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Review Article

Efficacy of topical acne agents in the treatment of Acne Vulgaris: Insights from a meta-analysis

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Abstract

Topical therapies are essential for controlling Acne Vulgaris because they have specific therapeutic effects on the skin. Through a meta-analysis, this study seeks to determine the effectiveness of topical acne treatments in the management of Acne Vulgaris. Data extraction and systematic study of literatures were both included in the methodology utilized for this meta-analysis. Controlled clinical trials and randomized controlled trials comparing topical acne treatments with placebos were included as inclusion criteria. The search strategy used techniques for assessing the quality of results, additional sources, and electronic databases. The pooled effect sizes and publication bias were computed using a random effects model. The results were presented as effect estimates, confidence ranges, and significance levels. The RR estimate for the common effect model is 5.1986, and the 95% confidence interval is [3.8070; 7.0990]. According to this, persons who receive topical acne treatments have a 5.1986 times higher chance of getting a good result than those who receive a placebo. Overall, there isn't much proof of publication bias in the meta-analysis of topical pharmaceutical therapies for Acne Vulgaris, according to the findings of the linear regression test of funnel plot asymmetry. These results provide useful insights into the use of topical treatments for Acne Vulgaris and highlight the targeted mechanism of action, rigorous clinical study designs, consideration of heterogeneity, and statistical significance of the topical acne agents.

Keywords

Meta-analysis, Acne Vulgaris, topical acne agents, common effect model, random effect model

Introduction

Katz et al. (2018) claim that Acne Vulgaris is a typical dermatological disorder that manifests as comedones, papules, pustules, and sporadically nodules or cysts on the skin. A person's quality of life and psychological health can be seriously affected. All ages are affected, but adolescents and young adults are primarily affected (Dunn et al. 2011). Treatment for Acne Vulgaris involves a multimodal approach that may involve dietary modifications, topical drugs, oral medications, and surgical procedures (Williams et al. 2012; Gollnick and Zouboulis 2014).

Topical therapies are crucial in the treatment of Acne Vulgaris due to their focused therapeutic effects on the skin (Wang et al. 2022).

These treatments, which are applied topically to the affected areas, target the underlying causes of acne, such

as excessive sebum production, follicular hyperkeratinization, bacterial overgrowth, and inflammation (Huang et al. 2022; Khakimova et al. 2022). Topical acne therapies that are widely accessible include retinoids, benzoyl peroxide, salicylic acid, antibiotics, and combination formulations (Zaenglein et al. 2016). These compounds are said to function by correcting keratinocyte differentiation, reducing sebum production, having antibacterial activity, and having anti-inflammatory properties, according to Thielitz and Gollnick (2009), Strauss et al. (2007), and Burkhart and Burkhart (2003).

In order to evaluate the efficacy of topical therapies for acne, numerous clinical trials have been conducted. However, individual studies may have minimal statistical power because of variations in study design, patient groups, treatment regimens, and outcome measures. A thorough and quantitative method for evaluating therapy efficacy is provided by meta-analysis, a statistical technique that incorporates data from various trials (Higgins and Green 2011).

The objective of the current meta-analysis is to compile the available data on the effectiveness of topical acne medications in the management of Acne Vulgaris. It will be possible to conduct a thorough review of the efficacy across various patient demographics and treatment modalities by combining data from numerous clinical studies, which will give a more reliable estimate of the treatment effect. Numerous outcome measures, such as lesion counts, changes in clinical severity, patient-reported outcomes, and adverse events will be considered during the study. The meta-analysis will also evaluate factors that might affect treatment response and address potential causes of heterogeneity.

The knowledge gathered from this meta-analysis will help in the better understanding of the effectiveness of topical acne treatments and guide clinical judgment in the treatment of Acne Vulgaris. The results may help medical providers choose appropriate topical therapies and assist patients in making decisions about their acne management tactics. In the end, boosting topical treatment efficiency can result in better outcomes and improved quality of life for those with Acne Vulgaris.

