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Correlation between Serum Brain-Derived Neurotrophic Factor Level and Depression Severity in Psoriasis Vulgaris Patients

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Abstract

BACKGROUND: Psoriasis vulgaris is a chronic inflammatory skin disorder that can lead to depression. There is a similarity in neurotrophic substance in the pathogenesis of psoriasis and depression; it's called brain-derived neurotrophic factor (BDNF). BDNF level imbalance potentially affects the severity of psoriasis and depression.

AIM: This study aims to know the correlation between serum BDNF level and depression severity in psoriasis vulgaris patient and also the correlation between serum BDNF level and psoriasis vulgaris severity.

METHODS: This is an analytical cross-sectional study that 23 psoriasis vulgaris patients participated. All participants have performed serum BDNF level examination with enzyme-linked immunosorbent assay (ELISA). Depression severity assessed with Beck depression inventory-II (BDI-II) and psoriasis severity assessed with psoriasis area and severity index. Correlation between all variables was analysed with Spearman's correlation test.

RESULTS: Serum BDNF level and depression severity are a strongly negative correlation in psoriasis vulgaris patients (r = -0.667 with significant value p = 0.001). There is a moderate negative correlation between serum BDNF level with psoriasis vulgaris severity (r = -0.595 with significant value p = 0.003).

CONCLUSION: In psoriasis vulgaris patients, a low level of serum BDNF may increase depression severity and psoriasis vulgaris severity.

Introduction

Psoriasis is a chronic inflammatory skin disease with genetic factors may greatly affecting this disease [1]. Characteristics of psoriasis are a disturbance of epidermal proliferation and differentiation that involves biochemical, immunological, vascular and nervous system [1]. In general, it can be assumed that psoriasis, brain-derived neurotrophic factor (BDNF) and depression are related to each other. In psoriasis and depression, BDNF level is decreased. This condition may contribute to similar pathogenesis between psoriasis and depression. Psoriasis can be caused depression, as does depression can trigger psoriasis [2], [3].

There is a similarity between skin embryogenesis and the nervous system, its called ectodermal. Its allowed the role of growth factors in controlling skin homeostasis and remodelling, in this case, the role of neurotrophin [2]. The relationship between the nervous system and psoriasis was proved by the remission of psoriasis lesions after the cutaneous sensory nerve had removed [4], [5]. Some studies focused on the role of neurotropic in psoriasis, possibly due to activation of mast cells that continue into skin inflammation and then stimulate other neuroinflammatory cytokines [6].

In psoriasis, epidermal proliferation and apoptosis are influenced by neuropeptides and their receptors. Through its main receptor tyrosine kinase B (TrkB), BDNF plays a role in keratinocyte proliferation

and apoptosis [2]. BDNF induces keratinocyte apoptosis but does not work on psoriatic transit-amplifying sub-population of basal keratinocytes [2].

In line with a low level of BDNF in psoriasis patients, research showed that BDNF level in depressed patients is also low. Psychological stress will reduce BDNF level through activation of the hypothalamic-pituitary-adrenal axis and sympathetic-adrenal-medullary axis which will increase cortisol and neuroinflammation cytokines and reduce BDNF level [7].

The problems of psoriasis are not limited to the skin. Psoriasis can result in psychological distress and a decrease in the quality of life [1]. Psychological stress, social stigma and embarrassment can lead to depression. The prevalence of depression in psoriasis patients is 10-62% [8]. A cross-sectional study found 32% of patients with psoriasis suffered from depression from a total of 265 psoriasis patients [9]. Psoriasis patients have a higher tendency to suffered from depression than leprosy, vitiligo and lichen planus [8]. Depression in psoriasis patients affects treatment adherence which remission is impossible to achieve. Based on these many studies, it is interesting to investigate the correlation between serum BDNF level and depression severity in psoriasis vulgaris patients.

Methods

This is an analytical cross-sectional study conducted from September 2016 to October 2017. This study was held at dermatology and venereology clinic Adam Malik General Hospital Medan Indonesia. The sample was taken using consecutive sampling method. This study was approved by the ethical commission of Faculty of Medicine Universitas Sumatra Utara Medan Indonesia.

