

Treatment of Acne Vulgaris with 1064 nm Nd:YAG Laser

Ruta Ganceviciene^{1,2}, Raimundas Meskauskas³, Austra Berzanskyte⁴

¹*Clinic of Infectious diseases, Thoracic diseases, Dermatovenereology and Allergology, Medical Faculty of Vilnius University, Vilnius, Lithuania*

²*Clinic of General and Aesthetic Dermatology, Vilnius, Lithuania*

³*National Center of Pathology, Affiliate of Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania*

⁴*Institute of Public Health, Vilnius University, Vilnius, Lithuania*

ABSTRACT

Acne vulgaris is one of the most common dermatologic diseases, affecting teenagers as well as adults, with a possibility to cause long-lasting psychosocial and physical effects. Since acne is a chronic inflammatory skin disorder, a long-lasting combined treatment as well as maintenance therapy are advised. Conventional treatments such as topical and oral medications are often associated with poor compliance, lack of durable remission and potential side effects. If untreated, acne may lead to scarring, dyspigmentation and physical discomfort.

Acne treatments using laser and light-based devices have been reported to have varying degrees of efficacy. 1064 nm Nd:YAG laser was tested as a potentially safe and side-effect-free novel treatment of acne vulgaris. A split-face study was performed on 19 patients with a diagnosed acne vulgaris condition. A reduction in inflammatory as well as non-inflammatory acne lesion counts on the treated as well as control side was observed and supported by histological examination, suggesting a systemic effect of this laser treatment on the skin. No significant adverse reactions were observed, with only transient post-treatment erythema. The treatment has the potential to become a well-tolerated, safe and effective alternative for mild to moderate inflammatory acne vulgaris.

Key words: acne vulgaris, acne treatment, Nd:YAG laser, light-based therapy.

Article: J. LA&HA, Vol. 2015, OnlineFirst

Received: June 1, 2015; Accepted: November 27, 2015

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Printed in Europe. www.laserandhealth.com

I. INTRODUCTION

Acne is the most common skin disease worldwide and the most common dermatological reason for medical consultation (1.1%). Around 70 to 95% of all adolescents have acne lesions [1]. The incidence of the

disease reaches a maximum at the age of 15 to 18 years. The majority of patients have a spontaneous regression after puberty, and 2 to 7% have significant scarring. In 10% of cases, the disease persists over the 25th year of age. Approximately 15-30% of acne patients need medical treatment because of the severity or duration of the illness [2].

Acne vulgaris is a chronic multifactorial inflammatory disease of pilosebaceous units. There are classical key factors of acne lesions development: an increased activity of the sebaceous glands leading to seborrhea, abnormal follicular differentiation and increased cornification as well as Propionibacterium acnes (*P. acnes*) colonization with inflammatory reaction and the subsequent immunological processes. Androgens, skin lipids and regulatory neuropeptides appear to be involved in this multifactorial process [2-4]. Hereditary factors are supposed to play an important but indirect role; in women, an irregular menstrual cycle and pregnancy exert an influence on the course of acne [4-5]. Environmental factors, such as smoking and diet, numerous medications and psychological factors are supposed to influence the course of the disease [3]. These factors interrupt the natural cyclic process in the sebaceous follicles and support the transition from microcomedones to comedones and inflammatory lesions, affecting mostly the face but also the back and chest [6, 7]. In severe cases they may evolve into deep inflammatory nodules with associated systemic symptoms [8]. Acne may cause long-lasting psychosocial and physical effects, with patients often showing anxiety and depression. The psychological effects usually improve with treatment. Therefore, acne patients should be evaluated by dermatologists in order to plan an efficient individual acne therapy [8].

Conventional treatments with combined topical/oral medications can be prolonged and are often associated with poor compliance, lack of durable remission, and potential side effects. Acne therapy should be determined by the extent, severity and duration of the disease, response to previous treatments and predisposition to scarring and post-

inflammatory hyperpigmentation (PIH), as well as patient preference and cost, and should combine standard treatments with adjunct therapy and cosmetic use [8].

