Comparative Trial of Silver Nanoparticle Gel and 1% Clindamycin Gel when Use in Combination with 2.5% Benzoyl Peroxide in Patients with Moderate Acne Vulgaris

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Background: *Treatments of acne vulgaris commonly use antimicrobials and comedolytic agents. Considering bacterial resistance to topical antibiotics, the alternative treatment such as silver manufactured into nanoparticle receives an attention. Silver nanoparticle has an antibacterial effect against Propionibacterium acnes and anti-inflammation. Clinical study of silver nanoparticle gel for the treatment of acne vulgaris is limited.*
Objective: *To compare the efficacy and safety between silver nanoparticle gel and 1% clindamycin gel both combine with 2.5% benzoyl peroxide for the treatment of moderate severity of acne vulgaris.*
Material and Method: *This was an experimental, double-blinded, randomized-controlled study. Sixty-four moderately severe acne patients were enrolled. They were randomized to receive either silver nanoparticle gel with 2.5% benzoyl peroxide or clindamycin gel with 2.5% benzoyl peroxide (32 patients each). The clinical outcomes were evaluated for inflammatory and non-inflammatory acne count, acne redness, the patients' satisfaction and patients' Dermatology Life Quality Index (DLQI) at the baseline, 2, 4, 6 and 8-week visit.*
Results: *After 8 weeks of follow-up period, the average mean percent change from the baseline of non-inflammatory and inflammatory acne counts were gradually declined in both silver nanoparticle and clindamycin group. At the study endpoint (8-week visit), average mean percent change from the baseline of inflammatory acne count was slightly better reduction in silver nanoparticle group (79.7%) than clindamycin group (72.6%) with no significant difference ($p = 0.18$). The average mean percent change from the baseline of non-inflammatory acne count reduction was also no difference from silver nanoparticle and clindamycin group (61.1% and 66.8% respectively, $p = 0.22$). For clinical erythema score and Mexameter erythema index to evaluate acne redness were no statistical difference between the 2 groups. Moreover, the patients' satisfaction to study medication and their quality of life of patients (DLQI score) were reported with better improvement from the baseline in both groups but there was no statistical significant difference. Except for average mean, patients' satisfaction to acne severity at 6-week visit showed that silver nanoparticle group had better satisfaction score than clindamycin group (4.6±0.6 vs. 4.2±0.6) with statistical significance ($p = 0.01$). Common adverse effects were skin dryness (28.1%) and skin irritation (4.7%) which might be caused by 2.5% benzoyl peroxide. There was no adverse effect for silver nanoparticle gel from the present study.*
Conclusion: *Silver nanoparticle gel is effective with good safety profile for the treatment of acne vulgaris. The present study demonstrated that there were no clinical significant differences between silver nanoparticle gel and clindamycin gel for the treatment of moderate severity of acne vulgaris when use in combination with 2.5% benzoyl peroxide. The clinical application as alternative treatment for acne is advised.*

Keywords: *Silver nanoparticle, 2.5% Benzoyl peroxide, Clindamycin, Acne vulgaris*

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Acne is a common skin disease. It both physically and psychologically affects to teenager and adolescence. The range of psychological impact varies from low self-esteem, social withdrawal to depressive mood and critically suicidal ideation[1,2]. Therefore, the concerning about the effects of acne to patients is crucial.

Usually, a reliable and acceptable acne grading is the Leeds-revised acne grading system[3]. The acne grading system defines treatment options which include topical and oral agents[4]. Topical agents for acne include topical benzoyl peroxide, retinoid, and antimicrobial. Due to the tremendous use of topical

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antibiotics, especially topical clindamycin, the incidence rate of topical antimicrobial resistance is rising over the years[5]. Moreover, some studies reported the occurrence of unusual, serious adverse effects of topical clindamycin such as pseudomembranous enterocolitis[6,7].

