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A Randomised Controlled Trial: The effect of oral astaxanthin as an anti-inflammatory agent on serum level of e-selectin in acne vulgaris



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Muhammad Eko Irawanto,^{1*} Harijono Kariosentono,¹ Bambang Purwanto,²
Eti Poncorini Pamungkasari³

ABSTRACT

Background: E-selectin plays a pivotal role in the inflammatory response of acne. Astaxanthin (AST), an supplement claimed having anti-inflammatory and antioxidant properties, has potential in inflammatory skin therapy. This study aims to determine the effect of oral AST as an anti-inflammatory agent on the serum level of e-selectin in acne vulgaris.

Methods: This is a double-blind, randomized controlled trial study with a pretest and posttest control group design. The participants were 34 acne vulgaris patients with inflammatory lesions (papulopustular acne). The participants are randomly assigned to the treatment or control group to receive oral tablet of 4 mg of AST or placebo in addition to standard acne therapy of tretinoin cream 0.025% and clindamycin cream 1.2%. Each group was measured for the serum level of E-selectin before therapy (pretest) and after one month of therapy (posttest).

Results: The pretest and posttest level of the mean serum e-selectin in the treatment group were 50.21 ± 21.12 ng/ml and 50.04 ± 22.99 ng/ml, respectively. There is no significant difference between the pretest and posttest of the mean e-selectin level in the treatment group ($p=0.943$). While, the pretest and posttest of mean serum e-selectin level in control group were 57.84 ± 20.71 ng/ml and 55.87 ± 15.98 ng/ml, respectively. There is no significant difference between the pretest and posttest of the mean e-selectin level in the control group ($p=0.453$). There was a decrease in the mean serum e-selectin level of the treatment and control groups one month after therapy. However, the decrease of the mean e-selectin level between treatment and control group is not significantly different ($p=0.547$).

Conclusion: The addition of oral AST to standard acne therapy shows no significant difference in reducing the serum e-selectin level compared to placebo.

Keywords: Oral astaxanthin, e-selectin, acne vulgaris.

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¹Department of Dermatology and Venereology,

²Department of Internal Medicine,

³Department of Public Health, Faculty of Medicine, Universitas Sebelas Maret, Dr. Moewardi General Hospital, Surakarta, Indonesia

INTRODUCTION

Acne vulgaris (AV) is a chronic multifactorial disorder of the pilosebaceous unit which occurs as a result of an interaction between the release of inflammatory mediators, follicular hyperkeratinization with subsequent plugging of the follicle, *Propionibacterium acnes* (*P. acnes*) follicular colonization and excess sebum production.^{1,2} The inflammation process is considered as a key component in the pathogenesis of acne as it occurs continuously in the early and late stage of acne vulgaris.³⁻⁵

In normal condition, the inflammation provide protection against infections and tissue damages through vasodilation and recruitment of immune cells and plasma proteins. However, the dysregulated inflammatory response can cause excessive or prolonged tissue damage, which plays a role in the development of acute or chronic inflammatory diseases. In the chronic inflammation, the nuclear factor-kappa beta (NF-κB) induces pro-inflammatory genes, innate and adaptive immune cells.⁶ The aberration in NF-κB activity is associated with

various inflammatory diseases. This process is targeted by anti-inflammatory drugs to suppress the expression of inflammatory cytokines.⁷ A similar response of NF-κB activation is found in acne lesion.⁸

The NF-κB activation is associated with inflammatory cytokines production. Inflammatory cytokines induce the expression of cell adhesion molecules.⁹ These molecules can be found in the surface of endothelial cells surface, such as e-selectin, intercellular cell adhesion molecules (ICAM)-1, and vascular cell adhesion molecules (VCAM)-1. They mediate the adhesion and extravasation of leukocytes. In response to pro-inflammatory cytokines, interleukin (IL)-1β and tumor necrosis factor (TNF)-α, endothelial cells express e-selectin.¹⁰ NF-κB pathway activation triggers the upregulation of the expression of the e-selectin, ICAM-1, and VCAM-1 in response to various inflammatory cytokines.¹¹ Then, e-selectin is synthesized and expressed on the endothelial cell surface within 1 to 2 hours in response to IL-1 and

*Correspondence to:
Muhammad Eko Irawanto,
Department of Dermatology and
Venereology
ekokepik@gmail.com

TNF.¹² Hence, e-selectin expression was elevated in acne lesions.¹³

Astaxanthin (AST) is an excellent agent with anti-inflammatory and antioxidant properties that suppresses pro-inflammatory cytokines, chemokine expression and NF- κ B activation.^{14,15} This agent prevents inflammatory processes by blocking pro-inflammatory genes expression as a consequence of suppressing NF- κ B activation.¹⁶ AST can be an exciting new strategy for treating inflammatory skin diseases.¹⁷

This study aimed to investigate the effect of oral astaxanthin as an anti-inflammatory agent on serum e-selectin level in acne vulgaris.

