

Probiotics *Lactobacillus Plantarum* PS128 Intervention in Two Patients with Major Depressive Disorder

The exact mechanisms responsible for depression are not clear, but immune dysregulation may be implicated. Meta-analyses have shown that patients with major depressive disorder (MDD) have higher levels of inflammation [1, 2]. Accumulating data have indicated that gut microbiota can communicate with the central nervous system, possibly through neural, endocrine, and immune pathways, thereby influencing brain function and behavior [3, 4]. Therefore, probiotics may be an alternative way to treat patients with depression through changing the composition of gut microbiota.

Lactobacillus plantarum PS128 (PS128) is one of the bacteria extracted from traditional fermented food, *Fu-Tsai* [5]. It alleviates depressive-like behavior and reduces inflammation level in mice with early life stress [6]. Here, we report the changes of depressive symptoms and levels of high-sensitivity C-reactive protein (hs-CRP) after an eight-week PS128 intervention in two patients with MDD.

Report of Two Cases

Both of our patients received one capsule of PS128 in the morning and another one in the afternoon for eight weeks. Each PS128 capsule contains 300 mg of probiotics, containing 3×10^{10} colony-forming unit of *L. plantarum* PS128. Because activity and diet may alter the composition of gut microbiota, we instructed patients not to change their lifestyle or dietary pattern. In addition, their psychotropic medications were kept unchanged during the intervention period. We compared the scores of both Hamilton Depression Rating Scale-17 items (HAMD-17) and serum hs-CRP levels at baseline and after eight weeks of PS128 intervention.

The first patient was a 50-year-old woman with the onset of MDD at the age of 40 years. Her daily medications were escitalopram 10 mg, trazodone 100 mg, zolpidem 10 mg, and diazepam 4 mg. Her HAMD-17 scores were 11 at baseline and 14 after an 8-week PS128 intervention. Serum hs-CRP levels were 4.4 mg/L at baseline and 1.0 mg/L after an eight-week PS128 intervention.

The second one was a 40-year-old woman patient with the onset of MDD at 31 years of age. Her HAMD-17 scores were 19 at baseline and nine after an eight-week PS128 intervention. Serum hs-CRP levels were 12.5 mg/L at baseline and 0.4 mg/L after an 8-week PS128 intervention. Although the patient had residual depressive symptoms, she did not take any psychotropics for three years.

Both patients did not report any side effects of PS128. We also found that serum hs-CRP was obviously dropped to normal level in these two patients after an eight-week PS128 intervention. It is worth to mention that in the second patient

with higher hs-CRP of 12.5 mg/L at baseline, depression severity was improved a lot after an eight-week PS128 intervention.

Comment

Until now, the results of probiotics use to alleviate depressive symptoms in clinical trials are inconsistent [7]. To the best of our knowledge, only three studies have evaluated the effects of probiotics in patients with MDD. Although all those studies used different strains or combinations of probiotics, they showed that probiotics can improve depression severity in patients with MDD compared with those treated with placebo [8-10].

Although serum hs-CRP level is significantly decreased in the article by Akkasheh et al., serum hs-CRP level at baseline is not available in their article [8]. Therefore, we cannot assure whether patients with higher levels of inflammation have good response to probiotics treatment.

This case report of two patients is limited because our study was an open trial without control group. Whether PS128 is effective in patients with high inflammation level needs to be verified using a randomized, double-blinded, placebo-controlled study in future. (The study protocol was approved by the Joint Institutional Review Board of Taipei Medical University with the requirement of obtaining signed informed consent from the participating patients.)

Financial Support and Sponsorship

The study was financially supported by the grant from the Ministry of Science and Technology, Taiwan (MOST 106-2314-B-038-051).

Conflicts of Interest

There are no conflicts of interest.

References

1. Dowlati Y, Herrmann N, Swardfager W, et al.: A meta-analysis of cytokines in major depression. *Biol Psychiatry* 2010; 67: 446-57.
2. Howren MB, Lamkin DM, Suls J: Associations of depression with C-reactive protein, IL-1, and IL-6: a meta-analysis. *Psychosom Med* 2009; 71: 171-86.
3. Cryan JF, Dinan TG: Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour. *Nat Rev Neurosci* 2012; 13: 701-12.
4. Rogers GB, Keating DJ, Young RL, et al.: From gut dysbiosis to altered brain function and mental illness: mechanisms and pathways. *Mol Psychiatry* 2016; 21: 738-48.
5. Chao SH, Wu RJ, Watanabe K, et al.: Diversity of lactic acid bacteria in suan-tsai and fu-tsai, traditional fermented mustard products of Taiwan. *Int J Food Microbiol* 2009; 135: 203-10.
6. Liu YW, Liu WH, Wu CC, et al.: Psychotropic effects of *Lactobacillus plantarum* PS128 in early life-stressed and naïve adult mice. *Brain Res* 2016; 1631: 1-2.

7. Ng QX, Peters C, Ho CY, et al.: A meta-analysis of the use of probiotics to alleviate depressive symptoms. *J Affect Disord* 2018; 228: 13-9.
8. Akkasheh G, Kashani-Poor Z, Tajabadi-Ebrahimi M, et al.: Clinical and metabolic response to probiotic administration in patients with major depressive disorder: a randomized, double-blind, placebo-controlled trial. *Nutrition* 2016; 32: 315-20.
9. Kazemi A, Noorbala AA, Azam K, et al.: Effect of probiotic and prebiotic vs. placebo on psychological outcomes in patients with major depressive disorder: a randomized clinical trial. *Clin Nutr* 2019; 38: 522-8.
10. Ghorbani Z, Nazari S, Etesam F, et al.: The effect of synbiotic as an adjuvant therapy to fluoxetine in moderate depression: a randomized multicenter trial. *Arch Neurosci* 2018; 5: e60507.

**Jr-Shian Chang, M.D.¹, Yi-Hang Chiu, M.D., M.S.¹, Chien-Chih Pan, M.D.^{1*},
Chun-Hsin Chen, M.D., M.S.^{1,2*}**

¹Department of Psychiatry, Municipal Wan-Fang Hospital, Taipei Medical University, ²Department of Psychiatry, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan

^{1*}Corresponding authors. No. 111, Section 3, Hsin-Long Road, Taipei 116, Taiwan.

E-mail: Chieh-Chih Pan <billypan101@gmail>, Chun-Hsin Chen <chunhsin57@yahoo.com.tw>

Received: Apr. 04, 2019 revised: Apr. 11, 2019 accepted: Apr. 12, 2019

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Access this article online

Quick Response Code:



Website:

www.e-tjp.org

DOI:

10.4103/TPSY.TPSY_22_19

How to cite this article: Chang JS, Chiu YH, Pan CC, Chen CH: Probiotics *Lactobacillus Plantarum* PS128 intervention in two patients with major depressive disorder. *Taiwan J Psychiatry* 2019; 33: 116-7.

© 2019 Taiwanese Journal of Psychiatry (Taipei) | Published by Wolters Kluwer - Medknow