Over the past decades, silver has been used as an antimicrobial agent, especially the use of silver sulfadiazine for burn wounds[8]. Silver has bactericidal property by attacking bacterial cell wall and formulating reactive oxygen species (ROS) inside bacterial cell[9]. There were some reported cases of side effect from topical silver treatment, the blue-grey discoloration so called argyria[10,11]. However, this side effect could only be seen in high concentration of silver was used. Nowadays, the application of nanotechnology in biomedical field leads to the development of nanoparticle drugs[12,13]. Using the nanotechnology for the production of silver nanoparticle, makes a robust efficacy in terms of better skin penetration with wider contact surface with bacterial cell wall than traditional silver. Moreover, it has fewer side effects because only small amount of its concentration requires to achieve bactericidal effect[9,14-16]. The study of Gupta et al[17] and Pandit et al[18] demonstrated that silver nanoparticle could inhibit the growth of *Propionibacterium acnes* (*p. acnes*) in vitro study. Furthermore, silver nanoparticle also had anti-inflammatory property[19,20].

Considering the serious adverse effects of clindamycin and the surge of bacterial resistance from topical antibiotics over the past decades, seeking alternative options for acne patients is inevitable. Our study aimed to determine the efficacy and safety of silver nanoparticle as an alternative treatment for the treatment of acne vulgaris.

Material and Method

This was an experimental, double-blinded, randomized-controlled study. The number of subjects was calculated by PS sample size program (version 3.0), according to the previous study of Seidler et al[21]. Finally, 64 patients with moderate acne vulgaris were enrolled. The study was conducted at the Skin Center, Srinakharinwirot University and was approved by the Clinical Research Ethical Committee of Srinakharinwirot University, Bangkok, Thailand. All patients were randomized to receive either silver nanoparticle gel or clindamycin gel in combination with daily 2.5% benzoyl peroxide (32 patients each) by using computer-generated block randomization. They were instructed to apply 2.5% benzoyl peroxide twice daily and wash off after 15-minute application. The tested drugs (silver nanoparticle gel or 1% clindamycin gel) were filled in identical tubes and blinded to both patients and study investigators. The concentration of silver nanoparticle gel (ASAP®) is 24 part per million. Patients were advised to use the tested drug only on facial acne lesions twice daily. The clinical outcome assessments were evaluated for non-inflammatory (comedones), inflammatory (papules, pustules and nodules) and total acne counts. We marked a single inflamed acne lesion (inflammatory papule) to evaluate improvements of acne erythema by using clinical erythema score and erythema index. Clinical erythema score assessed by four point rating score (grade 0, 1, 2 and 3). The average erythema index was measured three times on inflammatory papule by using Mexameter MX16® (Courage & Khazaka Electronic, Cologne, Germany). The patients' satisfaction and patients' Dermatology Life Quality Index (DLQI) were evaluated by using Thai DLQI version. The patients were examined at baseline, week 2, 4, 6 and 8.The adverse effects were also reported at each visit.

Inclusion criteria

The patients aged over 18 years old with moderate acne vulgaris by the Leeds-revised criteria[3] with voluntarily signed during informed consenting process.

Exclusion criteria

Patients who previously applied the following topical treatments: corticosteroids, silver-containing drug, erythromycin, clindamycin, benzoyl peroxide, retinoid, vitamin C, vitamin E and chemical peels, within 2 weeks prior to the study. Patients who took the following oral supplement or medicine: zinc, vitamin C, vitamin E, antibiotics, corticosteroids within 6 weeks prior to study or retinoid within 6 months prior to study. Patients who were allergic to silver-containing drug, benzoyl peroxide or topical clindamycin. Patients who are pregnant or lactating women. Patients who has active skin lesion on study site. Patients who are unable to follow-up according to the study protocol.

Table 1. Baseline demographics

Demographic data	Silver nanoparticle (n = 32)	Clindamycin (n = 32)	*p*-value
Female, n (%)	22 (68.8)	22 (68.8)	1.00
Male, n (%)	10 (31.2)	10 (31.2)	1.00
Mean age (years)±SD	22.6±4.9	22.0±5.0	0.62
Age range (years)	18-36	18-38	N/A
Positive medical illness, n (%)	3 (9.4)	3 (9.4)	1.00*
Concurrent medication, n (%)	0	1 (3.1)	1.00*
Mean non-inflammatory counts±SD	26.2±14.3	32.1±15.7	0.12
Mean inflammatory counts±SD	14.9±3.8	15.3±4.3	0.73
Mean nodular acne counts±SD	0.4±0.9	0.6±1.2	0.56
Mean total lesional counts±SD	41.5±16.2	47.9±16.5	0.12
Mean erythema score±SD	2.2±0.4	2.1±0.6	0.81
Mean Mexametererythema index±SD	643.4±25.2	656.5±33.1	0.08
Mean DLQI±SD	10.2±5.1	11.0±5.8	0.58