Methodology

Study objectives

- To evaluate the efficacy of topical acne agents in the treatment of Acne Vulgaris.
- To assess the pooled treatment effect across multiple studies.

Study design

- Conduct a thorough literature search to find research that is pertinent.
- Conduct a meta-analysis to compile information from a few chosen papers.

Inclusion criteria

- Controlled clinical trials (CCTs) and randomized controlled trials (RCTs).
- Research contrasting topical acne treatments with a placebo.
- Research involving people who have been diagnosed with Acne Vulgaris.
- Studies reporting treatment effectiveness outcome measures (such as lesion counts, changes in clinical severity, and patient-reported outcomes).

Search strategy

A thorough search of electronic databases (such as PubMed and Embase) was carried out using pertinent keywords and Medical Subject Headings (MeSH) phrases. The search phrases included the following domains: "efficacy", "therapeutic efficacy", "topical acne agents", "topicals", "Acne Vulgaris", and "placebo AND topicals". Accordingly, the Boolean operators "OR" and "AND" were used in this study to join concepts.

Study selection

The identified studies based on predefined inclusion criteria was screened.

Data extraction

- Using a standardized form, pertinent data from the included studies was retrieved.
- Data on participant demographics, intervention details, outcome measures, and results, as well as study characteristics (such as the author, year, and sample size), were gathered.

Statistical analysis

The following analysis utilized the R packages meta (Schwarzer 2007) and metasens (Balduzzi et al. 2019):

- Based on the types of reported outcome measures, the pooled effect size using the preferred measure (relative risk) was determined.
- A random effects model was applied to account for any potential study heterogeneity.
- A forest plot was created to show both the overall treatment effect as well as the results of each individual research.
- A funnel plot was used to evaluate publication bias.

Ethical considerations

- Since this study is a meta-analysis of already published data, ethical review is not necessary. However, ethical standards for conducting and reporting research were upheld.

Results

Studies and treatments

There were 197 potentially suitable papers found by a systematic literature search (65 from PubMed, 80 from Google Scholar, and 52 from Embase), of which 21 matched the eligibility requirements for the analysis (Fig. 1). Study characteristics are included in Suppl. material 1.

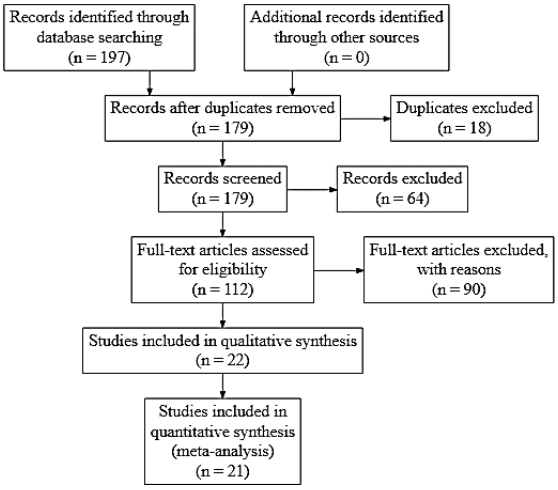

Figure 1. Flowchart diagram for selected plots.

According to the findings of this meta-analysis of topical pharmaceutical therapies for Acne Vulgaris, a total of 14 studies (out of 21 without missing values) were analyzed, amounting to a total of 2594 observations (Table 1). There were 601 events in these trials (Table 1), which normally denote the occurrence of an important result or event; in this case, the events in question had to do with the efficacy or reaction of topical therapies for Acne Vulgaris. The meta-analysis can determine the overall treatment impact and evaluate the efficacy of topical pharmacological therapies for Acne Vulgaris by considering the ratio of events to observations. In summary, 14 trials with a combined total of 2594 observations and 601 events make up the meta-analysis of topical pharmacological therapies for Acne Vulgaris. These findings point to a sizable body of data and offer a solid basis for assessing the efficacy of the treatments and making judgments about how well they manage Acne Vulgaris. Topical treatments analyzed in these studies include Salicylic acid, Benzoyl Peroxide, Adapalene, Azelaic acid gel, Fusidic acid lotion, Retinoic Acid, Clindamycin, Isotretinoin gel, Erythromycin gel, Tazarotene gel, Chloroxylenol and Zinc Oxide cream, Tretinoin topical gel, Retinaldehyde/Glycolic acid combination, Triethyl citrate and Ethyl linoleate combination lotion, Zinc acetate, Ketoconazole cream and Superoxidized solution. Their mechanisms of action are described in Suppl. material 1.