METHODS

This research was a double-blind randomized control trial with a pre- and post-test control group design. This research is approved by the RSUD Dr Moewardi Ethical Committee (Ethical Clearance No.1.138/X/HREC/2019). The written informed consent was obtained from the participants before the research is conducted. The participants were acne vulgaris patients of RSUD Dr Moewardi outpatient clinic from October to November 2019. The exclusion criteria were acne vulgaris patients with other inflammatory diseases, obesity, smoking, or patients were taking medications such as benzodiazepines, lithium, cyclosporine, ramipril, isoniazid, iodides, bromides, vitamin B-type complexes, serotonin uptake inhibitors, epidermal growth receptor inhibitors, progestin contraceptives, corticosteroids and anti-acne. The participants were randomly allocated into two equally numbered groups. Both groups received topical acne standard therapy of tretinoin cream 0.025% and clindamycin cream 1.2%. The cream was applied at night. The treatment group receive an additional oral therapy of 4 mg of AST, while the control group receive an AST-similar-looking-placebo containing 4 mg of lactulose. Neither the researcher nor the subject knew whether the subject was receiving the treatment or a placebo. The serum level of e-selectin was measured before (pretest) and after a month after (posttest) therapy. The serum levels of e-selectin were

determined by ELISA using a standard kit (Human sE-selectin Quantikine ELISA Kit, R&D Systems, Minneapolis, USA). The data was analysed using SPSS software version 21.0. The data distribution was determined using the Saphiro-Wilk test. The data was analysed according to intention-to-treat principle. The comparison of data within- and between-group was done using paired t-test and student t-test, respectively. If the data distribution is not normal, the Wilcoxon and Mann-Whitney U test will be used for analysis.

RESULTS

A total of thirty-four acne vulgaris patients (15 males and 19 females with an age range of 14-36 years) were recruited (Table 1). The pretest and posttest level of the mean serum e-selectin in the treatment group were 50.21 ± 21.12 ng/ml and 50.04 ± 22.99 ng/ml, respectively. There is no significant difference between the pretest and posttest of the mean e-selectin level in the treatment group ($p=0.943$). While, the pretest and posttest of mean serum e-selectin level in control group were 57.84 ± 20.71 ng/ml and 55.87 ± 15.98 ng/ml, respectively. There is no significant difference between the pretest and posttest of the mean e-selectin level in the control group ($p=0.453$). There is a decrease in the mean serum e-selectin level of the treatment and control groups one month after therapy. However, the decrease of the mean e-selectin level between treatment and control group is not significantly different ($p=0.547$).

DISCUSSION

AST is an agent claimed with anti-inflammatory and antioxidant properties.¹⁴ AST suppresses NF- κ B activation. It prevents inflammatory processes by blocking pro-inflammatory genes expression as a consequence of suppressing NF- κ B activation.¹⁶ AST inhibits expression of e-selectin, ICAM-1 and VCAM-1 leading to inhibition of inflammatory cell infiltration.¹⁸

In this study, the addition of AST as an anti-inflammatory to standard acne therapy has shown no

Table 1 The subjects' characteristics

Characteristics	Treatment n=17	Control n=17	p-value
Age (mean \pm SD, years)	21.12 \pm 4.567	25.76 \pm 5.019	0.007
Male (n, %)	6 (35.3%)	9(52.9%)	0.300
Female n(%)	11 (64.7%)	8(47.1%)	
E-selectin level, (mean \pm SD, ng/mL)			
Pre-test	50,21 \pm 21.12	57.84 \pm 20.71	0.290
Post-test	50,04 \pm 22.99	55.88 \pm 15.98	0.259

significant difference in decreasing the e-selectin level compared to the placebo. This result might be due to the lack of dosage or less treatment time. Moreover, this can be resulted from the influence of other factors in the pathogenesis of acne.

The specific trigger that initiates the development of acne is unknown. Immune responses to *P. acnes* may play a larger role in acne than the pathogenicity of *P. acnes* itself.¹⁹ It activates the pilosebaceous unit via toll-like receptors (TLRs) and the cluster of differentiation (CD)14 and through CD1 molecules and can recognize altered lipid content in sebum, followed by inflammatory cytokines production.²⁰⁻²² TLRs stimulation leads to pro-inflammatory cytokines expression, and recruitment and activation of various immune cells, including Th1/Th17 cells.²² However, this study is not designed to identify the factor influencing the pathogenesis of acne as it is specifically measured e-selectin as the inflammatory marker. Therefore, further research are needed to confirm the result of the study.

CONCLUSION

The addition of oral AST to standard acne therapy compared to placebo, has no significant effect in reducing the serum level of e-selectin in acne vulgaris.

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The authors receive no funding or sponsorship in this research.

CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

AUTHOR CONTRIBUTION

The authors contributed equally in designing and conducting the study, analysing the data, and writing the manuscript.