Footnote:
Abbreviation: SD (standard deviation), DLQI (Dermatology Life Quality Index), N/A (not applicable)
**p*-value: Fisher's exact test
p-value $\leq$0.05, determined as significant value
Total lesional counts = non-inflammatory lesion + inflammatory lesion + nodular lesion

Statistical analysis

Descriptive statistics were used to describe clinical demographics and at baseline visit. Independent student t-test was used to compare the average mean for continuous data between the two groups. Pearson's Chi-square was used to test the difference for categorical data. Repeated, Analysis of variance (ANOVA) was used to compare the mean change from the baseline at different visits. Statistical data analysis using IBM statistical package for the social sciences (SPSS) version 19.0 was used.

Results

Demographics and the baseline data

Sixty-four patients were enrolled and conducted from December 16, 2015 to February 16, 2016. The present study was registered to the Thai Clinical Trial Registry (TCTR) (ID-TCTR number:20160216002). All participants were randomized by using pre-planned, blocked randomization to receive either silver nanoparticle (AgNP group) or 1% clindamycin (CM group) with 2.5% benzoyl peroxide (32 patients each). Forty-four (68.8%) patients were female and 20 (31.2%) patients were male. The average mean age±standard deviation (SD) of silver nanoparticle and clindamycin group was 22.6±4.9 and 22.0±5.0 years, respectively. The baseline non-inflammatory lesion count, inflammatory lesion count, total lesional count, clinical erythema score, erythema index, patients' satisfaction, physician's satisfaction and Dermatology Life Quality Index (DLQI) score were reported. However, no significant differences at baseline characteristics were detected between the groups (Table 1). Five patients (7.8%) did not complete the study protocol due to protocol withdrawal [3 patients (4.5%) in CM group and 1 patient (1.5%) in AgNP group, and 1 patient for severe worsening acne (1.5%) in CM group].

Primary outcomes

Regarding inflammatory acne counts (papules and pustules), the lesion counts were consecutively reduced in both groups. The percent reduction of

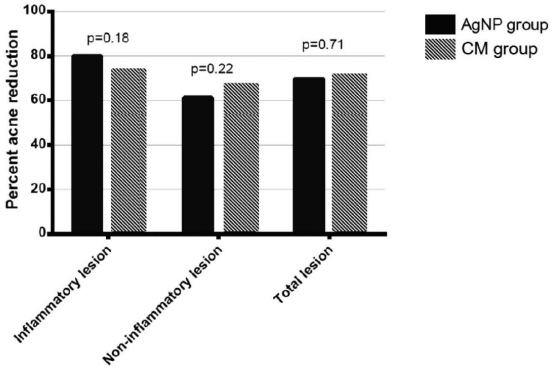

Fig. 1 The percent reduction of inflammatory, non-inflammatory and total acne count from the baseline to at 8-week visit between AgNP and CM group.

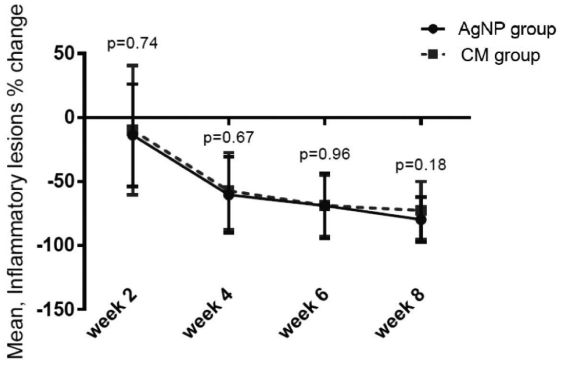

Fig. 2 The percent reduction of inflammatory acne count from the baseline to at 2-week, 4-week and 8-week visit between AgNP and CM group.

