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Is Glycolic Acid Safe And Effective In The Treatment Of Mild to Moderate Acne?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

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Abstract

Objective: The objective of this selective EMB review is to determine whether or not the use of glycolic acid is effective in the treatment of inflammatory and non-inflammatory acne.

Study Design: The review of three randomized, double-blind, controlled trials all published in English language between the years of 2008-2010.

Data Sources: Three randomized, double-blind, controlled trails comparing glycolic acid to a visually matched placebo or pharmaceutical therapy in improvement of acne. All articles were found using PubMed and EBSCO.

Outcomes Measured: The improvement of inflammatory and non-inflammatory acne and tolerance/ safety of the intervention. Efficacy was measure via patients' preference/ assessment, Wilcoxon signed rank test, number of lesions, and Paired T-Test.

Results: Abels demonstrated a significant improvement in the appearance of acne with monotherapy of oil-in-water emulsion and 10% glycolic acid verum. The patient and physician subjects' evaluations indicated the verum was both well tolerated and efficacious. The report showed no statistically significant difference between verum and placebo of oil-in-water emulsion without glycolic acid in reported adverse effects. I. LKNUR established a statistically significant decrease in the number of non-inflamed and inflamed lesions with glycolic acid peel. When compared to the amino acid fruit placebo peel, the report detailed a non-significant difference in improvement of non-inflamed and inflamed lesions. Kessler demonstrated glycolic acid peels as well as the visually matched therapy salicylic acid peels were significantly effective by the second treatment. Additionally, the differences in effectiveness between the two peels were found to be non-significant. The report detailed more adverse events reported with the glycolic acid peel.

Conclusions: The results of these three studies show conclusive evidence that the use of glycolic acid is effective in the treatment of acne. Each study demonstrated both a significant quantitative and qualitative improvement. Varying reports of tolerability and adverse effects are possibly due to differing preparations and applications between studies. Most commonly these included reports of desquamation and erythema. The results do not encourage future research since no significant efficacy was found between glycolic acid and the comparable placebo or pharmaceutical therapy.

Key Words: glycolic acid and acne

Introduction

Acne vulgaris is chronic skin condition responsible for many dermatologist visits annually. Acne most commonly affects adolescents, although it can be present at any age.⁶ It is often considered an exclusively dermatological concern; however, it can be associated with developmental issues of body image, socialization, and sexuality.⁶ Due to the multifactorial pathologies of acne, treatment of acne vulgaris can be challenging. One such treatment, glycolic skin preparations, can be effective however its benefit in use remains in question due to concerns for tolerability with frequent use.²

Acne vulgaris is one of the most common skin diseases. The peak incidence occurs in adolescence. It is estimated that acne affects approximately 85% of males and females between 12 and 24 years old.² The global acne market was worth 2.8 billion in 2009. It is estimated to reach revenues of 3.02 billion by 2016.^{2,3,6} Acne is commonly treated by a variation of medical professionals including primary care, emergency room, dermatology, and gynecology practitioners.⁶ Additionally many first line acne treatments are available over-the-counter. Due to variation of physiologic causes and treatment options, Acne-related health care visits have proven challenging to track. There has not been an estimate within the past few years. Nearly 20% of dermatology visits is for the treatment of acne.⁵

Acne is defined as a multifactorial chronic inflammatory disease of the pilosebaceous units.⁵ The clinical presentation can vary. It may include seborrhea, comedones, erythematous, papules, and pustules. Less commonly, one may present with nodules, deep pustules, or pseudocysts.^{1,2,6} Acne has four pathogenic causes. They are sebum overproduction, follicular hyperkeratinization, *Propionibacterium acne*'s colonization, and inflammation. The initiating factor of acne is unknown.⁴

The successful management of acne requires individualized care according to clinical presentation.⁶ A variety of treatment modalities are available for treatment of acne. Topical medications are the mainstay treatment for acne. Topical treatment options include benzoyl peroxide, antibiotics, and retinoid. Systemic options include oral antibiotics, hormonal therapy, and isotretinoin.⁶