REFERENCES

- Korkmaz S, Fiçıcıoğlu SK. Calprotectin can play an inflammatory role in acne vulgaris. *Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii*. 2018;35(4):397.
- Agak GW, Qin M, Nobe J, Kim M-H, Krutzik SR, Tristan GR, et al. Propionibacterium acnes induces an IL-17 response in acne vulgaris that is regulated by vitamin A and vitamin D. *Journal of Investigative Dermatology*. 2014;134(2):366-73.
- Bhat YJ, Latief I, Hassan I. Update on etiopathogenesis and treatment of Acne. *Indian Journal of Dermatology, Venereology, and Leprology*. 2017;83(3):298.
- Mochtar M, Murasmita A, Irawanto ME, Julianto I, Kariosentono H, Waskito F. The Difference in Interleukin-19 Serum on Degrees of Acne Vulgaris Severity. *International journal of inflammation*. 2018;2018.
- Szabó K, Tax G, Teodorescu-Brinzeu D, Koreck A, Kemény L. TNF α gene polymorphisms in the pathogenesis of acne vulgaris. *Archives of dermatological research*. 2011;303(1):19-27.
- Liu T, Zhang L, Joo D, Sun S-C. NF- κ B signaling in inflammation. *Signal transduction and targeted therapy*. 2017;2:17023.
- Lee S, Bai S, Lee Ks, Namkng s, Na Hj, Ha KS, et al. Astaxanthin Inhibits Nitric Oxide Production and Inflammatory Gene Expression by Suppressing I (κ)B Kinase-dependent NF-(κ)B Activation. *Mol Cells*. 2003;16(1):97-105.
- Zouboulis C, Jourdan E, Picardo M. Acne is an inflammatory disease and alterations of sebum composition initiate acne lesions. *Journal of the European Academy of Dermatology and Venereology*. 2014;28(5):527-32.
- Chew W, Mathison BD, Kimble LL, Mixer PF, Chew BP. Astaxanthin decreases inflammatory biomarkers associated with cardiovascular disease in human umbilical vein endothelial cells. *Am J Adv Food Sci Technol*. 2013;1:1-17.
- Zhong L, Simard MJ, Huot J. Endothelial microRNAs regulating the NF- κ B pathway and cell adhesion molecules during inflammation. *The FASEB Journal*. 2018;32(8):4070-84.
- Maria AG, Graziano R, Nicolantonio DO. Carotenoids: potential allies of cardiovascular health? *Food & nutrition research*. 2015;59(1):26762.
- Abbas AK, Lichtman AH, Pillai S. *Cellular and molecular immunology E-book: Elsevier Health Sciences*; 2014.
- Layton A, Morris C, Cunliffe W, Ingham E. Immunohistochemical investigation of evolving inflammation in lesions of acne vulgaris. *Experimental dermatology*. 1998;7(4):191-7.
- Park JH, Yeo IJ, Han JH, Suh JW, Lee HP, Hong JT. Anti-inflammatory effect of astaxanthin in phthalic anhydride induced atopic dermatitis animal model. *Experimental dermatology*. 2018;27(4):378-85.
- Farruggia C, Kim M-B, Bae M, Lee Y, Pham TX, Yang Y, et al. Astaxanthin exerts anti-inflammatory and antioxidant effects in macrophages in NRF2-dependent and independent manners. *The Journal of nutritional biochemistry*. 2018;62:202-9.
- Priyadarshini L, Aggarwal A. Astaxanthin inhibits cytokines production and inflammatory gene expression by suppressing I κ B kinase-dependent nuclear factor κ B activation in pre and postpartum Murrah buffaloes during different seasons. *Veterinary world*. 2018;11(6):782.
- Davinelli S, Nielsen ME, Scapagnini G. Astaxanthin in skin health, repair, and disease: A comprehensive review. *Nutrients*. 2018;10(4):522.
- Gerondakis S, Fulford TS, Messina NL, Grumont RJ. NF- κ B control of T cell development. *Nature immunology*. 2014;15(1):15.
- Dispenza MC, Wolpert EB, Gilliland KL, Dai JP, Cong Z, Nelson AM, et al. Systemic isotretinoin therapy normalizes exaggerated TLR-2-mediated innate immune responses in acne patients. *Journal of Investigative Dermatology*. 2012;132(9):2198-205.
- Dreno B, Gollnick H, Kang S, Thiboutot D, Bettoli V, Torres V, et al. Understanding innate immunity and inflammation in acne: implications for management. *Journal of the European Academy of Dermatology and Venereology*. 2015;29:3-11.
- Kurokawa I, Danby FW, Ju Q, Wang X, Xiang LF, Xia L, et al. New developments in our understanding of acne pathogenesis and treatment. *Experimental dermatology*. 2009;18(10):821-32.
- Lwin SM, Kimber I, McFadden JP. Acne, quorum sensing and danger. *Clinical and Experimental Dermatology*. 2014;39(2):162-7.



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