Table 1. Summary statistics of analyzed studies.

Number of studies combined: k	14
Number of observations: o	2594
Number of events: e	601

The forest plot (Fig. 2) displays the results of a meta-analysis of topical pharmacological treatments for Acne Vulgaris, showing that topical acne agents are preferred to placebo. The results include the relative risk (RR) estimates and their respective 95% confidence intervals (95%-CI) for each study, as well as the percentage weights assigned to each study in both the common effect model (%W(common)) and random effects model (%W(random)).Similar results were found by Eichenfield et al. (2013) and Iraji et al. (2007), with RR estimates of 61.4296 [8.6332; 437.1013] and 13.0000 [1.8130; 93.2178] and all demonstrating a significant decline in acne with topical therapy, respectively.

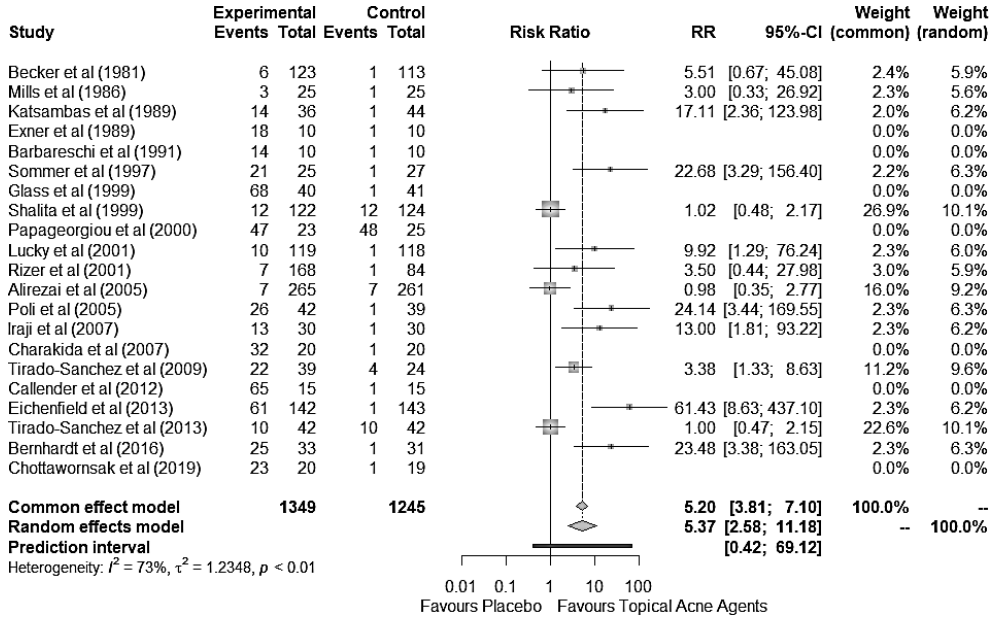

Figure 2. Forest plot showing risk ratio and 95% confidence interval for each study along with study weight.

It is crucial to keep in mind that a few studies, including Barbareschi et al. (1991), Glass et al. (1999), Papageorgiou and Chu (2000), Charakida et al. (2007), Exner et al. (1983), and Chottawornsak et al. (2019), include missing data that is marked as "NA." These studies might not offer precise RR values; therefore, they can't be used to assess the overall treatment effect.

