individually to each participant and their caregivers. All the participants gave their written consent before the onset of interventions.

Randomization

Block randomization allowed to assign the participants to the distinct groups. SAS software (version 9.4 or above) was used to generate single random numbers for each participant. Once the subjects had been enrolled successfully, the researchers obtained the group allocation number through the central randomization system and applied the treatment following the instructions.

Procedures

Studied wound areas were determined according to the study protocol (Protocol p.10). Clinicians were instructed to debride and wash each wound with standard procedures before applying the investigated or control drugs. For the treatment groups, PL-5 spray was administered evenly on the wounds, then covered with 2 layers of sterilized gauzes soaked with PL-5, subsequently covered with vaseline gauze, and bandaged with sterile gauzes. The dressing change was performed daily, at a fixed hour, and repeated for 7 consecutive days. For the patients receiving control treatment, the SSD cream was directly and evenly smeared on the wound surface, and covered with double layers of sterile gauze rubbed with SSD cream. Vaseline gauze and sterile gauze dressings were covered similarly. Exactly as the treatment groups, the dressing change was performed once a day at a fixed hour and repeated for 7 consecutive days. Standard wound care was given to the other nonstudied wound areas. During the observation period of the trial (D1–D8), drugs that could potentially promote wound healing, including growth

factors, peeling cream, and growth hormones were not applied to the wounds under study. Also, during the trial administration period, the topical and systemic application of any other antibiotic was not permitted.

Outcomes

On the fifth day (D5) and eighth day (D8) after the treatment onset, at each center, 1 or 2 assessors, who were not aware of the patients' grouping information, evaluated the wounds using the SIRS. The drugs on the wounds were cleansed before the evaluation. Photographs of each wound were taken using standard procedures. The clinical efficacy was evaluated through comprehensively considering SIRS scores, patient's clinical symptoms, physical examinations, and laboratory tests results. The investigator who was in charge of the individual patient (usually the attending physician) reached the decision about the efficacy regarding the treatment. The criteria for "effective" were reduced SIRS scores and improved symptoms, physical examinations signs, and nonmicrobiological laboratory test results. The treatments with unchanged or increased SIRS scores, or showing new signs of infection, or having used other antimicrobial treatments were all considered as "lacking efficacy."

Microbiological efficacy was evaluated by comparing bacteria culture results from wound swab samples taken on D1, D5, and D8. The examination results were categorized as: pathogen clearance (no pathogenic bacteria were cultured from the original infection site); assumed clearance (wound healed, with no culture sample obtained); nonclearance; assumed nonclearance; partial clearance; recurrence; bacterial flora alternation; superinfection; and colonization." The bacterial clearance rate was calculated by combining "clearance" and "assumed clearance" counts.

The overall efficacy was evaluated by a comprehensive consideration of clinical results and bacteriological results, which included 2 categories: effective and ineffective. The subject with clinical efficacy and "clearance" or "assumed clearance" bacteriological results belongs to the overall effective category. The overall ineffective category included the subject who was clinically ineffective, or the bacteriological result had one of these situations: nonclearance, assumed nonclearance, partial clearance, recurrence, bacterial flora alternation, superinfection, colonization, or both. If one item of the subject's clinical and bacteriological results was ineffective and the other was missing, the comprehensive efficacy should be ineffective.

For the PK group, blood was drawn at the designated time points (Protocol p.5).

The primary efficacy outcome was the clinical effective rate on D8. The secondary efficacy outcome included clinical, microbiological, and overall efficacy evaluations. Specifically, the clinical efficacy on D5, the bacteria clearance rates on D5 and D8, and the overall efficacy on D5 and D8.

The safety outcomes included patients' vital signs, physical examinations, 12-lead electrocardiogram, laboratory tests, adverse reactions, and posttreatment PK analysis. Any adverse event (AE) was monitored and recorded through the whole period of the study.

The data collection and management of the study was performed using the Electronic Data Collection (EDC) system. The data management process complied with Good Clinical Practice (GCP) requirements and was in accordance with the standard operating procedures of the data management department, to ensure true, accurate, complete, reliable, and traceable clinical data.