Inclusion criteria in this study were patients diagnosed clinically as psoriasis vulgaris, age 20-65 years old, willing to take part in the study and sign an informed consent letter. Exclusion criteria were pregnant and breastfeeding patient, using topical drugs to treat psoriasis vulgaris such as a topical corticosteroid, calcipotriol, tazarotene and tar 2 weeks before this study was conducted. And patients who used systemic drugs such as methotrexate, acitretin, cyclosporine, corticosteroid 6 weeks before this study was conducted. Patients who suffered from bipolar disorder, schizophrenia and used antidepressant drugs are also excluded.

Blood sampling was taken at 8-9 am to avoid variations due to circadian rhythm. Measurement of BDNF serum level was done at the Clinical Pathology Laboratory of Adam Malik General Hospital Medan Indonesia using human brain-derived neurotrophic factor kit (R&D®, USA) and ELISA method. Measurement of depression severity was performed using Beck depression inventory-II (BDI-II). In this study, psoriasis severity was also evaluated using the psoriasis area and severity index (PASI).

The collected data was analysed to determine the relationship between variables using computer software. Correlation between serum BDNF level and depression severity and psoriasis severity was analysed with the Spearman correlation test. Significant correlation indicated by p-value ≤ 0.05.

Results

Psoriasis vulgaris patients characteristics

In this study 23 psoriasis vulgaris patients were participated and fulfil the inclusion and exclusion criteria. Characteristic of subjects were reported based on the gender, age, education, psoriasis and depression severity (Table 1).

Table 1: Psoriasis vulgaris patient's characteristic

No.	Characteristic	Amount (n)	(%)
1.	Gender		
	Male	12	52.2
	Female	11	47.8
2.	Age group		
	20-29	3	13
	30-39	7	30.4
	40-49	7	30.4
	50-59	5	21.7
	≥ 60	1	4.3
3.	Education		
	Elementary	0	0
	Junior high school	2	8.7
	High school	10	43.5
	Undergraduate	11	47.8
4.	Psoriasis severity		
	Mild	13	56,5
	Moderate	4	17,4
	Severe	6	26,1
5.	Depression severity		
	Minimal	7	30.4
	Mild	7	30.4
	Moderate	9	39.1
	Severe	0	0

The frequency difference between male and female patients was only 1 patient (4.4%). Based on the age group, the highest frequency are at the group 30-39 and 40-49 years old and have the same frequency of 7 patients (30.4%). The lowest frequency is in the age group ≥ 60 years old, who is only 1 patient (4.3%). Based on education, this study found the highest frequency is undergraduate patients that are 11 patients (47.8%). The lowest frequency is junior high school that is 2 patients (8.7%). It can be concluded that the subjects in this study were well-educated patients.

Based on the psoriasis severity, the highest frequency in this study was mild psoriasis, that is 13 patients (56.5%). While the lowest frequency is moderate psoriasis, that is 4 patients (17.4%).

The highest frequency of depression severity in this study was moderate depression that is 9 patients (39.1%).

Correlation between BDNF Levels and Depression Severity in Psoriasis Vulgaris Patients

This study found that the average serum BDNF level was 912.45 ± 180.94 pg/ml (Table 2).

Table 2: Correlation between serum brain-derived neurotrophic factor level and depression Severity in psoriasis vulgaris Patients and psoriasis severity

1. Serum BDNF level (Mean ± SD)	912,45 ± 180,94		
	p	r	r^2
2.Serum BDNF level and depression severity	0,001	-0,667	0,445
3. Serum BDNF level and psoriasis severity	0,003	-0,595	0,354

*Spearman's correlation test.

Serum BDNF level and depression severity were analysed with Spearman correlation, the value of the correlation coefficient (r) was -0.667 with a significance value (*p*) of 0.001 (Table 2). There is a strong negative correlation between serum BDNF level with depression severity. The lower serum BDNF level, the higher the severity of depression will be [14]. The coefficient of determination (r^2) in this analysis was found 45%, which indicate that 45% factor that influence severity of depression was serum BDNF level, and the remaining 55% are other factors (Table 2).

Discussion

Man and woman have the same opportunity to suffered from psoriasis [1], [10]. Psoriasis affects all age, but in children, the incidence is low (0.71%) [11]. Similar to the study by Kundacki et al., Who reported that psoriasis in childhood is rare, only 5.7% under the age of 10 years [12]. In this study, we have only recruited patients with psoriasis vulgaris at the age of more than 20 years old.