The use of glycolic acid in the treatment of acne has been shown to be successful although not common.¹ Glycolic acid is the most stable alpha hydroxyl acid and is found naturally in grapes and sugar cane juice.^{1,2} Glycolic acid is commonly used for its desquamation properties in the treatment of acne. With concentration dependent efficacy, alpha hydroxyl acids reduce the coherence of the superficial and follicular corneocytes.^{1, 2, 4} The pH value typically ranges from 2-8. The low pH of the Glycolic acid containing products is responsible for the comedolytic and antimicrobial effects. There are varying products and treatments available containing 5-20% glycolic acid; however, products for frequent to daily use are scarce due to concerns for tolerability.¹ Common adverse effects include stinging, skin redness, mild skin irritation, and dryness.^{1, 2, 4}

This selective evidence-based medicine review evaluated two randomized, double blind studies and one single blind study to examine the efficacy and tolerability of glycolic acid in the treatment of inflammatory and non-inflammatory acne.

Objective

The objective of this selective EBM review is to determine whether or not the use of glycolic acid is effective in the treatment of inflammatory and non-inflammatory acne.

Methods

The population chosen was men and woman over the age of 12 with moderate to severe acne. ILKNUR further selected subjects without inflammatory acne. All interventions studied in the RCTs involved glycolic acid skin preparations. Abels' investigated an oil-in-water emulsion containing 10% glycolic acid regarding clinical efficacy and tolerability for 90 days. Kessler's intervention incorporated 30% glycolic acid peels. The peels were applied contra-laterally every two weeks for a total of six treatments. ILKNOR's single-blind, randomized study investigated the use of glycolic acid peels on the face at two-week intervals for 6 months. On one half of the face Glycolic acid was applied at varying concentrations of 20%, 30%, 50%, and 70% from lowest to highest.² In the Abels' study, comparisons were made between glycolic acid and visually matched placebo.¹ The remanding RCTs (ILKNOR and Kessler) compared the efficacy and tolerability of glycolic acid to a visually match pharmaceutical therapy. Measured outcomes included: the improvement of acne, tolerance of the intervention, efficacy in the treatment of moderately severe acne, and efficacy as a monotherapy.^{1, 2, 4}

Key words used in the searches were "glycolic acid" and "acne." All articles were published in peer-review journals and in the English language. The author searched the articles through PubMed and EBSCO October 1, 2012- December 1, 2012. The selection of articles was based on relevance to the clinical question and inclusion of patient-oriented outcomes. These included improvement of acne, and tolerability of the glycolic acid dermatological intervention. Inclusion criteria were randomized studies that were either double or single-blind. Each included patient-oriented outcomes of a subject population ≥ 12 years of age with mild to moderate acne. Exclusion criteria consisted of studies with exclusively diseased-oriented outcome, and those that included subjects <12 or having severe acne. The statistics utilized in the studies were relative

benefit increase (RBI), absolute benefit increase (ABI), and numbers needed to treat (NNT), and p-values.^{1, 2,4}

Table 1- Demographic & Characteristics of the included studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
İLKNUR (2010)	Double Blind RCT	24	≥12 yo	Men and Women 12 year old and older with .25-2 grade Acne Vulgaris	pregnant and nursing women, oral contraceptive and hormone replacement in the past 6 months	0	GA solution- (Glycolic Acid Peels; Neostrata, Princeton, NJ, USA) at concentrations from the lowest to the highest (20%, 35%, 50%, 70%) on the two halves of the face at 2-week intervals for 6 months
Kessler (2008)	Double Blind RCT	20	13-38 yo	Males and Females ages 13 to 38 with mild to moderatel y severe facial acne vulgaris	active infections, herpes simplex or zoster, bacterial folliculitis, current isotretinoin usage, use of isotretinoin within 12 mo	0	An α-hydroxy acid (30% glycolic acid) was applied to one-half of the face and a β-hydroxy acid peel (30% salicylic acid) was applied contralaterally every 2 weeks for a total of six treatments
Abels (2011)	Double Blind RCT	120	≥ 12 yo	Men and Women ages 12 and older with mild acne	History of hypersensitivit y against a ingredient of the study preparations; Sandpaper-acne; Additional facial skin therapy	5	An oil-in-water emulsion-containing 10% glycolic acid (pH 4; Dr.AugustWolffGmbH&C. KGArzneimittel, Bielefeld,Germany) as monotherapy in mild acne for 90 days.