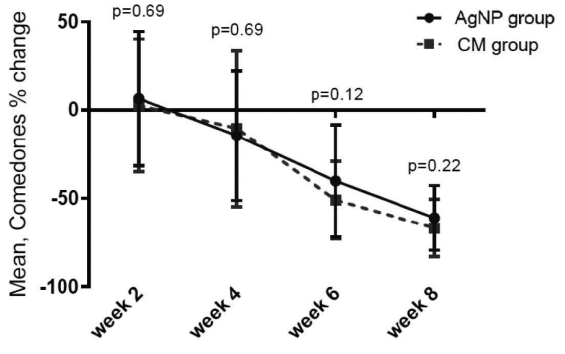

Fig. 3 The percent reduction of non-inflammatory acne counts from the baseline to at 2-week, 4-week and 8-week visit between AgNP and CM group.

inflammatory acne count from the baseline to 8-week visit (study endpoint) was 79.7% [95% confidence interval (CI): 73.6%-85.9%] that were slightly greater in AgNP group than CM group with 72.6% [95%CI: 64.2%-81%]; however, there was no difference between the two groups ($p = 0.18$) (Fig. 1,2).

For non-inflammatory comedonal count, it gradually declined in both groups. After 8 weeks, the percent reduction of comedonal counts from baseline of AgNP group and CM group were 61.1%[95% CI: 54.6%-67.6%] and 66.8% [60.7%-72.8%] with no difference, $p = 0.22$ (Fig. 1,3).

The average mean of total lesional count (sum of inflammatory and non-inflammatory acne count) gradually reduced in both groups but did not show the difference between the two groups. The percent reduction of total lesional counts from the baseline to 8-week visit in AgNP group and CM group were 69.5% [95%CI: 64%-74.7%] and 70.7% [95%CI: 66.5%-75.0%], respectively ($p = 0.71$) (Fig. 1).

Secondary outcomes

For acne redness, the authors used clinical erythema score and Mexameter erythema index to evaluate acne redness and follow the same lesions to compare on different visits. After 8 weeks, both groups showed better improvement in both erythema score and Mexamete rerythema index but there were no difference between the two groups ($p>0.05$).

Throughout the study, patients' satisfaction score to study medication and acne severity improved in both groups but no statistical significance except at 6-week visit to show that AgNP group had better satisfaction score comparing to CM group with statistical significance ($p = 0.01$). Moreover, the improvement of physician's satisfaction score and patients' Dermatology Life Quality Index (DLQI) score from the baseline to at 8-week visit were not difference in both groups ($p>0.05$) (Table 2).

The common adverse effects included skin dryness (27.9%) and skin irritation (4.9%) which might be caused by 2.5% benzoyl peroxide, except one patient reported with skin dryness from 1% clindamycin. Side effects occurred in the study were not different between silver nanoparticle and clindamycin group ($p>0.05$). Treatments with moisturizer (physiogel® cream) were prescribed for skin dryness and irritation. All symp-

Table 2. Comparison of the change from baseline to 8-week visit betweenAgNP and CM group

Outcome data	Silver nanoparticle (n = 31)	Clindamycin (n = 28)	*p*-value
Mean, change of erythema score±SD	-1.2±0.6	-1.1±0.6	0.57
Mean change of Mexameter erythema index±SD	-4.5±25.8	-15.1±23.8	0.11
Mean change of patients satisfaction score	+0.6±0.8	+0.7±0.6	0.59
Mean change of physicians satisfaction score	+0.8±0.7	+0.8±0.7	0.92
Mean change of DLQI score±SD	-7.0±4.9	-8.3±5.8	0.34

Footnote:
Abbreviation: SD (standard deviation), DLQI (Dermatology Life Quality Index, 95% CI (95% confidence interval)

toms resolved completely within 8 weeks. No topical corticosteroids was prescribed during the study period. There was no abnormal discoloration occurred. There was no report for adverse effect of silver nanoparticle.

Discussion

The present study was the first presenting clinical study to determine an efficacy and safety of silver nanoparticle gel for the treatment of acne vulgaris. For 8 weeks follow-up period, silver nanoparticle gel in combination with 2.5% benzoyl peroxide showed a better improvement for substantial reduction of non-inflammatory, inflammatory and total acne lesional counts with equal efficacy by comparison with 1% clindamycin group. There were 4 patients (6.3%); three patients in clindamycin group and one patient in silver nanoparticle group, reported loss to follow-up due to protocol withdrawal. Moreover, there was one patient (1.6%) in clindamycin group was discontinued from the study due to worsening of acne, she wasfurther treated with oral isotretinoin.