Fathy et al. reported that 90 psoriasis vulgaris patients had the average of PASI score was 20.8 ± 18.8, 70% of patients were categorised as moderate to severe psoriasis with a PASI score > 10 [13].

In this study, there were no psoriasis vulgaris patients with a severe degree of depression. Fatthy et al. reported that severe depression was higher in psoriasis vulgaris patients [13].

Fatthy et al. reported that BDNF level was lower in both groups of psoriasis (without depression 25.2 ± 6.5; with depression 16.9 ± 2.5) compared to the healthy control group (26.5 ± 3.6) [13]. BDNF level was significantly lower in psoriasis vulgaris patients with depression compared to psoriasis patients who did not suffer from depression (mean difference 8.3; $p < 0.001$) [13]. BDNF level was also significantly lower in psoriasis vulgaris patients with depression and depressed patients without psoriasis compared to healthy controls ($p < 0.0001$ and $p < 0.001$) [13]. The mean BDNF level was significantly lower ($p < 0.01$) in the group of psoriasis patients with depression (16.9 ± 2.5) compared to depressed patients without psoriasis vulgaris (21.5 ± 5.8) [13].

Duclot et al. reported that low BDNF level was known to play a role in depression pathophysiology, but can be increased by antidepressant [15]. However, BDNF level in serum does not correlate with depression severity. Therefore, utilisation of BDNF as a biomarker of depression is still unclear [15].

The role of BDNF in depression is proven by the presence of four things [16]. First, depression causes a decrease in BDNF level in the hippocampus and the prefrontal cortex. Second, depression triggers atrophy of the nerve dendrites in the hippocampus and the prefrontal cortex. Third, there is evidence of increased BDNF level in the hippocampus and the prefrontal cortex after administration of antidepressant. Fourth, the BDNF level increased in the amygdala and neural accumbent area which facilitate symptoms of depression. Therefore, Yu et al. concluded that depressive symptoms depend on BDNF level in the affected anatomic location [16].

BDNF level and psoriasis vulgaris severity were analysed with the Spearman correlation test; the correlation coefficient (r) was -0.595 with significant value (*p*) 0.003 (Table. 2). This result showed a moderate negative correlation between BDNF level and psoriasis vulgaris severity. The lower serum BDNF level, the higher psoriasis severity will be [14]. The coefficient of determination (r^2) in this analysis was found 35%, which indicate 35% factor that influences psoriasis severity was serum BDNF level and the remaining 65% were influenced by other factors.

Fatthy et al., reported that there was no correlation between BDNF level and PASI score ($r = 0.217$; $p = 0.250$) [13]. Similarly, Narbutt et al. reported that there was no correlation between BDNF level and PASI score [17]. The mean BDNF level in their study were 14.5 ng/ml and the mean of PASI score was 14.3 ($p > 0.05$) [17].

A study conducted by Brunoni et al. reported that there was no difference ($p = 0.59$) BDNF level in patients with mild psoriasis (3649 ± 3653 pg/ml) and severe psoriasis (3280 ± 2837 pg/ml) [2]. However, in their study psoriasis severity was not assessed with the PASI score, but was classified according to the presence of psoriatic arthritis and the used of systemic therapy such as methotrexate, cyclosporine, mycophenolate mofetil, biological agents and phototherapy [2]. Raap et al. reported that there was no correlation between BDNF level and PASI score

[18]. However, in their published article did not mention the mean of BDNF level in psoriasis patients, maybe because it was not the main purpose of their study.

It can be concluded from this study that the lower serum BDNF level, the higher the severity of depression and psoriasis will be. Serum BDNF level might be considered as a biomarker of depression severity as well as a biomarker of psoriasis severity in patients with psoriasis vulgaris. BDNF might be the new psoriasis treatment target. However, further investigations with better design are still needed to prove this result.

References

1. Gudjonson JE, Elder JT. Psoriasis. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K, editor. Fitzpatrick's dermatology in general medicine. 8th Ed. New york: Mcgraw Hill Companies Inc., 2012:197 – 231.