There is a lack of standard protocols, experience and clinical trials for the treatment of acne with laser and light sources. Nevertheless, laser therapy may offer an alternative to conventional acne treatments, in particular for non-responders or non-compliant patients or in patients with antibiotic-resistant bacterial strains. Methods involve the use of 585- and 595-nm pulsed dye lasers [9, 10], the 1450-nm diode laser [11], the potassium titanyl phosphate laser – KTP [12-14], radiofrequency devices [15], intense pulsed light (IPL, 400-1200 nm) sources [16], and photodynamic therapy (PDT) [17]. Regarding the use of 1064 nm Nd:YAG laser, studies are very limited. Some studies report it to be a safe, effective, and well-tolerated alternative for patients with acne who have contraindications to the use of systemic anti-acne therapies [18]. The above light-base devices are thought to either indirectly target the bacterium *P.acnes*, through photo-excitation of porphyrins, inducing a bactericidal effect on *P. acnes* by release of reactive free radicals, or cause phototoxic and/or photothermal damage to the sebaceous gland, resulting in reduced gland size and sebum production [19, 20]. Apart from numerous small uncontrolled studies, reports are very limited and the true mechanisms of action remain unclear. Therefore, the aim of our study was to evaluate the clinical efficacy, safety, and histological changes of a new method of treatment of mild to moderate acne with 1064 nm Nd:YAG laser.

II. MATERIALS AND METHODS

a) Study design

This study was conducted according to the ethical standards of the Lithuanian Bioethical Committee (The Lithuanian Bioethical Committee on research involving human subjects; protocol No.1, version No.2, authorization No.158200-13-640-212).

19 patients, aged >18 years with Fitzpatrick skin type I-III and clinically diagnosed mild to moderate facial acne vulgaris visiting the General and Aesthetic Clinic of Dermatology in Vilnius, Lithuania were enrolled in the study. Exclusion criteria were underage, pregnancy and lactation, prior therapy with isotretinoin within 6 months, systemic antibiotic therapy (for any indication) within 1 month or use of topical acne preparation/intra-lesional steroid injection within 1 month before the laser treatment. Patients were interviewed for past skin diseases and were not allowed to use any systemic, topical, or phototherapy-based

acne treatment during the course of this study.

A split-face study design was used; the side of the face to receive the intervention was randomized with the other side acting as a within-patient control.

b) Laser treatment

Patients were treated with the 1064 nm Nd:YAG laser wavelength (Fotona SP Dynamis, Ljubljana, Slovenia), using an S11 scanner with OPTimal scanning pattern, 6 mm spot size, 25-40 ms pulse duration, 30-50 J/cm² fluence and frequency of 3.2-3.8 Hz. Treatment was performed on one side of the face, with one pass without overlapping the single pulses. Cold air cooling was used throughout the treatment and moisturizing cream and/or sunscreen was applied immediately after treatment to ensure comfort and safety at the highest level. Altogether, 5 treatment sessions were performed with 1 week intervals.

c) Clinical outcome assessment

Based on disease activity and the predominant type of acne lesions, a simple 4-group clinical classification of patients (Nast et al. 2012) was used, which is based on EU Guidelines (1 – Comedonal acne, 2 - Mild–moderate papulopustular acne, 3 - Severe papulopustular acne, moderate nodular acne, 4 - Severe nodular acne, conglobate acne). The progress of treatment and acne lesion counts were evaluated by standardized high-resolution digital photographs (MVC-FD97, Sony, Tokyo, Japan), which were taken before each treatment, at every laser treatment, as well as 1 week (and also 1 month in some patients) after the last treatment session (total 6 visits), with the same settings and lighting conditions throughout the study. The clinical outcome was assessed also by inflammatory and non-inflammatory acne counts by an independent dermatologist. The duration and type of adverse reactions, such as erythema, edema, exfoliation or hyper- and hypo-pigmentation, were documented at every follow-up visit with a 1-5 VAS scale (1-none, 2-mild, 3-moderate, 4-severe, 5-very severe), which was used also for self-assessment of the pain level during and after the treatment (stinging, burning, itching, dryness).