The percentage weights allocated to each study are also shown in the forest plot (Fig. 2), indicating their influence on the evaluation of the treatment's overall effectiveness. The estimated effect is more affected by studies with heavier weights. For instance, Tirado-Sanchez et al. (2013) and Alirezai et al. (2005) have considerably greater weights in both models, indicating that they significantly contributed to the calculation of the overall treatment impact.

The forest plot is consistent with the finding that topical pharmaceutical treatments for Acne Vulgaris are preferred to placebo. Strong support for the efficiency of topical acne medications in treating Acne Vulgaris is shown by the significant RR estimates and the condensed confidence intervals in several of the included trials.

The RR estimate for the common effect model is 5.1986 with a 95% confidence interval of [3.8070; 7.0990] (Fig. 2; Table 2). According to this, persons who receive topical acne treatments have a 5.1986 times higher chance of getting a good result than those who receive a placebo. The RR estimate is statistically different from the null hypothesis that there is no difference between the treatments, according to the z-score of 10.37. Strong evidence is presented against the null hypothesis by the p-value, which is less than 0.0001, which shows a substantial treatment effect in favor of topical acne treatments.

Additionally, a significant treatment impact in favor of topical acne medications is seen in the random effects model (Fig. 2; Table 2). With a 95% confidence interval of [2.5820; 11.1790], the RR estimate is 5.3725. This implies that the treatment impact is of a similar size to the common effect model. The occurrence of a substantial treatment effect is supported by the z-score of 4.50, which shows that the RR estimate significantly differs from the null hypothesis, and the p-value of less than 0.0001.

Table 2. Models associated with study outcome.

Model	RR	95%-CI	z	p-value
Common effect model	5.1986	[3.8070; 7.0990]	10.37	< 0.0001
Random effects model	5.3725	[2.5820; 11.1790]	4.50	< 0.0001

Whether the common effect model or the random effects model is applied, the forest plot findings consistently show that topical acne treatments are linked with a much higher likelihood of good outcomes compared to placebo. These results offer solid proof of the efficiency of topical pharmaceutical therapies for treating Acne Vulgaris. The plot also offers measures of heterogeneity, which aid in evaluating the degree of variation in the outcomes across the included studies, in addition to treatment effect estimates.

The metrics of heterogeneity presented in the forest plot are tau2, tau, I2, and H, which are quantified as tau2 = 1.2348 [0.4110; 4.0914]; tau = 1.1112 [0.6411; 2.0227]; I2 = 73.3% [54.5%; 84.3%]; and H = 1.93 [1.48; 2.52]. The anticipated amount of variation in treatment effects that goes beyond pure chance is represented by tau2 (Pustejovsky and Tipton 2022). Tau2 is estimated to be 1.2348 in this meta-analysis, with a 95% confidence interval of [0.4110; 4.0914]. Tau is 1.1112 with a 95% confidence interval of [0.6411; 2.0227], where tau is the square root of tau2. These numbers show how heterogeneous the studies' data are.

I2 describes the percentage of overall treatment effect variance that can be attributed to heterogeneity (Higgins and Thompson 2002). The I2 score in this situation is 73.3%, and the 95% confidence interval is [54.5%; 84.3%]. This shows that there is heterogeneity between the trials which accounts for a sizable portion of the diversity in treatment outcomes. Greater heterogeneity is indicated by higher I2 values.

Another measure of heterogeneity is H, which, according to Mittlböck and Heinzl (2006), is the ratio of overall variability (which includes both within-study and between-study variability) to within-study variability. The H value for this meta-analysis is 1.93, and the 95% confidence interval is [1.48; 2.52]. Significant heterogeneity is indicated by values larger than 1.

The findings show that the papers included in the meta-analysis of topical pharmacological therapies for Acne Vulgaris exhibit moderate to significant heterogeneity. This heterogeneity shows that variables other than pure chance may have an impact on the diversity in treatment outcomes seen across studies. Different study designs, patient demographics, treatment regimens, or outcome measures could all be potential causes of variation (Benjamin et al. 2017).