2. Botchkarev VA et al. Neurotrophin in skin biology and pathology. Journal of investigative dermatology. 2006; 126:1719–1727. https://doi.org/10.1038/sj.jid.5700270 PMid:16845411

3. Katzung BG, Masters SB, Trevor AJ. Farmakologi Dasar dan Klinik. 12th edition. Jakarta: EGC, 2014:199 – 209.

4. Raychaudhuri SP, Farber EM. Neuroimmunologic aspects of psoriasis. Cutis. 2000; 66:357–362. PMid:11107521

5. Reich A, Orda A, Wis´nicka B, Szepietowski JC. Plasma neuropeptides and perception of pruritus in psoriasis. Acta Derm Venereol. 2007; 87:299–304. https://doi.org/10.2340/00015555-0265 PMid:17598031

6. Timmusk T, et al. Multiple promoters direct tissue-specific expression of the rat BDNF gene. Neuron. 1993; 10:475–489. https://doi.org/10.1016/0896-6273(93)90335-O

7. Bath KG, Schilit A, Lee FS. Stress effects on BDNF expression: effects of age, sex, and form of stress. Neuroscience. 2013; 239:149-156. https://doi.org/10.1016/j.neuroscience.2013.01.074 PMid:23402850

8. Meffert J. Psoriasis [internet]. USA: [publisher unknown]; [date unknown] [2015 January 22; cited 2016 Juli 3]. Available from: http://emedicine.medscape.com/article/1943419-overview

9. Schmitt J, Ford DE. Understanding the relationship between obejctive disease severity, psoriatic symptoms, illness-related stress, health-related quality of life and depressive symptoms in patients with psoriasis – a structural equations modeling approach. Gen Hosp Psychiatry. 2007; 29(2):134-140. https://doi.org/10.1016/j.genhosppsych.2006.12.004 PMid:17336662

10. Griffiths CE, Barker JN. Psoriasis. dalam: Burns T, Breathnach SM, Cox NH, Griffiths CE, editor. Rook's textbook of dermatology. Edisi ke-8. UK:Wiley Blackwell, 2010:20.1-60.

11. Ibrahim G, Waxman R, Helliwell PS. The prevalence of psoriatic arthritis in people with psoriasis. Arthritis and Rheumatism. 2009; 61(10):1373-8. https://doi.org/10.1002/art.24608 PMid:19790120

12. Kundacki N, Ursen UT, Babiker MO, Urgey EG. The evaluation of the sociodemographic and clinical features of turkish psoriasis patients. International journal of dermatology. 2002; 59(1):19-24.

13. Fatthy H, Tawfik AA, Madbouly N. Evaluation of serum brain-derived neurotrophic factor to assess the association between psoriasis and depression. J Egypt Women Dermatol. 2015; 12:186–190. https://doi.org/10.1097/01.EWX.0000466467.93686.0d

14. Mukaka MM. A guide to approriate use of correlation coefficient in medical research. Malawi Med J. 2012; 24(3):69-71. PMid:23638278 PMCid:PMC3576830

15. Duclot F, Kabbaj M. Epigenetic mechanisms underlying the role of brain-derived neurotrophic factor in depression and response to antidepressants. J Exp Biol. 2015; 218:21-31. https://doi.org/10.1242/jeb.107086 PMid:25568448 PMCid:PMC4286703

16. Yu H, Chen Z. The role of BDNF in depression on the basis of its location in the neural circuitry. Acta Pharmacol. 2011; 32:3–11. https://doi.org/10.1038/aps.2010.184 PMid:21131999 PMCid:PMC4003317

17. Narbutt J, Olejniczak I, Sztychny SD, Jedrzejowska SA, Kwiatkowska SI, Hawro T, et al. Narrow band ultraviolet B irradiations cause alteration in interleukin-31 serum level in psoriatic patients. Arch Dermatol Res. 2013; 305:191–195. https://doi.org/10.1007/s00403-012-1293-6 PMid:23108364 PMCid:PMC3606511

18. Raap U, Werfel T, Goltz C, Deneka N, Langer K, Bruder M, et al. Circulating levels of brain-derived neurotrophic factor correlate with disease severity in the intrinsic type of atopic dermatitis. Allergy. 2006; 61:1416–1418. https://doi.org/10.1111/j.1398-9995.2006.01210.x PMid:17073871