Skin specimens were obtained from the facial skin with inflamed acne lesions (papules or pustules) of 3 patients before the treatment and 1 week after the last treatment, by performing 3 mm-cylinder punch biopsies. Tissue samples were subjected to hematoxylin and eosin (HE) staining before histopathologic evaluation by an independent pathologist.

d) Statistical analysis

Statistical analysis was performed using the SPSS statistical package (IBM Statistics SPSS Version 22).

The paired t-test with $P < 0.05$ was used to assess changes in acne counts before and after the treatments. The non-parametric Wilcoxon signed-rank test was used for paired change evaluation on one side. The Mann–Whitney U test was used for difference evaluation between the treated and control sides of the face. Regression analysis was done for all types of lesions on each facial side.

III. RESULTS AND DISCUSSION

Seventeen (17; 2 men, 15 women) of 19 initially enrolled subjects with acne completed the study; two dropped out for personal reasons. The mean age of subjects was 20.4 years (18 to 30 years). The subjects had Fitzpatrick skin types I-II. Patients were identified with mild to moderate facial acne, severity - grade 2.

a) Acne counts

The number of acne lesions reduced significantly from visit to visit during the entire period in each of facial sides ($P < 0.001$). The median lesion count reduced by 56 lesions in the laser-treated facial side and by 34 lesions in the control side, as seen in Figure 1, but the difference between the facial sides was not significant ($P = 0.179$). At the final visit, 1 week after the final treatment, total acne lesions were reduced by 75% on both the treated and control sides ($P < 0.001$) as seen in Table 1.

Table 1: Percentage reduction of acne lesions (median) with weekly 1064 nm Nd:YAG laser treatments. After 5 weeks (1 week after the final treatment), total acne lesions were reduced by 75% on both the treated and control sides.

	Laser-treated side		Control side	
	Median	P value	Median	P value
After 1 week	12.1%	0.001	9.5%	0.006
After 2 weeks	34.8%	0.001	21.3%	0.001
After 3 weeks	41.6%	<0.001	35.4%	<0.001
After 4 weeks	45.9%	<0.001	36.4%	<0.001
After 5 weeks	74.7%	<0.001	75.4%	<0.001

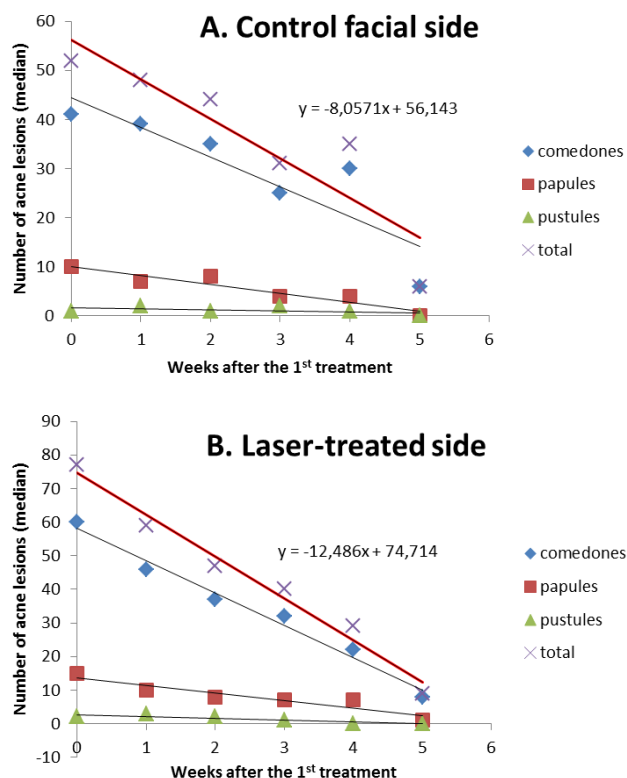


Fig. 1: Change in number of acne lesions on the control (A) and 1064 nm Nd:YAG laser-treated side (B), during 5 weekly treatments. Follow-up was made 5 weeks after the 1st treatment session (1 week after the last treatment). The number of acne lesions reduced significantly from visit to visit during the entire period on both facial sides. The median lesion count reduced on both sides, but the difference between facial sides was not significant.

b) Histopathological examination

Before the treatment, histopathological examination showed typical acne-associated findings. Foreign-body large cells were recognized in the dermis, with dilated follicles with abundant infiltration of PMN (polymorphonuclears - neutrophils, solitary, sporadic eosinophils) and MMN (monomorphonuclears consisting of lymphocytes and plasma cells) as well as micro-abscesses and horny cells aggregation (Figures 2A, 2B, 2C). After the treatment, very spare focal MMN infiltration, undamaged, practically normal pilosebaceous units (PSU) and very few PMN in the stratum corneum were observed. Generally, a significant reduction of inflammation severity with reduced quantity of inflammatory cells and disappearing of granulomas was observed after laser treatment. Inflammation densities were significantly decreased and became non-active (Figures 2D and 2E).