Statistical Analysis

SAS 9.4 (SAS Institute Inc.) was used for statistical analysis. Continuous variables were analyzed by case number, mean, SD, median, quartile, minimum and maximum values. Categorical variables were analyzed by case number and percentage. Sample size was decided according to the results of the phase IIa study, of which the clinical cure rate of the experimental group was $>80\%$, and that of the control group was 70% (unpublished data). Setting the clinical cure rate of the experimental group as no $<60\%$, $\alpha = 0.05$ (bilateral test), power $(1-\beta) = 85\%$, then each dose of the experimental group required 39 subjects, and the number of cured subjects was not <29. Therefore, taking shedding and other factors into account, each dose group was increased to 60 cases. The main analysis of the primary and secondary outcomes was performed in all patients who underwent randomization. The analysis of the safety outcomes included all patients who received at least 1 treatment, and their safety data was recorded.

The baseline characteristics of the participants and protocol adherence are provided as descriptive data: qualitative variables are expressed as percentages and quantitative variables as either means with SDs or medians with interquartile ranges, as appropriate.

RESULTS

Patients

Between July 29, 2020, and May 10, 2021, 338 patients across 27 centers in China underwent screening and 220 underwent randomization in part 1 of the trial. The enrolled patients were randomly assigned to receive 1‰ PL-5 (59), 2‰ PL-5 (61), 4‰ PL-5 (60), or 1% SSD (40) as treatment. Overall, 59 (100%) of the patients in the 1‰ PL-5 group, 57 (93.4%) of those in the 2‰ PL-5 group, 59 (98.3%) of those in the 4‰ PL-5 group, and 36 (90.0%) of those in the 1% SSD control group completed the trial. The CONSORT flow diagram was shown in Figure 1. The demographic and clinical characteristics of the patients at baseline were similar across the groups (Table S3, Supplemental Digital Content 1, http://links.lww.com/SLA/D862). In part 2 of the trial, 6 patients were recruited to the PK group, and all of the subjects successfully completed the study.

Primary Outcome

On D8, the clinical efficacy rates were 100.0% (59/59), 96.7% (59/61), 96.7% (58/60), and 87.5% (35/40) across the 4 groups (ie, 1‰ PL-5, 2‰ PL-5, 4‰ PL-5, and 1% SSD, respectively) in terms of reduced SIRS scores as compared with baseline, and improved symptoms, signs, and nonmicrobiological indexes (Table 1). There were significant differences among the 4 groups about the clinical efficacy rate ($P = 0.0193$). At the same time point, the clinical efficacy rates were 91.5% (54/59), 83.6% (51/61), 85.0% (51/60), and 60.0% (24/40) across the 4 groups in terms of a $>50\%$ reduction of SIRS scores as compared with baseline, in addition to improved symptoms, signs, and nonmicrobiological indexes (Fig. 2). The stratified analysis of SIRS scores in terms of each evaluation items were listed in Table S4 (Supplemental Digital Content 1, http://links.lww.com/SLA/D862).

Secondary Outcome

Clinical Efficacy Evaluation

On D5, the clinical efficacy rates were 100.0% (59/59), 93.4% (57/61), 98.3% (59/60), and 82.5% (33/40) across the 4 groups, respectively in terms of reduced SIRS scores as compared with baseline, and improved symptoms, signs, and

nonmicrobiological indexes (Table 1). There were significant differences among the 4 groups about the clinical efficacy rate ($P = 0.0009$). Considering a $> 50\%$ reduction of SIRS scores as compared with baseline, in addition to improved symptoms, signs, and nonmicrobiological indexes, the clinical efficacy rates across the 4 groups were 64.4% (38/59), 68.9% (42/61), 53.3% (32/60), and 40.0% (16/40), respectively (Fig. 3). The stratified analysis of SIRS scores in terms of each evaluation items were listed in Table S4 (Supplemental Digital Content 1, http://links.lww.com/SLA/D862). On both D5 and D8, there was no significant difference of overall efficacy between each PL-5 groups and the control group (Table 1).

Microbiological Efficacy Evaluation

On both D5 and D8, there was no significant difference in bacteria clearance rates between each PL-5 groups and the control group (Table 1). The results of bacteria cultures at baseline are shown in Table S5 (Supplemental Digital Content 1, http://links.lww.com/SLA/D862).