Outcomes Measure

Outcomes were measured using a combination of five techniques. Patient's preference was determined via asking each participant which method or treatment was preferred. Patient self-assessment was measured by questionnaire. The number of lesions was used to measure efficacy. A comparison was done using photos before and after intervention. Additionally a count of visible lesions was completed. Another method utilized by Kessler is the paired t-test. This was performed by calculating the difference between observations for each pair. The mean and standard error of the differences are calculated. Dividing the mean by the standard error yields a test statistic, t_s . T_s is t-distributed with degrees of freedom equal to one less than the number of pairs. Wilcoxon signed rank test was also utilized in the ILNKUR study. The absolute value of the difference between observations is ranked from smallest to largest. The smallest difference getting the rank of 1, then the next difference ranked 2, etc. Abels utilized Leeds score. Leeds score grading system provides a photographic standard for grading acne. Published in 1998, the Leeds system ranks acne on a 0-10 scale on the basis of severity and types of lesions visualized.²

Results

The study by Edward Kessler was a split-face, double-blind, randomized, controlled study. Twenty subjects were recruited between the ages of 13 and 38. Participants included seven (35%) male and 13 (65%) females. The mean number of acne lesions was 27. Two participants failed to follow-up after the fourth and sixth (final) treatments. The drop outs were not due to adverse events. T-test from an independent group noted no significant difference

between the glycolic acid and salicylic acid peels in efficacy through the first month ($p > .05$). Patient self-assessment questionnaires revealed the glycolic acid side had greater improvement. 41% of subjects thought the glycolic acid peel was most improved, while 35% indicated a greater improvement with the salicylic acid peel. Of the remaining participants 12% reported equal improvement and 12% noted no improvement. Adverse events of redness, scaling, peeling, crusting, blister formation, and hyperpigmentation were reported with both chemical skin treatments. The highest frequency was reported after two treatment visits and appeared to decrease over the treatment period. The study notes a greater degree of desquamation with the glycolic acid peel than reported with the salicylic acid peel. This was noted via patients' self-assessment. Table 2 shows the incidence of positive outcomes with glycolic acid intervention compared to salicylic acid peel. There was a small difference in AE incidence with the glycolic acid peel (41%) compared to the amino fruit acid (35%). The relative benefit increase (RBI) was calculated to be 0.17. Absolute benefit increase was 0.06. Numbers needed to treat was found to be 17. This can be interpreted as 17 patients need to be treated with the intervention to reap a positive outcome.

Table 2: Incidence of positive outcomes with intervention

P-value	CER	EER	RBI	ABI	NNT
>.05	35%	41%	.17	.06	17

The study by TURNA ILKUR was a single-blind randomized, right to left comparison study. 30 patients were selected, although 6 were excluded due to none compliancy with inclusion requirements. 7 males and 17 females completed the six month study. The patients received 12 serial facial peels at a two week interval. Glycolic acid was applied to one side of the

face at concentrations from lowest to highest. The concentrations used were 20%, 35%, 50, and 70%. The first peel was initiated with the least concentrated at a minimal contact period of 2 minutes to a maximum of 6 minutes with respect to tolerability noted by erythema. At each treatment the contact time and concentration was increased. The amino fruit acid peel was applied similarly with concentrations of 20, 30, 40, 50, and 60. Clinical assessment was evaluated by a doctor blinded monthly. The assessment was a quantitative comparison from baseline. Tolerability was assessed via evaluations of erythema, edema, and frosting.