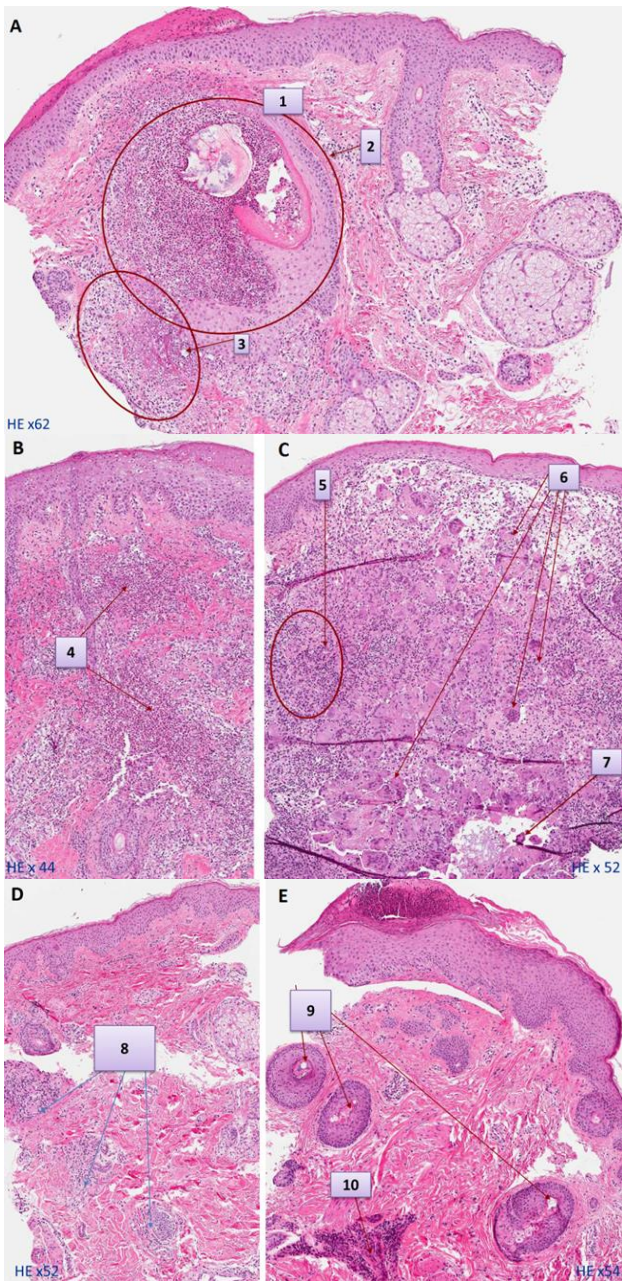


Fig. 2: Histopathological examination of facial skin specimen with inflamed acne lesion, obtained with 3 mm-cylinder punch biopsies and subjected to hematoxylin and eosin (HE) staining, before (A, B, C,) and 1 week after (D, E) 1064 nm Nd:YAG laser treatment. A significant reduction in inflammation severity, with disappearance of granulomas, very spare focal MMN infiltration and undamaged PSUs were observed after the laser treatment, compared to the situation before the treatment. Legend: 1 - foreign body type granuloma; 2 - dilated follicle with abundant infiltration of PMN & MMN; 3- perifollicular inflammatory infiltration; 4 - focal infiltration of PMN & MMN (PMN - neutrophils, MMN - lymphocytes and plasma cells), micro-abscesses; 5 - perifollicular inflammatory infiltration consisting of lymphocytes and plasma cells; 6 - foreign body giant cells; 7 - horny cells aggregation, former follicle; 8 - several residual dermal periadnexal inflammatory infiltrates; 9 - practically normal PSUs; 10 - perivascular inflammatory infiltration.