Concerning microbiological tests, in total, we examined minimum inhibitory concentration (MIC) for 838 strains of identified microbes, including 9 species accounting for 87.0% of the examined microbes, which are also the main species of clinically pathogenic bacteria causing wound infections. The results showed those 9 species of bacteria were all sensitive to PL-5 spray except for *Enterococcus faecalis*. The MIC_{50} and MIC_{90} of PL-5 against the 9 species of microbe strains and their resistance to 4 control antibiotics are listed in Table 2.

Overall Efficacy Evaluation

On both D5 and D8, there was no significant difference of overall efficacy between each PL-5 groups and the control group (Table 1).

Safety Outcome

There were no specific findings to report regarding patients' vital signs, physical examination, electrocardiogram, and laboratory tests among different groups. The PK analysis of the PK group and AEs are reported as follows.

PK Group

Concerning the PK group patients, after the administration of PL-5 on the wound, the blood concentration of PL-5 was not detectable (ie, below the detectable concentration 1 ng/mL) in all 6 patients, suggesting that PL-5 spray did not enter the blood circulation system after its local administration at the wound.

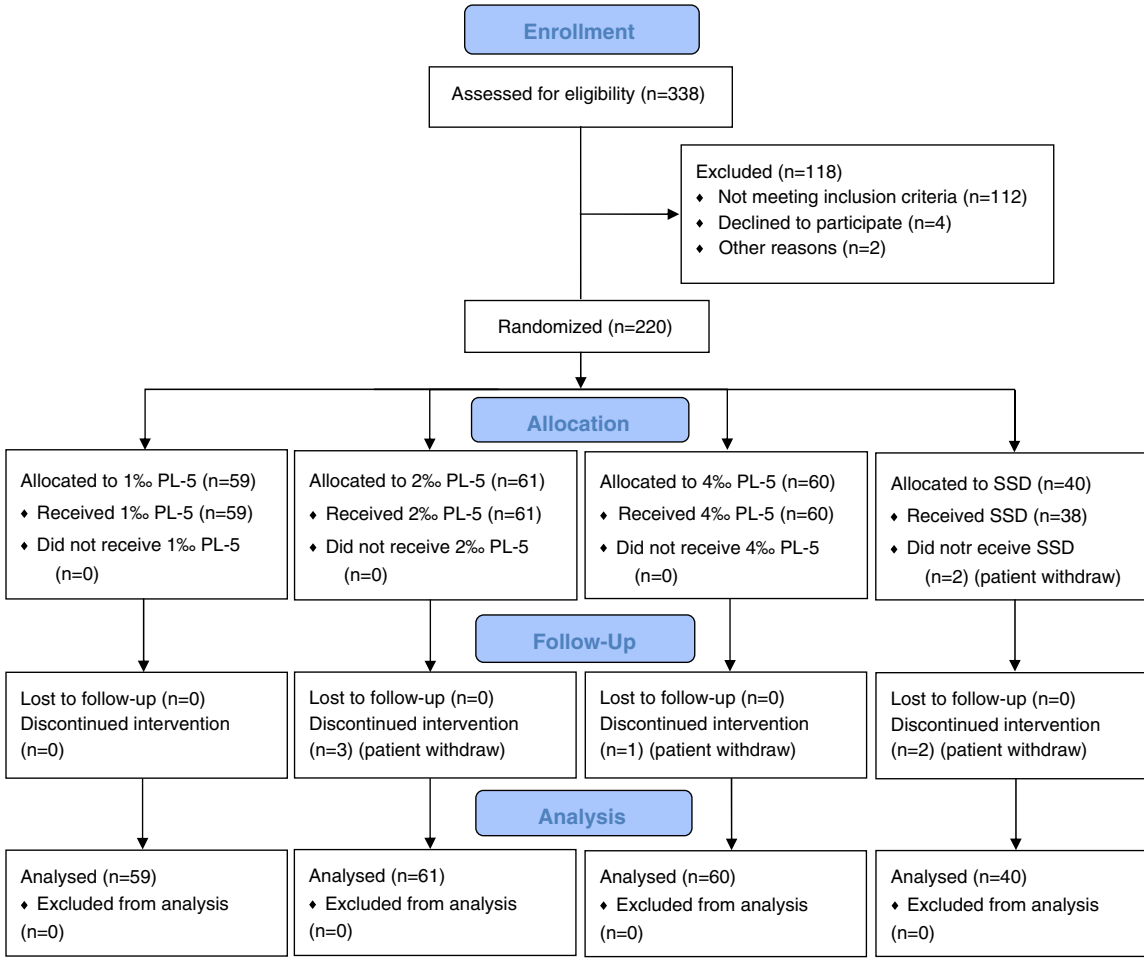

FIGURE 1. CONSORT flow diagram of the enrollment and randomization of the subjects.

TABLE 1. Primary and Secondary Outcomes in the Intention-to-treat Population

	1‰ PL-5 (N = 59)	2‰ PL-5 (N = 61)	4‰ PL-5 (N = 60)	1% SSD (N = 40)	*P* (χ^2 Test)
Clinical efficacy rate (D8)					
n (%)	59 (100.0)	59 (96.7)	58 (96.7)	35 (87.5)	0.0193
95% CI	93.9–100.0	88.7–99.6	88.5–99.6	73.2–95.8	
Clinical efficacy rate (D5)					
n (%)	59 (100.0)	57 (93.4)	59 (98.3)	33 (82.5)	0.0009
95% CI	93.9–100.0	84.1–98.2	91.1–100.0	67.2–92.7	
Bacteria clearance rate (D8)					
n (%)	9 (15.3)	13 (21.3)	10 (16.7)	11 (27.5)	0.4339
95% CI	7.2–27.0	11.9–33.7	8.3–28.5	14.6–43.9	
Bacteria clearance rate (D5)					
