Comparison of brain-derived neurotrophic factor (BDNF) serum level in inflammatory and non-inflammatory acne vulgaris

Sweet Caroline Marpaung¹*, Nelva Karmila Jusuf², Imam Budi Putra³

ABSTRACT

Background: Acne vulgaris is a chronic and self-limiting inflammation disorder of the pilosebaceous unit, generally manifested in adolescents with polymorphic lesions, such as comedones, papules, nodules, and cyst. Brain-derived neurotrophic factor (BDNF) is a member of neurotrophins that can be downregulated because of stress. It is suspected that a lower BDNF level is induced inflammatory process, although its relationship with acne vulgaris has not been widely studied. This study compared BDNF serum levels in the inflammatory and non-inflammatory type of acne vulgaris.

Methods: This is an analytical observational research with a cross-sectional design that involved 31 acne vulgaris patients with inflammatory lesions and 31 acne vulgaris patients with non-inflammatory lesions. Each subject was interviewed and going through dermatology examinations, followed by blood sampling to assessed their BDNF serum levels through the ELISA test. The collected data were analyzed statistically using an independent T-test. P<0.05 was significant.

Result: The mean BDNF serum levels in acne vulgaris patients were 32.53±6.32 ng/ml. In subjects with inflammatory-type lesions, the mean BDNF level is 27.55±3.31 ng/ml. While, in the non-inflammatory type lesions group, the mean BDNF is 37.51±4.37 ng/ml. The BDNF serum level is significantly lower in inflammatory-type subjects than in non-inflammatory type (p < 0.001).

Conclusion: There was a significant difference in serum BDNF levels between the inflammatory and non-inflammatory type acne groups.

Keywords: acne vulgaris, brain-derived neurotrophic factor, BDNF, stress.

INTRODUCTION

Acne vulgaris is a skin-related problem that is mainly found in adolescents and adults. Globally, the prevalence of acne vulgaris is approximately 86%.¹ According Indonesian Cosmetic Dermatology Study Group (ICDSG) in 2015, acne vulgaris is one of the top three most common skin diseases.²

Acne vulgaris is related to inflammation of the pilosebaceous unit.³ The pathogenesis of acne vulgaris is multifactorial, including follicle hyperproliferation, sebum hypersecretion, bacterial colonization, follicular infundibulum hyperkeratinosis, and inflammation. Other factors contributing to acne vulgaris pathogenesis are genetic, race, hormone, environment, cosmetic use, diet, and stress.⁴⁵

Cutibacterium acnes (C. acnes) is a critical causative and associated with other pathophysiological phenomena.⁶ A study by Jusuf et al. in 2020 showed the differences in bacterial isolates both in non-inflammatory and inflammatory lesions of acne vulgaris. The study reported that C. acnes play a role in the inflammatory process in acne vulgaris, but other bacteria such as Staphylococcus epidermidis (S. epidermidis) are also more abundant in an inflammatory type of acne vulgaris lesions.⁷

Neurotrophin is a neurotrophic growth factor and one of the critical factors in the pathogenesis of inflammation. It can affect not only the central nervous system but also the endocrine and immune system. One of the neurotrophins currently being studied in many types of research is a brain-derived neurotrophic factor (BDNF), secreted as a neurotrophic factor into extracellular space.⁸⁹

Human sebocytes expressed functional receptors to many neuroendocrine factors. Several receptors mediate androgen metabolism in sebocytes and produce multiple inflammatory cytokines, which can modulate acne vulgaris. Human basal keratinocytes can secrete active BDNF. The BDNF can stimulate apoptosis of keratinocytes through p75NTR.¹⁰¹¹

Mikhal et al. in 2019 showed that the mean BDNF serum in the acne vulgaris group is significantly lower than the control group (p<0.001). They also found that patients with severe acne vulgaris...
have significantly lower BDNF level compared to moderate and mild acne vulgaris patients with p<0,001. The relationship between acne vulgaris and the inflammatory process and BDNF is one factor in inflammation. Not many studies evaluating serum BDNF levels and acne vulgaris caused researchers to examine the comparison of serum BDNF levels in patients with inflammatory and non-inflammatory acne vulgaris.