The histopathologic findings correlated well with the clinical acne treatment response. Interestingly, both the treated as well as untreated sides of the face improved with laser treatment (Figure 3 and 4), suggesting the possibility of a systemic effect of the laser on the skin. A systemic effect of red and infrared laser on the repair of skin wounds in rats has been previously observed also by Rodrigo et al. [21].

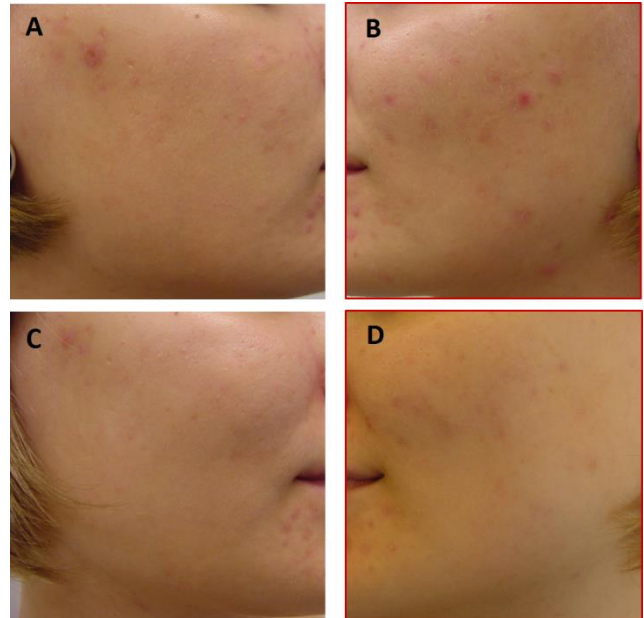


Figure 3: Patient with inflammatory acne before (A, B) and 1 week after (C, D) a series of 5 treatments with 1064 nm Nd:YAG laser. Improvement is visible on both the treated (B, D) as well as control sides (A, C).

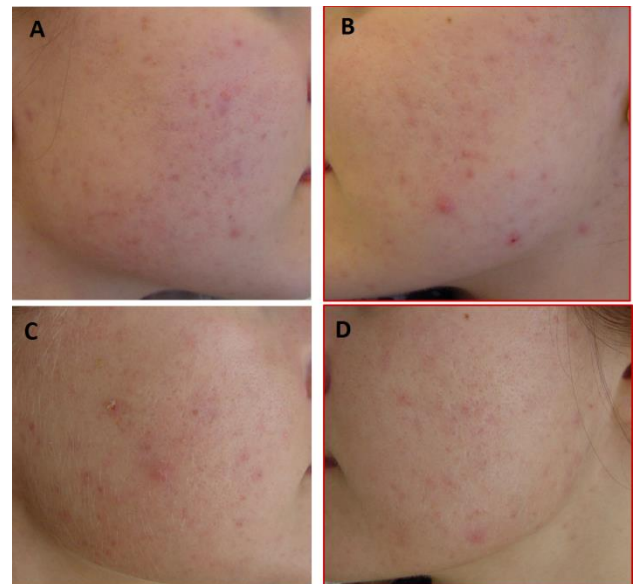


Figure 4: Patient with inflammatory acne before (A, B) and 1 month after (C, D) a series of 5 treatments with 1064 nm Nd:YAG laser. Improvement is visible on both the treated (B, D) as well as control sides (A, C).

No significant adverse reactions like blistering, hyper/hypopigmentation, or scarring were reported. All patients reported mild transient erythema that resolved a few hours after treatment in all cases. The mean VAS score of pain was approximately 2-3 (mild to moderate) at each session and was well tolerated by the patients.

IV. CONCLUSIONS

Treatment of acne vulgaris with 1064 nm Nd:YAG laser showed to be effective for treating not only inflammatory but also non-inflammatory acne lesions, with improvement on the treated as well as control sides, suggesting a systemic effect on the skin from this laser treatment. The treatment can be a well-tolerated, safe and effective alternative for inflammatory mild to moderate acne, and further studies are encouraged.

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