n (%)	6 (10.2)	10 (16.4)	5 (8.3)	8 (20.0)	0.2753
95% CI	3.8–20.8	8.2–28.1	2.8–18.4	9.1–35.6	
Overall efficacy rate (D8)					
n (%)	9 (15.3)	14 (23.0)	10 (16.7)	11 (27.5)	0.3939
95% CI	7.2–27.0	13.2–35.5	8.3–28.5	14.6–43.9	
Overall efficacy rate (D5)					
n (%)	6 (10.2)	10 (16.4)	5 (8.3)	7 (17.5)	0.3996
95% CI	3.8–20.8	8.2–28.1	2.8–18.4	7.3–32.8	

CI indicates confidence interval.

AEs

The incidence of AEs during the treatment period was similar across the 4 groups. Fever and wound site pain were the most often reported AEs. The details of the AEs are listed in Table S6 (Supplemental Digital Content 1, http://links.lww.com/SLA/D862). Only 3 patients had a severe adverse event (SAE). One patient in 1‰ PL-5 group developed grade 3 SAE (allergic purpura), which was later found to be irrelevant to the administered drug. One patient in 2‰ PL-5 group had grade 3 SAE (cerebral infarction), and no causal relationship with the administered drug could be found. Finally, 1 patient in the 1% SSD (control) group developed grade 4 SAE (dyspnea), and no causal relationship with the administered drug could be found.

DISCUSSION

In the context of the worldwide threat from growing antimicrobial resistance, the biological activity of AMPs, particularly their ability to kill multidrug-resistant bacteria has drawn special attention.2,17 Powerful AMPs such as vancomycin, daptomycin, dalbavancin, oritavancin, and telavancin, have demonstrated their strong antibiotic efficacy against severe even fatal infections.18–21 However, topical AMPs for treating local wound infections are less frequent. According to the literature and registered clinical trial records, Polymyxin B ointment is the only clinically available topical AMPs drug for the treatment of wound infections, while other 2 AMPs, Pexiganan and LL-37 are still at the clinical trial stage9 without updates for years.22,23

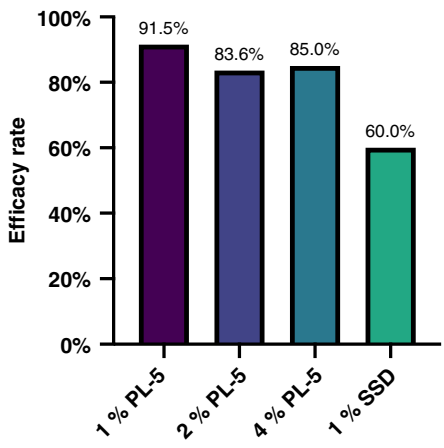

FIGURE 2. Clinical efficacy rates on D8 in terms of > 50% reduction of SIRS scores.

