2013

# Is Dapsone Gel Safe and Effective for the Treatment of Acne Vulgaris?

Amy Patel
*Philadelphia College of Osteopathic Medicine*, amypat@pcom.edu

# Is Dapsone Gel Safe and Effective for the Treatment of Acne Vulgaris?

Amy Patel, PA-S

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

December 14,2012

**ABSTRACT**

OBJECTIVE: The objective of this selective EBM review is to determine whether or not dapsone gel is safe and effective for the treatment of acne vulgaris.

STUDY DESIGN: A review of three English language studies published in 2007. Includes two randomized, double-blind, controlled trials and one open label, noncomparative study.

DATA SOURCES: Randomized, controlled trials comparing dapsone gel to vehicle gel control were found using PubMed and Cochrane database.

OUTCOMES MEASURED: Success on the Global Acne Assessment Score (GAAS) and reduction in acne lesion counts

RESULTS: The two randomized, controlled trials and the open-label noncomparative study showed that dapsone gel was effective in the treatment of acne vulgaris. Results from the Draelos et al and Raimer et al studies showed patients had success on the GAAS and had a reduction in acne lesion counts. The Lucky et al study showed that patients had a reduction in acne lesions counts. All three studies also demonstrated that dapsone gel was safe when used to treat acne vulgaris.

CONCLUSIONS: The results of the randomized, controlled trials and open-label noncomparative study indicate that dapsone gel for the treatment of acne vulgaris is safe and effective.

KEY WORDS: Dapsone, acne.

**INTRODUCTION**

Acne vulgaris is a common dermatologic condition that presents in adolescence and is characterized by inflammatory lesions (papules and pustules) and non-inflammatory lesions (comedones).[1] Acne vulgaris can be chronic for some individuals but self-limiting in other cases. Acne vulgaris tends to be more severe in males than females. Contributing factors to developing acne include stress, genetics, and environment. Acne vulgaris may negatively impact body image, self-esteem, and mood.[2] Successful and prompt treatment of acne vulgaris can improve an individual's quality of life.[2]

In the United States, acne is the most common skin disorder affecting 40 to 50 million individuals.[3] The prevalence of acne vulgaris peaks during the middle to late teenage period and then steadily decreases. The incidence of acne vulgaris is 30% to 60% of 10-12 year olds and 80% to 95% of 16-18-year olds that are affected.[4] The direct costs associated with acne vulgaris surpass $2.2 billion each year in the United States.[5] Due to the numerous individuals affected by acne vulgaris, this condition is commonly encountered in the scope of PA practice. It is important to be able to correctly diagnose and treat acne vulgaris.

The pathogenesis of acne vulgaris includes many factors and the series of events in the process of development of acne are unclear.[6] Acne development is initiated during menarche when there is increasing sebum production in the sebaceous glands.[6] During menarche, the adrenal glands, ovaries, and testes secrete androgens. This subsequently leads to an increase in sebum production, causing hair follicles to be plugged with oil and dead skin cells that further stimulate the development of acne.[6] Other known factors that contribute to acne vulgaris are

inflammation, follicular hyperproliferation, and Propionibacterium acnes.[6] Common locations for acne to develop include the face, neck, chest, shoulders, and back.

Acne vulgaris can be treated with a variety of medications or, simply, self-care. Treatment of acne will help to fight bacterial infections, accelerate skin turnover, reduce inflammation, and/or reduce oil production. Treatment options vary with each patient, depending on the severity of acne. Some options include accutane, tretinoin, azelaic acid, benzoyl peroxide, sulfer, salicyclic acid, resorcinol, or routine face washing with mild soap.[4] Antibiotics that can be used for acne include tetracycline, doxycycline, erythromycin, trimethoprim, and clindamycin.[4] Prompt treatment is crucial because acne vulgaris can cause psychological or social dysfunction and long-lasting deformity.

The treatment options that are listed above are all successful ways of treating acne. Dapsone is a sulfone that has anti-inflammatory and antimicrobial properties. Dapsone has been used orally for the treatment of acne, but is limited in use due to the potential for systemic absorption leading to toxicity. Recently, topical dapsone gel was developed for treatment of acne, which would offer the same antimicrobial and anti-inflammatory advantage with minimal systemic absorption. Thus, dapsone gel offers a new treatment option for acne vulgaris.

**OBJECTIVE**

The objective of this selective EBM review is to determine whether or not "Is dapsone gel safe and effective for the treatment of acne vulgaris?"