Regarding inflammatory acne, silver nanoparticle showed anti-bacterial and anti-inflammation effects. At 8 weeks duration, AgNP group demonstrated slightly better inflammatory lesion reduction than CM group. But there was no significant difference. For non-inflammatory comedonal acne, AgNP group equally showed an efficacy for non-inflammatory lesional reduction with CM group. The results of both groups may be due to the synergistic effect of 2.5%BP with AgNP and with CM[21]. The power to detect the difference between the two groups may be affected by patient's drop-out from the study, especially in CM group.

In About the acne redness, the clinical erythema score and Mexameter erythema index, both AgNP group and CM group showed better improvement. Regarding the subjective evaluations, both groups showed better patients' satisfaction score and Dermatology Life Quality Index (DLQI) score but no statistical significant difference between the two groups. Except for patients' satisfaction to acne severity score at 6-week visit, AgNP group had better satisfaction than CM group with statistical significance ($p = 0.01$). According to Kulthanan et al[22], acne has a significant impact on patients' quality of life. In the present study, AgNP group showed reduction of DLQI score which meant that this study confirm that silver nanoparticle could help improve acne patients' quality of life. Nevertheless, patient's response to both patients' satisfaction and DLQI questionnaire may vary due to individual judgment.

The most common side effects were dryness and skin irritation from 2.5% benzoyl peroxide which were not different in the two groups and gradually subsided within 8 weeks by moisturizing cream. Adverse effects were self-limited and not different comparing to previous studies[23,24]. There was no abnormal skin discoloration at the application site.

Prescribing combination treatment for acne patients shows better efficacy and tolerability comparing with prescribing monotherapy treatment. Neverthe-

less, it also helps reducing bacterial resistance to acne medication, especially topical antibiotics[25,26]. Moreover, it demonstrates the synergistic effect between the combined treatment which shares the same concept as in the study of Leyden et al[23] and Thiboutot et al[24].

The present study is the first clinical trial using silver nanoparticle in combination with frequently prescribed 2.5% benzoyl peroxide for moderate acne patients. Moreover, the follow-up interval in this study was more frequent (2-week period) compared to other studies (4-week period)[23,24,27]. However, the study period of the present study was shorter (8-week period) compared to other studies (10 to 12-week period)[23,24].

Concerning the strengths of the study, this is a randomized, double-blinded, controlled study with well-defined methodology. Baseline demographics of both groups were equally balanced. The follow-up period was properly adequate witht otal duration of 8 weeks in every 2-week visit. This made it easier to detect any subtle changes of clinical outcome more precisely.

Regarding the weakness of the trial, the present study only enrolled patients with moderate acne vulgaris and predominatel female. As a consequence, the results may have limitations if infer to patients with different acne severity or male patients. Some patients had poor compliance to studied medications. In addition, the issues of contamination and co-intervention may also affect the study results. There were some confounding factors such as psychological stress, hormonal changes, and also food consumption that cannot be strictly controlled throughout the study period. Concerning the acne redness, primary investigator was the sole Mexameter evaluator. The use of Mexameter may subject to intra-rater validity concern since measuring acne redness in soft areas such as cheek, was difficult. Five patients (7.8%) were lost to follow-up which could lead to attrition bias especially in clindamycin group. We conducted a trial in 8 weeks, as a result, the failure to prove the primary hypothesis that AgNP has better efficacy comparing to CM may be due to insufficient study period.

In the future, we suggest enrolling more male patients and more diverse acne severity such as, mild to moderate or moderate to severe acne. Contamination, co-intervention and poor compliance should be managed by more frequent patient advice either by direct verbal contact or text messaging. Some confounding factors such as food consumption may be strictly controlled and monitored in the future trial.

In conclusion, silver nanoparticle gel is effective with good safety profile for the treatment of moderate acne vulgaris. The present study demonstrated that there were no clinical significant differences with topical clindamycin for the treatment of moderate acne vulgaris. The clinical application as alternative treatment in acne is advised.

What is already known on this topic?

Bacterial resistance to topical antibiotics in acne patients has been rising over the past decades[28]. Silver nanoparticle shows antibacterial property against *P. acnes*[17] and anti-inflammatory property[19]. Seeking alternative option for acne patient needs more attention. Silver has been used as an antibacterial treatment in burn patients. However, it has never been used to treat acne vulgaris.

What is this study adds?

Silver nanoparticle gel is effective with good safety profile for the treatment of acne vulgaris.The clinical application as alternative treatment in acne is advised.

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Potential conflicts of interest

Silver nanoparticle gel (ASAP®) was provided by Specialty Tech Corporation Co., Ltd. and Proaxtive Care Co., Ltd.