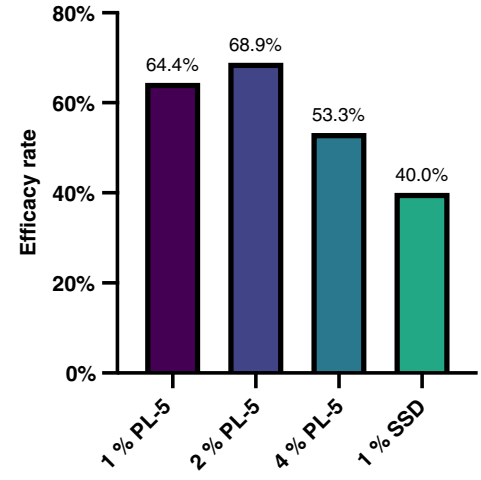

FIGURE 3. Clinical efficacy rates on D5 in terms of > 50% reduction of SIRS scores.

Polymyxin B ointment has been widely used for treating wound infections.24 However, it has a narrow antimicrobial spectrum, narrow range of treatment dosage, renal, and neurotoxicity which limited its application in extensive wound infections.25,26 In addition, Polymyxin B is a cyclic heptapeptide with a tripeptide side chain which is not easy to be degraded, resulting in higher systematic toxicity and chances of inducing antimicrobial resistance. PL-5 is different from Polymyxin B in that it shows random coil structure in preparations, and the peptide sequence is easy to be degraded, therefore less likely to cause toxicity and antimicrobial resistance. Also, the peptide were induced into α-helical structure when attaching on the surface of bacterial phospholipid bilayers through electrostatic interactions, and the integrity of the cytoplasmic membrane was disrupted in a detergent-like "carpet" way, causing the rapid death of bacteria.16 Since the cytoplasmic membrane is the sole target of PL-5, it shows antimicrobial activity against both Gram-positive and Gram-negative bacteria. Our in vitro studies proved that the therapeutic effects of PL-5 on drug-resistant strains are similar to those on sensitive strains, therefore it has greater advantages in the treatment of infections caused by drug-resistant bacteria. Also, the low MIC_{50} of PL-5 proved its ability to kill bacteria at a lower dosage as compared with other traditional antibiotics or AMPs, together with the PK group's data which showed that PL-5 administered to the wound site at its highest testing concentration was not detectable in the blood, PL-5 proved to be a safer AMP drug which is less likely to cause systematic toxicity when applied to large area wounds.

The current phase IIb clinical trial showed that for the treatment of wound infections, PL-5 spray at all the 3 concentrations (1‰, 2‰, 4‰) is more effective in terms of reduced SIRS evaluations than the active control drug SSD. The stratified analysis of SIRS scores showed that PL-5 spray was

TABLE 2. MIC_{50} and MIC_{90} of PL-5 Against the 9 Species of Microbe Strains

Microbial Species	Strain Count	MIC_{50} (μg/mL)	MIC_{90} (μg/mL)	Strains Resistant to Control Antibiotics [n (%)]			
				Ceftriaxone	Imipenem	Vancomycin	Levofloxacin
Staphylococcus aureus	320	4	8	No	NA	0	56 (17.5)
Staphylococcus epidermidis	126	4	4	No	NA	0	41 (32.5)
Pseudomonas aeruginosa	74	4	8	74 (100)	2	NA	8
Enterobacter cloacae	63	8	16	8	8	NA	2
Klebsiella pneumoniae	45	16	16	18 (40.0)	1	NA	14 (31.1)
Acinetobacter baumannii	31	4	8	14 (45.2)	15 (48.4)	NA	5
Enterococcus faecalis	25	64	128	25 (100)	NA	0	2
Staphylococcus haemolyticus	23	2	8	No	NA	0	14 (60.9)
Escherichia coli	22	8	16	13 (59.1)	0	NA	13 (59.1)

The predominant 9 species of microbe strains included > 20 strains each. In total, there were 729 strains accounting for 87.0% of the 838 examined microbes. The results showed those 9 species of bacteria were sensitive to PL-5 spray with MIC_{50} values <16 μg/mL, except for *Enterococcus faecalis*. The resistance strains of those 9 species of pathogenic bacteria to 4 control antibiotics (ceftriaxone, imipenem, vancomycin, levofloxacin) were examined, and the result showed that those drug-resistant strains of ceftriaxone, imipenem, and levofloxacin (except for *Enterococcus faecalis*) are sensitive to PL-5.