Additionally patient preference test was given to each patient at the conclusion of the study. As monotherapies, the amino fruit acid and glycolic acid both proved to be effective with $p < .05$. However, there was not a statistically significant difference when the two treatments were compared with one another ($p > .05$). Patient preferences noted 100% discomfort affecting daily life with the glycolic acid solution. There was no notable difference in preference for future treatment (GA, 45.8%; AFA, 54.2%). Table 3 shows the incidence of positive outcomes with glycolic acid intervention compared to amino fruit acid peel. There was a small difference in AE incidence with the glycolic acid peel (51.72) compared to the amino fruit acid (42.11). The relative benefit increase (RBI) was calculated to be -0.186. Absolute benefit increase was -9.61. Numbers needed to treat was found to be -10. This can be interpreted as -10 patients need to be treated with the intervention to reap a positive outcome.

Table 3: Incidence of positive outcomes with intervention

P-value	CER	EER	RBI	ABI	NNT
>.05	51.72	42.11	-0.186	-9.61	-10

The study by Christoph Abels was a double-blind, randomized study of 120 patients. All participants had mild facial acne noted by a Leads score between 0.25-1.00. 115 completed the study. Five participants did not complete the study due to poor compliance. The study utilized intention to treat analysis and no difference was found regarding the number of patients in the group as compared to the per-protocol- analysis. The placebo and experimental groups were randomly selected. Fifty-nine participants of 39 females (66.1%) and 20 males (33.9%) applied the 10% glycolic acid containing oil-in-water. The remaining 61 subjects or 34 females (55.7%) and 27 males (44.3%) applied the oil-in-water visually matched placebo without glycolic acid. The participants were instructed to apply the solution once a day at bedtime over a period of 90 days. Subjects were monitored at 3 equally spaced intervals for efficacy and tolerability. Acne improved in all participants receiving the 10% glycolic acid solution had reduced acne on the completion of the 90 day trial ($P < 0.0001$). The improvement of acne with the placebo group was less; however, the difference when compared to the experimental date was not significant ($P = 0.078$). Patients and physicians reported tolerability. There was no significant difference between the two treatments. At 51.2% to 42.11%, the placebo was marginally favored. Table 2 shows the incidence of positive outcomes with glycolic acid intervention compared to amino fruit acid peel. There was a small difference in AE incidence with the glycolic acid peel (54.2%) compared to the placebo (45.8). The relative benefit increase (RBI) was calculated to be -0.155. Absolute benefit increase was -0.084. Numbers needed to treat was found to be -11. This can be interpreted as -11 patients need to be treated with the intervention to reap a positive outcome.

Table 4: Incidence of positive outcomes with intervention

P-value	CER	EER	RBI	ABI	NNT
0.078	54.2%	45.8%	-0.155	-0.084	-11

Discussion

Glycolic acid, an alpha-hydroxy acid, is often used in the treatment of acne due to its antimicrobial and desquamation properties.^{1, 2, 4} Products and methods of application can vary. Outcomes appear to be concentration dependent. Dermatologists commonly use glycolic acid at high concentrations as a chemical peel.² This technique not only proves effective in improving the appearance of acne but additionally wrinkles, hyperpigmentation, and texture may be improved. Most insurance companies will not cover the procedure since it is considered not medically necessary. Over the counter products with a low concentration of glycolic acid are available for self-application.⁷

This literature review studied the efficacy and tolerability of glycolic acid in the treatment of acne. Studies reviewed were randomized and controlled that failed to find significant difference between patients using glycolic acid and those using the visually identical therapy or placebo. There were limitations that could have impacted the studies' results. Compared to the GA peel, the AFA peel used in the ILKNUR study is less irritating and better tolerated.² This may be reflected in the participants preference of acne interventions regardless of which is most effective in the treatment of the acne. This is especially true in the Abels study where an insignificant difference in efficacy and tolerability was found between the placebo of oil-in-water emulsion and the verum containing the glycolic acid solution.¹

Conclusion

Each study reviewed was conclusive that glycolic acid is a viable treatment for mild to moderate acne. Glycolic acid peel and oil-emulsion both proved effective in the treatment of acne vulgaris. There were significant reports of adverse events including redness, peeling, and scarring when compared to the placebo or visually identical dermatological therapy. Difference in the improvement of acne was found to be insignificant. The difference in treatment medium did not appear to impact the effectiveness or tolerability of the therapy. Further research should be designed to study the effect of changing application techniques for the purpose of increasing tolerability of the glycolic acid skin preparations.

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