**METHODS**

This study was conducted after being approved by the Ethics Committee, Faculty of Medicine, Universitas Sumatera Utara (292/KEP/USU/2020). This analytic observational study with a cross-sectional design involved 31 acne vulgaris patients with inflammatory lesions and 31 acne vulgaris patients with non-inflammatory lesions in outpatient clinic Dermatology Venerology Department, Universitas Sumatera Utara General Hospital from June 2020 until February 2021. The inclusion criteria are patients diagnosed with acne vulgaris, age more than 18 years old, and agree to participate in this study by signing the informed consent. The exclusion criteria are patients that have a psychological disorder such as schizophrenia, depression, mood disorder, and others; suffers from systemic or skin chronic disease such as psoriasis, diabetes mellitus, and others; receiving medication such as a statin, anti-depressant, corticosteroid, contraception, psychotropic drugs, and beta-blocker agents in the last six months; receiving systemic or topical treatment for acne vulgaris; doing high intensity exercise regularly; on calorie restriction diet, and pregnant or breastfeeding.

Each subject was interviewed and underwent a dermatologic examination. Demographic data, such as age and gender, were taken from the medical record. Each patient’s dermatologic examination was done to determine whether they were grouped into an inflammatory or non-inflammatory lesion group. Then, the subjects got their blood taken to assess their BDNF level using ELISA. The collected data were analyzed statistically using an independent T-test. The p-value <0.05 was significant.

### Table 1. Demographic characteristics of subjects.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Acne vulgaris with inflammatory lesions</th>
<th>Acne vulgaris with non-inflammatory lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 – 23 years old</td>
<td>16</td>
<td>51.6</td>
</tr>
<tr>
<td>24 – 29 years old</td>
<td>8</td>
<td>25.8</td>
</tr>
<tr>
<td>30 – 35 years old</td>
<td>7</td>
<td>22.6</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9</td>
<td>29</td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
<td>71</td>
</tr>
</tbody>
</table>

### Table 2. The mean level of BDNF serum in acne vulgaris.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>BDNF serum level (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>Acne Vulgaris</td>
<td>62</td>
<td>32.53</td>
</tr>
</tbody>
</table>

### Table 3. Comparison between BDNF serum level in acne vulgaris patients with inflammatory and non-inflammatory lesions.

<table>
<thead>
<tr>
<th>BDNF serum level (ng/ml)</th>
<th>Acne vulgaris with inflammatory lesions</th>
<th>Acne vulgaris with non-inflammatory lesions</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>27.55</td>
<td>37.51</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>3.31</td>
<td>4.37</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>27.60</td>
<td>37.12</td>
</tr>
<tr>
<td></td>
<td>Min-max</td>
<td>20,90-32,89</td>
<td>30,21-49,23</td>
</tr>
</tbody>
</table>

### RESULT

The demographic characteristics of subjects can be seen in Table 1. Samples were taken from 31 acne vulgaris patients with inflammatory lesions and 31 patients with non-inflammatory lesions. The majority of subjects in both groups are 18 – 23 years old, with 16 subjects (51.6%) in the acne vulgaris with inflammatory lesions and 24 subjects (77.4%) in the acne vulgaris non-inflammatory lesions group. Based on gender, most acne vulgaris with inflammatory lesions are female, with 22 subjects (71%) compared to males with nine subjects (29%). While, in the acne vulgaris with non-inflammatory lesions group, the majority are male with 16 subjects (51.6%) and female with 15 subjects (48,4%). The mean BDNF serum level in acne vulgaris can be seen in Table 2. In this study, the mean BDNF serum level in acne vulgaris is 32,53 ± 6,32 ng/ml. The comparison between BDNF serum levels in acne vulgaris with inflammatory and non-inflammatory lesions can be seen in Table 3. This study shows that in acne vulgaris patients with inflammatory lesions, the mean BDNF serum level is 27,55 ± 3,31 ng/ml, with the lowest level is 20,90 ng/ml and the highest level is 32,89 ng/ml. In acne vulgaris patients with non-inflammatory lesions, the mean BDNF serum level is higher, 37,51 ± 4,37 ng/ml, with the lowest level is 30,21 ng/ml, and the highest level is 49,23 ng/ml. The independent T-test showed a significant difference in BDNF levels between both study groups (p<0.001).

### DISCUSSION

This study was done in 31 acne vulgaris patients with inflammatory lesions and 31 acne vulgaris patients with non-inflammatory lesions. Acne vulgaris primarily found in 18-23 years old, with most females (71%) in the inflammatory lesions group and males (51,6%) in non-inflammatory groups.