NA indicates not available.

especially advantageous in reducing exudate/pus scores, erythema/inflammation scores, edema scores, and tissue warmth scores compared with the control drug SSD. Regarding microbiological efficacy and overall efficacy, PL-5 spray at all the 3 concentrations is comparable to the control drug SSD cream. It is well known that SSD has a broad antibiotic spectrum and rarely causes drug resistance.16,27,28 The efficacy rate of SSD in our study is similar as previous ones,29,30 therefore the comparable bacteria clearance rates between PL-5 spray and SSD cream demonstrated that PL-5 was as powerful as SSD in clearing bacteria at the wound site. Also, PL-5 successfully met the safety outcomes of this clinical trial by showing no SAE related to its application and having an incidence of AEs comparable to that of SSD. However, considering the toxicity of serum silver ions through systematic absorption which contributes to the toxicity of SSD, the cytotoxicity of local silver ions which could delay the wound healing, and patients with sulfonamide allergies could not use SSD,16,27,28 PL-5 spray is a significant innovation to complete the current wound infection treatment regime/strategy with topical antibiotics.

Regarding the optimal dosage of PL-5 spray, our results showed the 2‰ PL-5 group had the highest bacterial clearance and overall efficacy rate, while 1‰ PL-5 group showed a higher clinical efficacy rate than 2‰ PL-5 group did. We considered the lower clinical efficacy of 2‰ PL-5 than 1‰ PL-5 might be related to the different dynamic equilibrium of the peptide structures in the preparation of different concentrations. As the formation of dimers are more likely to occur in higher concentration, therefore reduced its ability to destroy the bacterial membrane. However, the primary outcome showed that the difference of clinical efficacy rate between 1‰ PL-5 and 2‰ PL-5 was not significant. Altogether, in the current clinical trial, the PL-5 spray at 2‰ concentration showed the highest comprehensive efficacy rate among the 3 PL-5 groups, and hence was the dosage chosen for the phase III clinical trials.

Strengths and Limitations of This Study

Our study has the following strengths. As available topical antimicrobial agents for treating skin wound infections are few, with increasing incidence of antibiotic resistance globally, PL-5 (Peceleganan) spray is the first topical AMPs spray agent for the treatment of wound infections. PL-5 spray has shown to be safe and effective in treating skin wound infections, with less chances of inducing antibiotic resistance, which provide more options for clinical treatment, especially in cases of wound infections caused by antibiotic-resistant bacteria.

The limitations of the current study include the relatively less severity of the treated wound infections which no systematic antibiotics were needed. Therefore, the efficacy of PL-5 at this stage could not be applied on serious infections. Since it was only a phase IIb clinical trial, systematic antibiotics were not given to the patients to explore the independent anti-infective effects of the novel AMP drug. Extensive wound infections which generally need systematic antibiotic treatments may provide more information regarding the advantages of the topical AMP drug, which will be explored in future studies. Also, we have not specifically evaluated the application of PL-5 on surgical site infections and necrotizing infections, which may limit its application in these respective cases at this stage. The applicability of different categories of wound infections other than those listed in this study will be more specifically addressed so as to improve the generalizability of its application in the upcoming phase III study. At the same time, other commonly used active control drugs, such as nanocrystalline silver, mupirocin, etc., were not compared with PL-5 and further studies could be meaningful to perform more extensive explorations.

CONCLUSIONS

In conclusion, PL-5 (Peceleganan) spray is the first topical AMPs spray agent developed for the treatment of wound infections. The results of this phase IIb clinical trial showed that PL-5 spray is safe and effective for the treatment of skin wound infections, with 2‰ being its optimal concentration.

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