**METHODS**

This review includes two randomized controlled trials and one open-label non-comparative study. The intervention used was dapsone gel 5%. The treatment groups receiving dapsone gel were compared to those receiving vehicle gel control treatment. The population in these studies consisted of men and women over the age of 12 years with acne vulgaris. The outcomes measured were those of patient-oriented evidence. The efficacy and safety of dapsone gel for the treatment of acne vulgaris was measured through success on the GAAS (global acne assessment score) and reduction in acne lesion count. Safety of dapsone gel was specifically evaluated through adverse events and physical examination findings.

The three studies in this review were researched using PubMed and Cochrane database by the author. Keywords used in literature search were “dapsone” and “acne”. All articles were published in English in peer-reviewed journals in 2007. Articles were selected by the author based on their relevance and outcome to the patient. Inclusion criteria were randomized, controlled, double-blind studies based on an outcome which was important to the patient. Studies were excluded if they included patients under the age of 12 years old. Table 1 demonstrates the demographics of the studies included. Statistics included in the studies were relative risk reduction (RRR), absolute risk reduction (ARR), relative risk increase (RRI), absolute risk increase (ARI), number needed to treat (NNT), number needed to harm (NNH), and p-values.

Both Draelos et al and Raimer et al studies were designed in a similar way. Patients were randomly assigned dapsone gel or vehicle gel and then instructed to apply a thin layer of dapsone or vehicle gel to the acne-affected areas for 12 weeks. In Lucky et al study, patients applied dapsone gel to acne-involved areas for 12 months. In this study, if acne cleared up in a particular area, treatment could be discontinued but if acne recurred, then dapsone gel was reapplied.

**OUTCOMES MEASURED**

Outcomes measured were those of patient-oriented evidence that matters. Draelos et al and Raimer et al studies assessed efficacy based on success rates on the GAAS from 0 to 4 (0=none, 1=minimal, 2=mild, 3=moderate,4=severe) and reduction from baseline in acne lesion counts. Success on the GAAS is defined as a score of 0 or 1. Patients went through a dermatologic examination at baseline and weeks 2, 4, 6, 8, and 12. At these visits, a Global Acne Assessment Score was recorded. In addition, at baseline and week 12, inflammatory, non-inflammatory and total lesions were counted. The Lucky et al study assessed efficacy based on reduction of acne count lesions during a dermatological examination at baseline and months 1, 3, 6, 9, and 12.

Another outcome measured was safety of dapsone gel. This was evaluated by the adverse events and physical examination findings. All three studies assessed patients for dryness, peeling, and erythema. Additionally, blood was drawn for routine laboratory tests and patients were screened for G6PD deficiency.

Table 1: Demographics & Characteristics of included studies

| Study | Type | # Pts | Age | Inclusion Criteria | Exclusion Criteria | W/D | Intervention |
|---|---|---|---|---|---|---|---|
| Draelos[6] (2007) | Double blind, RCT | 3010 | > 12 years old | - Atleast 12 years old with a clinical diagnosis of acne vulgaris involving face<br>- 20-50 inflammatory lesions and 20-100 noninflammatory lesions above the mandibular baseline | - Severe cystic acne or active/ developing nodules<br>- Use of drugs that affect acne<br>- Allergy to dapsone or sulfa drugs<br>- Pregnant or nursing women | 503 | dapsone gel 5% twice daily or vehicle gel control |
| Raimer[2] (2007) | Double blind, RCT | 1306 | >12 years old (sub-group presented in this study is 12-15 years old) | - 12 years or older with acne vulgaris;<br>- presence of 20-50 inflammatory lesions and 20-100 noninflammatory lesions above the mandibular line at baseline | N/A | 22 | dapsone gel 5% twice daily or vehicle gel control |
| Lucky[1] (2007) | Open label, noncom-parative | 506 | >12 years old | - 12 years or older with a clinical diagnosis of moderate to moderately severe acne vulgaris defined as at least 20 inflammatory lesions at baseline | - Severe cystic acne, acne conglobate, or active/developi ng nodules<br>- Use of drugs that affect acne<br>- Allergy to dapsone or sulfa drugs<br>- Pregnant or nursing women | 166 | dapsone gel 5% twice daily |

**RESULTS**

This EBM review was done on two randomized controlled trials and one open-label non-comparative study. The results in these reviews were presented as dichotomous data. Data from the studies was analyzed with the intention to treat. The inclusion criteria for all three studies was similar. All participants were at least 12 years old with a clinical diagnosis of acne vulgaris and had the presence of at least 20 inflammatory lesions at baseline. The Draelos et al and Lucky et al studies had similar exclusion criteria whereas the Raimer et al study did not have an exclusion criteria noted. Exclusion criteria included severe cystic acne, active/developing nodules, pregnant or nursing women, allergy to dapsone or sulfa drugs, or the use of other drugs that affect acne.