A test of heterogeneity, which determines if the observed variation in treatment effects across the studies is statistically significant, is shown in the forest plot based on the meta-analysis of topical pharmacological therapies for Acne Vulgaris. A Q value of 48.60 with 13 degrees of freedom and a p-value of less than 0.0001 are reported in this instance by the test of heterogeneity. According to Barili et al. (2018), the Q statistic is a measurement of the overall variability in treatment effects across trials, considering both within-study and between-study variability. The number of independent pieces of information that can be used to estimate the variability is indicated by the degrees of freedom. The Q value of 48.60 in this meta-analysis indicates high heterogeneity among the studies. The statistical significance of the heterogeneity is indicated by the p-value attached to the Q statistics. The p-value in this instance is less than 0.0001, indicating that it is unlikely that the observed heterogeneity could have happened by chance alone.

Test of publication bias

A test of funnel plot asymmetry using linear regression is included in these results (Fig. 3). This test evaluates the potential for publication bias, which is the selective publication of studies based on their findings (Hunter et al. 2014).

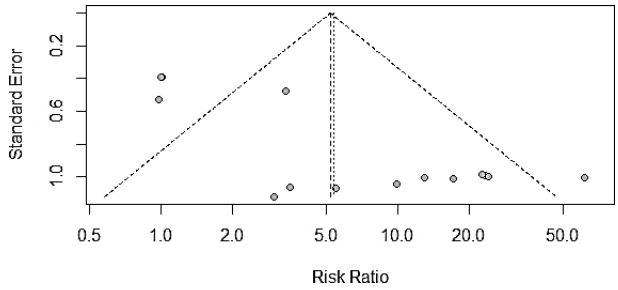

Figure 3. Funnel plot assessment of publication bias.

The test's findings for linear regression are as follows: The corresponding p-value is 0.2196, the degrees of freedom (df) are 12, and the test statistic (t-value) is -1.30. The link between the asymmetry of the funnel plot and the standard error of the treatment effect estimates is measured by the t-value (Stanley 2005). The funnel plot may be asymmetric in this instance, but the negative t-value does not statistically signify this.

Additional details concerning the bias and intercept of the linear regression model are revealed by the sample estimates. The bias estimate is -1.8713, suggesting that there may be a systematic bias in the way that studies are published. The standard error of the bias estimate (se. bias), however, is 1.4449, which suggests that there is some ambiguity surrounding this estimate. The standard error of the intercept (se. intercept) is 0.5538, while the estimated intercept is 2.0444.

Overall, there isn't much proof of publication bias in the meta-analysis of topical pharmaceutical therapies for Acne Vulgaris, according to the findings of the linear regression test of funnel plot asymmetry.

Discussion

With their targeted therapeutic effects on the skin, topical therapies are essential in the therapy of Acne Vulgaris (Elman and Lebzelter 2004). These treatments have varying efficacies, and clinical studies and meta-analyses can be used to evaluate their efficacy (Moher et al. 1998).

According to the meta-analysis study, both the common effect model and the random effects model show that topical acne treatments are effective in treating Acne Vulgaris. These findings suggest that topical acne treatments are superior to a placebo in terms of treating Acne Vulgaris. The meta-analysis, which considers several studies and study heterogeneity, offers solid proof of the treatment impact. Individual responses to topical treatments can vary, so it's vital to consider other aspects like acne severity and skin type when choosing the best course of action for each patient (Callender 2004; Gollnick 2015). The findings emphasize the value of adding these medicines in acne management regimens and support topical therapies as a feasible choice for those looking for relief from Acne Vulgaris.