According to Global Burden of Diseases, acne vulgaris is adolescent mainly to young adults age 12 – 25 years old. Studies by Snast et al. and Alshammari et al.
reported that acne vulgaris could be found primarily in females than males.\textsuperscript{15,16} This study found that the mean BDNF serum level in acne vulgaris is 32.53 ± 6.32 ng/ml. He et al. showed that BDNF serum level in patients with acne vulgaris is 13.35 ± 2.65 ng/ml. This study also highlights the lower BDNF serum level in acne vulgaris subjects with depression. Therefore, it concluded that BDNF serum level could be a promising non-invasive biomarker to detect depression in young adults with acne vulgaris.\textsuperscript{1} Study by Mikhael et al. found that female acne vulgaris patients have a mean BDNF serum level of 13.48 ± 2.73 ng/ml, while the mean BDNF serum level in male acne vulgaris is 8.62 ± 3.30 ng/ml.\textsuperscript{13}

This study found that in acne vulgaris with inflammatory lesions, the mean BDNF level is 27.55 ng/ml. While in other groups, the mean BDNF level is higher with 37.51 ng/ml. Independent T-test showed that the difference in BDNF level in both study groups is statistically significant (p<0.001).

Mikhael et al. stated that the mean BDNF serum level in mild acne vulgaris is 11.22 ng/ml, higher than moderate and severe acne vulgaris with each BDNF level 10.18 ng/ml and 4.85 ng/ml.\textsuperscript{13} This may be caused by inflammatory lesions, such as papulopustular lesions, mainly in severe acne vulgaris. Another study by He et al. also found that BDNF serum level is lower in acne vulgaris, 13.35±2.65 ng/ml compared with BDNF level in the control group 14.35 ± 2.70 ng/ml.\textsuperscript{13}

In vitro study done by Liang et al. on mice with spinal cord injury showed that decrease level of BDNF and TrkB inhibitor level could induce phosphorylation of (p-) p38 and inflammation process that marked by the increase of TNF-α, IL-1β, IL-6, IL-18, nitric oxide synthase (iNOS) and (COX)-2.\textsuperscript{17}

The strength of this study is that we compare the BDNF level in inflammatory and non-inflammatory acne vulgaris patients. Therefore, it could be more specific to see the significant differences between the two groups. The BDNF can be produced by human monocyte.\textsuperscript{18} Inflammatory cytokine can affect BDNF (TrkB) receptor phosphorylation causing disturbances in BDNF signal.\textsuperscript{19}

Stress can down-regulate BDNF serum level.\textsuperscript{20} It is also one of many factors that causing acne vulgaris. The skin sebaceous gland has CRH receptors, and the increase of CRH in stress can induce sebum production that clogs the pilosebaceous gland.\textsuperscript{21,22} Research by Sutrisno et al. found a relationship between stress degree and severity of acne vulgaris.\textsuperscript{23} Stress can induce other neuropeptides that cause neurogenic inflammation. The binding of neuropeptides, such as substance P with their receptors, will cause an increase in the production of proinflammatory cytokines resulting in proliferation, differentiation, and lipogenesis of the pilosebaceous glands.\textsuperscript{21,22}

This study proved differences in BDNF serum levels in inflammatory type acne vulgaris patients with non-inflammatory types acne vulgaris, which had a milder degree of severity, indicating a role BDNF in the inflammatory process the pathogenesis of acne vulgaris. This result was in line with the research conducted by Liang et al., which states that decreased levels of BDNF and TrkB inhibitors can induce phosphorylation (p-) p38 and an inflammatory process.\textsuperscript{17} This suggests that serum BDNF can be used as a biological marker of the inflammatory process in acne vulgaris.

However, this study is not without limitations. One of the factors that affect the value of BDNF levels is the time of blood sampling. In this study, the time for blood sampling was not the same for each subject, so could affect the differences in the results of BDNF levels. Another is the number of subjects in this study is still relatively small, further studies with a larger number of subjects are highly recommended.

**CONCLUSION**

There was a difference in serum BDNF levels significantly lower in the inflammatory type acne group than the non-inflammatory type acne group.

**DISCLOSURE**

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**Conflict Of Interest**

The authors declare no conflict of interest regarding the publication of this article.

**Author Contribution**

All authors have contributed to all processes in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

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**REFERENCES**