In the study done by Draelos et al, patients treated with dapsone gel had significantly greater reduction in inflammatory, non-inflammatory, and total lesion counts from baseline to 12 weeks and achieved success on the GAAS. The relative risk reduction (RRR) was 23% and absolute risk reduction (AAR) was 8.3%. The number needed to treat (NNT) was 13 patients. This implies that 13 people needed to be treated with dapsone gel in order to improve acne vulgaris in one patient. The difference in control and experimental group was a p-value less than 0.001, making it statistically significant.

In the study done by Raimer et al, dapsone gel was more effective than vehicle gel. At week 12 patients achieved GAAS success and reduction in acne lesion counts from baseline. The relative risk reduction (RRR) was 42% and absolute risk reduction was 11.9%. The number needed to treat was 9 patients. Thus, 9 patients needed to be treated with dapsone gel to improve acne vulgaris in one patient. Testing was statistically significant with a p-value less than 0.001.

In the open-label non-comparative study done by Lucky et al, there was a reduction in acne count lesions from baseline to 12 months with the use of dapsone gel. Inflammatory lesions decreased the greatest by 58.2% and non-inflammatory lesions decreased by 19.5%. Total acne lesion counts decreased by 49.0%. The test was statistically significant with a p-value of less than 0.001. **Table 2** shows the efficacy of dapsone gel in the treatment of acne vulgaris in two of the three studies. The study done by Lucky et al is not included in **Table 2** because it did not use the GAAS score to evaluate effectiveness.

**Table 2**. Clinical efficacy of dapsone gel in the treatment of acne vulgaris

| Study | EER (Dapsone gel; Individuals achieving success on GAAS) | CER (Vehicle gel control; Individuals achieving success on GAAS) | p-value | RRR | ARR | NNT |
|---|---|---|---|---|---|---|
| Draelos et al (2007) | 44.2% | 35.9% | p<0.001 | 23% | 8.3% | 13 |
| Raimer et al (2007) | 40.1% | 28.2% | p<0.001 | 42% | 11.9% | 9 |
| Lucky et al (2007) | - | - | - | - | - | - |

EER – experimental event rate, CER – control event rate, RRR – relative risk reduction, ARR – absolute risk reduction, NNT – number needed to treat

The incidence of adverse events was also calculated by each study in regards to the safety of dapsone gel. In the study done by Draelos et al, both dapsone gel and vehicle gel treated groups experienced similar rates of adverse events. Patients treated with dapsone gel had an

incidence of 58.2% and patients treated with vehicle gel had an incidence of 58.6% in terms of adverse events. Erythema occurred in 16.3% of dapsone treated patients and 16.1% of vehicle gel treated patients. The relative risk increase (RRI) was 1.2% and the absolute risk increase (ARI) was 0.2%. The number needed to harm (NNH) was 500 patients. Thus, 500 patients need to be treated with dapsone gel for one person to have erythema as an adverse event.

In the study done by Raimer et al, erythema was one of the most common adverse events occurring at week 12. The relative risk increase (RRI) was -11.4% and absolute risk increase (ARI) was -4.3%. The number needed to harm (NNH) was 23 patients.

The study conducted by Lucky et al found 68% of patients experienced at least one adverse event. About 1.6% of patients experienced erythema at application site. Erythema was a common adverse event in all three studies. **Table 3** shows the incidence of erythema in patients treated with dapsone gel versus vehicle gel treated groups.