1. Mechanism of Action: According to Tuchayi et al. (2015), topical acne treatments are specifically developed to attack the root causes of acne, such as increased sebum production, clogged pores, and inflammation. These substances often contain active components that function directly on the skin to eliminate acne lesions and enhance overall skin condition, such as retinoids, benzoyl peroxide, salicylic acid, or antibiotics (Fox et al. 2016). These medications' effectiveness in treating acne is a result of their tailored actions (Renzi et al. 2022).
2. Clinical Trials: By combining data from many clinical trials, the meta-analysis increases the sample size and statistical power to identify treatment effects. These studies aim to assess the efficacy of topical acne treatments in comparison to placebo or other control groups. The meta-analysis can find consistent patterns of efficacy across various demographics and situations by combining the results of numerous research (Planès et al. 2016).
3. Placebo-Controlled Design: The meta-analysis's inclusion of placebo-controlled studies aids in identifying the precise effects of topical acne treatments. To ensure that any treatment effects are not just the result of the placebo effect or other confounding variables, the treatment group is compared to a placebo group (Goetz et al. 2000). The topical acne agent group's recovery is greater than would be anticipated from a placebo effect alone, according to the significant treatment impact.
4. Evaluation of Heterogeneity: The heterogeneity among the included studies is taken into consideration by the meta-analysis. The analysis's random effects model considers both variances within and across studies. The meta-analysis gives a more conservative estimate of the treatment impact by taking heterogeneity into account, ensuring that the reported benefit is not being driven by single research or a particular subgroup.
5. Statistical Significance: The RR estimates' z-scores and p-values show the treatment effect's statistical significance. A z-score indicates how far the RR estimate is from the null hypothesis of no difference by the number of standard deviations. Strong evidence against the null hypothesis is indicated by the low p-values, which are less than 0.0001. This suggests a considerable treatment effect in favor of topical acne treatments.

In some of the studies, the unique combination of topical treatments showed better efficacy than the single use of one agent. For example, Tirado-Sanchez et al. (2013) "Tretinoin 0.05% and adapalene 0.3% were more effective than adapalene 0.1% and placebo in the reduction of both inflammatory and noninflammatory lesions.". Combined therapy of isotretinoin (0.05%) and erythromycin (2%) gels showed better efficacy than either of the agents alone (Glass et al. 1999).

In conclusion, the focused mechanism of action, the meticulous design of clinical studies, the inclusion of placebo-controlled trials, the consideration of heterogeneity, and the statistical significance of the data are likely respon-

sible for the considerable treatment effect in favor of topical acne medications. The common mechanisms of action of these topical agents are anti-inflammatory, antibacterial and keratolytic. While this meta-analysis is not exhaustive of all available topical treatments, it clearly shows that the use of topical therapies (with efficacy varying from individual to individual) alone or in addition to oral therapy, is very likely to produce significant benefits by reducing skin lesions in the management of Acne vulgaris. Together, these elements lend credence to the effectiveness of topical acne medications in the management of Acne Vulgaris.

Conclusion

In conclusion, the results of the meta-analysis offer convincing proof of the effectiveness of topical acne treatments in the management of Acne Vulgaris. A significant treatment effect in favor of topical treatments over a placebo is seen in both the common effect model and random effects model outcomes. This suggests that people who are treated with topical acne medications have a considerably higher chance of seeing their acne become better.

The inclusion of several clinical trials, which increases the sample size and statistical power, supports the reliability of the results. The meta-analysis considers study heterogeneity to make sure that no single study or subgroup is responsible for the reported treatment effect. The research' placebo-controlled layout further confirms the precise effects of topical acne treatments outside of the realm of chance.

Topical acne treatments are helpful in treating acne because of their specific mechanisms of action, which include their capacity to deal with excessive sebum production, clogged pores, and irritation. The results' statistical significance, as shown by the low p-values and substantial z-scores, boosts the belief in the effectiveness of the treatment.

The results of this meta-analysis highlight the significance of incorporating topical acne agents into acne management strategies, providing an effective therapeutic option for people seeking relief from Acne Vulgaris. However, it is important to note that individual responses to topical treatments may vary, and other factors such as acne severity and skin type should be considered when determining the most suitable treatment approach for each patient.

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Supplementary material 1

Characteristics of studies included in the meta-analysis, and full references

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Data type: docx

Explanation note: Characteristics of clinical trials studies included in the meta-analysis, and full references.

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