References

1. Do JE, Cho SM, In SI, Lim KY, Lee S, Lee ES. Psychosocial Aspects of Acne Vulgaris: A Community-based Study with Korean Adolescents. Ann Dermatol 2009; 21: 125-9.
2. Uhlenhake E, Yentzer BA, Feldman SR. Acne vulgaris and depression: a retrospective examination. J CosmetDermatol 2010; 9: 59-63.

3. O'Brien SC, Lewis JB, Cunliffe WJ. The leeds revised acne grading system. J Dermatol Treat 1998; 9:215-20.
4. Noppakun N, Timpatanamongkol P, SindhuphakW, Wattanakrai P, Akaraphanth R,Sutthipisal N, et al. Clinical practice guideline in acne [Internet]. 2011 [cited 2015 Mar 20]. Available from: http://www.dst.or.th/files_news/001-Guideline_Acne_2011.pdf. [in Thai].
5. Eady EA, Gloor M, Leyden JJ. Propionibacterium acnes resistance: a worldwide problem. Dermatology 2003; 206: 54-6.
6. Milstone EB, McDonald AJ, Scholhamer CF Jr. Pseudomembranous colitis after topical application of clindamycin. Arch Dermatol 1981; 117: 154-5.
7. Parry MF, Rha CK. Pseudomembranous colitis caused by topical clindamycin phosphate. Arch Dermatol 1986; 122: 583-4.
8. Atiyeh BS, Costagliola M, Hayek SN, Dibo SA. Effect of silver on burn wound infection control and healing: review of the literature. Burns 2007; 33: 139-48.
9. Huh AJ, Kwon YJ. "Nanoantibiotics": a new paradigm for treating infectious diseases using nanomaterials in the antibiotics resistant era. J Control Release 2011; 156: 128-45.
10. Flohr C, Heague J, Leach I, English J. Topical silver sulfadiazine-induced systemic argyria in a patient with severe generalized dystrophic epidermolysisbullosa. Br J Dermatol 2008; 159: 740-1.
11. Payne CM, Bladin C, Colchester AC, Bland J, Lapworth R, Lane D. Argyria from excessive use of topical silver sulphadiazine. Lancet 1992; 340: 126.
12. Parveen S, Misra R, Sahoo SK. Nanoparticles: a boon to drug delivery, therapeutics, diagnostics and imaging. Nanomedicine 2012; 8: 147-66.
13. Cevc G, Vierl U. Nanotechnology and the transdermal route: A state of the art review and critical appraisal. J Control Release 2010; 141: 277-99.
14. Sharma VK, Yngard RA, Lin Y. Silver nanoparticles: green synthesis and their antimicrobial activities. Adv Colloid Interface Sci 2009; 145: 83-96.
15. Munger MA, Radwanski P, Hadlock GC, Stoddard G, Shaaban A, Falconer J, et al. In vivo human time-exposure study of orally dosed commercial silver nanoparticles. Nanomedicine 2014; 10: 1-9.
16. Trop M. The safety of nanocrystalline silver dressing on burns: a study of systemic silver absorption. Burns 2009; 35: 306.
17. Gupta A, Bonde SR, Gaikwad S, Ingle A, Gade AK, Rai M. Lawsonia inermis-mediated synthesis of silver nanoparticles: activity against human pathogenic fungi and bacteria with special reference to formulation of an antimicrobial nanogel. IET Nanobiotechnol 2014; 8: 172-8.
18. Pandit RS. Green synthesis of silver nanoparticles from seed extract of *Brassica nigra* and its antibacterial activity. Nusantara Bioscience 2015;7:15-9.
19. Nadworny PL, Wang J, Tredget EE, Burrell RE. Anti-inflammatory activity of nanocrystalline silver in a porcine contact dermatitis model. Nanomedicine 2008; 4: 241-51.
20. David L, Moldovan B, Vulcu A, Olenic L, Perde-Schrepler M, Fischer-Fodor E, et al. Green synthesis, characterization and anti-inflammatory activity of silver nanoparticles using European black elderberry fruits extract. Colloids Surf B Biointerfaces 2014; 122: 767-77.
21. Seidler EM, Kimball AB. Meta-analysis comparing efficacy of benzoyl peroxide, clindamycin, benzoyl peroxide with salicylic acid, and combination benzoyl peroxide/clindamycin in acne. J Am AcadDermatol 2010; 63: 52-62.
22. Kulthanan K, Jiamton S, Wanitpakdeedecha R, Chantarujikaphong S. The validity and reliability of dermatology life quality index (DLQI) in Thais. Thai J Dermatol 2004; 20: 113-23.
23. Leyden JJ, Berger RS, Dunlap FE, Ellis CN, Connolly MA, Levy SF. Comparison of the efficacy and safety of a combination topical gel formulation of benzoyl peroxide and clindamycin with benzoyl peroxide, clindamycin and vehicle gel in the treatments of acne vulgaris. Am J ClinDermatol 2001; 2: 33-9.
24. Thiboutot D, ZaengleinA, Weiss J, Webster G, Calvarese B, Chen D. An aqueous gel fixed combination of clindamycin phosphate 1.2% and benzoyl peroxide 2.5% for the once-daily treatment of moderate to severe acne vulgaris: assessment of efficacy and safety in 2813 patients. J Am AcadDermatol 2008; 59: 792-800.
25. Thevarajah S, Balkrishnan R, Camacho FT, Feldman SR, Fleischer AB Jr. Trends in prescription of acne medication in the US: shift from antibiotic to non-antibiotic treatment. J Dermatolog Treat 2005; 16: 224-8.
26. Hoover WD, Davis SA, Fleischer AB, Feldman SR. Topical antibiotic monotherapy prescribing practices in acne vulgaris. J Dermatolog Treat 2014; 25: 97-9.