**Table 3**. Incidence of erythema in dapsone gel group versus vehicle gel control group.

| Study | EER (dapsone gel) | CER (vehicle gel control) | RRI | ARI | NNH |
|---|---|---|---|---|---|
| Draelos et al (2007) | 16.3% | 16.1% | 1.2% | 0.02% | 500 |
| Raimer et al (2007) | 33.4% | 37.7% | -11.4% | -4.3% | -23 |
| Lucky et al (2007) | 1.6% | N/A | N/A | N/A | N/A |

EER – experimental event rate, CER – control event rate, RRI – relative risk increase, ARI – absolute risk increase, NNH – number needed to harm, N/A – not applicable

**DISCUSSION**

Dapsone was shown to be effective for the treatment of acne vulgaris years ago, but was not widespread in use due to its systemic toxicity. Dapsone has antimicrobial and anti-inflammatory properties. Dapsone was known to cause adverse hemolytic reactions, more commonly in patients with G6PD deficiency.[6]

The two randomized controlled trials and one open-label noncomparative study showed that dapsone gel 5% is safe and effective for the treatment of acne vulgaris. Topical dapsone gel has minimal systemic absorption, as noted by the studies discussed. Adverse events and routine blood laboratory values were monitored on patients during the study, which showed similar results between the dapsone gel treated group and vehicle gel treated group. A major concern was patients diagnosed with G6PD deficiency, but no mean change from baseline was seen in the hematology results.

The study done by Draelos et al showed a higher percentage of people having minimal to no acne at the end of the treatment in patients treated with dapsone gel. In addition, those treated with dapsone gel had greater success on the GAAS and a reduction in acne lesion counts. Erythema was a common adverse reaction seen in both groups that were treated but declined with the course of treatment. In the study conducted by Raimer et al, dapsone gel also caused improvement of acne based on GAAS success and reduction in acne count lesions. Greatest improvement was seen in inflammatory lesions. In the study done by Lucky et al, it is difficult to assess efficacy without a control group. However, this study did assess the use of dapsone gel for twelve months rather than only twelve weeks.

The studies in this review have some limitations. The studies done by Draelos et al and Raimer et al were twelve weeks long, which may not be enough time to thoroughly assess

efficacy of dapsone gel. For many patients, acne can be a chronically debilitating condition where a longer treatment period may be needed. Also, the study done by Raimer et al only focused on a subgroup of participants from 12 to 15 years of age. Even though acne vulgaris is more common in young teenagers and adolescents, many older individuals are also affected and should have been represented. In addition, the study done by Lucky et al lacked a control group. Lack of a control group can limit findings and be inconclusive about the efficacy and safety of dapsone.

## CONCLUSION

The trials reviewed imply that dapsone gel is safe and effective for the treatment of acne vulgaris. Patients in all three studies showed improvement in acne vulgaris when applying topical dapsone gel. It was also suggested from these studies that dapsone gel is well-tolerated, as it does not cause significant adverse events. Additionally, dapsone gel has a rapid onset of action, which truly matters to the patient. Dapsone gel provides a new treatment option for medial providers and those diagnosed with acne vulgaris. Although these studies do conclude the use of dapsone gel is safe and effective, more trials should be done to assess the safety of using dapsone gel over a chronic time period. Regardless of the need for additional studies, dapsone gel is a safe and effective way of treating acne vulgaris.

References


1. Lucky AW, Maloney JM, Roberts J, et al. Dapsone gel 5% for the treatment of acne vulgaris: Safety and efficacy of long-term (1 year) treatment. *J Drugs Dermatol*. 2007;6(10):981-987.
2. Draelos ZD, Carter E, Maloney JM, et al. Two randomized studies demonstrate the efficacy and safety of dapsone gel, 5% for the treatment of acne vulgaris. *J Am Acad Dermatol*. 2007;56(3):439.e1-439.10. doi: 10.1016/j.jaad.2006.10.005.
3. American Academy of Dermatology. Acne. American Academy of Dermatology Web site. http://www.aad.org/media-resources/stats-and-facts/conditions/acne. Updated 2012. Accessed September 24, 2012.
4. Knox MA. Chapter 6. Skin Diseases in Infants & Children. In: South-Paul JE, Matheny SC, Lewis EL, eds. *CURRENT Diagnosis & Treatment in Family Medicine*. 3rd ed. New York: McGraw-Hill; 2011. http://www.accessmedicine.com/content.aspx?aID=8149632. Accessed September 29, 2012.
5. Bhambri S, Del Rosso JQ, Bhambri A. Pathogenesis of acne vulgaris: Recent advances. *J Drugs Dermatol*. 2009;8(7):615-618.
6. Raimer S, Maloney JM, Bourcier M, et al. Efficacy and safety of dapsone gel 5% for the treatment of acne vulgaris in adolescents. *Cutis*. 2008;81(2):171-178.