27. Thiboutot DM, Weiss J, Bucko A, Eichenfield L, Jones T, Clark S, et al. Adapalene-benzoyl peroxide, a fixed-dose combination for the treatment of acne vulgaris: results of a multicenter, randomized double-blind, controlled study. J Am AcadDermatol 2007; 57: 791-9.

28. Walsh TR, Efthimiou J, Dreno B. Systematic review of antibiotic resistance in acne: an increasing topical and oral threat. Lancet Infect Dis 2016; 16: e23-e33.

การศึกษาเปรียบเทียบเจลอนุภาคระดับนาโนของแร่เงินกับเจลคลินดามัยซิน 1% เมื่อใช้ร่วมกับเบนโซอิลเปอร์ออกไซด์ 2.5% ในผู้ป่วยโรคสิวความรุนแรงระดับปานกลาง

ณัฐชาต จุไรรัตนาภรณ์, เทพ เฉลิมชัย, สุวิรากร โอภาสวงศ์, มนตรี อุดมเพทายกุล

ภูมิหลัง: *การรักษาสิวส่วนมากใช้ยาปฏิชีวนะชนิดทา และยาที่มีฤทธิ์ลดสิวหัวดำ และสิวหัวขาว ปัจจุบันพบว่า ยาปฏิชีวนะชนิดทาเริ่มพบอัตราการดื้อยาสูงขึ้น จึงมีการศึกษายาใหม่ที่น่าสนใจซึ่งเป็นยาทางเลือกโดยมีฤทธิ์การต้านเชื้อจุลชีพ เช่น แร่เงิน ที่ผ่านกระบวนการผลิตทำให้มีอนุภาคขนาดเล็กระดับนาโนเมตร อนุภาคระดับนาโนของแร่เงินมีฤทธิ์ในการต้านเชื้อแบคทีเรีย Propionibacterium acnes ได้ และสามารถลดอาการอักเสบได้ด้วย โดยยังไม่เคยมีการศึกษาทางคลินิกในการนำอนุภาคระดับนาโนของแร่เงินในการรักษาสิวมาก่อน*

วัตถุประสงค์: *เพื่อศึกษาเปรียบเทียบประสิทธิภาพและความปลอดภัยของเจลทาเฉพาะที่อนุภาคระดับนาโนของแร่เงินเทียบกับยาปฏิชีวนะชนิดทาคลินดามัยซิน 1% เมื่อใช้ร่วมกับเบนโซอิลเปอร์ออกไซด์ 2.5% ในการรักษาสิวที่มีความรุนแรงระดับปานกลาง*

วัสดุและวิธีการ: *งานวิจัยนี้เป็นการทดลองแบบสุ่มโดยมีกลุ่มเปรียบเทียบ และอำพรางทั้งสองฝ่าย ผู้วิจัยได้คัดเลือกอาสาสมัครที่มีความรุนแรงของสิวระดับปานกลาง จำนวน 64 คน แบ่งออกเป็น 2 กลุ่มแบบสุ่มเลือก กลุ่มละ 32 คน เป็นกลุ่มที่ได้รับยาทาอนุภาคระดับนาโนของแร่เงินร่วมกับ 2.5% เบนโซอิลเปอร์ออกไซด์ และกลุ่มที่ได้รับยาทาคลินดามัยซินร่วมกับเบนโซอิลเปอร์ออกไซด์ 2.5% ติดตามและเปรียบเทียบผลการรักษาของทั้งสองกลุ่มเปรียบเทียบจำนวนเม็ดสิวอักเสบ จำนวนสิวหัวดำและสิวหัวขาว ความแดงของสิวความพึงพอใจของอาสาสมัคร และคุณภาพชีวิตของอาสาสมัครที่เปลี่ยนแปลงไป ที่ระยะเวลาเริ่มต้น, 2, 4, 6 และ 8 สัปดาห์*

ผลการศึกษา: *หลังสิ้นสุดการศึกษาที่ 8 สัปดาห์ พบว่าเม็ดสิวหัวดำ สิวหัวขาว และจำนวนสิวอักเสบของทั้งสองกลุ่มมีค่าลดลงทั้งในกลุ่มอนุภาคระดับนาโนของแร่เงิน และกลุ่มคลินดามัยซิน เมื่อศึกษาเปรียบเทียบค่าเฉลี่ยของการเปลี่ยนแปลงของจำนวนสิวอักเสบที่ 8 สัปดาห์ เทียบกับสัปดาห์แรก พบว่ากลุ่มแร่เงิน(ร้อยละ 79.7) มีการลดลงดีกว่ากลุ่มคลินดามัยซิน (ร้อยละ 72.6) เล็กน้อยแต่ไม่พบความแตกต่างอย่างมีนัยสำคัญ (p = 0.18) ค่าเฉลี่ยของการเปลี่ยนแปลงของจำนวนสิวหัวดำและสิวหัวขาวไม่แตกต่างกันระหว่างกลุ่มแร่เงิน (ร้อยละ 61.1) และกลุ่มคลินดามัยซิน (ร้อยละ 66.8) (p = 0.22) สำหรับการประเมินความแดงโดยใช้ erythema score และ erythema index ไม่พบความแตกต่างกันระหว่างสองกลุ่ม นอกจากนี้การประเมินความพึงพอใจของอาสาสมัครต่อยาและคุณภาพชีวิตที่เปลี่ยนไป พบว่ามีการเปลี่ยนแปลงในทางที่ดีขึ้นทั้งสองกลุ่ม แต่ไม่พบความแตกต่างอย่างมีนัยสำคัญ ยกเว้นค่าเฉลี่ยของคะแนนความพึงพอใจของอาสาสมัครต่อระดับความรุนแรงสิวที่ 6 สัปดาห์ พบว่ากลุ่มแร่เงินมีความพึงพอใจดีกว่ากลุ่มคลินดามัยซิน (4.6±0.6 และ 4.2±0.6 คะแนนตามลำดับ) อย่างมีนัยสำคัญทางสถิติ (p = 0.01) ผลข้างเคียงที่เกิดขึ้นได้แก่ ผิวแห้ง (ร้อยละ 28.1) และอาการแสบระคายเคือง (ร้อยละ 4.7) ซึ่งอาจเกิดจากเบนโซอิลเปอร์ออกไซด์ 2.5% ไม่พบผลข้างเคียงจากการใช้เจลอนุภาคระดับนาโนของแร่เงินในการศึกษานี้*

สรุป: *เจลอนุภาคระดับนาโนของแร่เงินมีประสิทธิผลและความปลอดภัยดีสำหรับการรักษาสิว จากการศึกษานี้แสดงให้เห็นว่าเจลอนุภาคระดับนาโนของแร่เงินไม่มีความแตกต่างจากยาปฏิชีวนะชนิดทาคลินดามัยซินในแง่ของการเปลี่ยนแปลงทางคลินิก ผู้นิพนธ์แนะนำว่าสามารถใช้เจลอนุภาคระดับนาโนของแร่เงินเป็นยาทางเลือกสำหรับการรักษาสิวได้*
