

Lower Serum Albumin Levels in Patients with Mood Disorders

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Background: Some physicians have reported lower serum albumin levels in patients with major depression in Western countries. In this study, the relationship between serum albumin levels and mood disorders (including mania and major depression) was investigated during the acute phases in Taiwanese psychiatric inpatients.

Methods: A review of medical charts during a 1-year period was carried out in a population of 213 Taiwanese psychiatric inpatients that included 61 patients with mood disorders (with or without suicide attempts). The collected data included age, body weight, height, serum albumin levels, and routine blood biochemistry examination results. These data were compared with data from a healthy control group (N=32) drawn from the staff of the psychiatric ward. Statistical analysis was done using covariance after age adjustment.

Results: The mean serum albumin levels were 40.2 ± 4.0 g/L in patients with mania (N=25), 39.8 ± 2.8 g/L in patients with major depression (N=36), and 45.8 ± 2.0 g/L in the control group. Patients with mania (F=64.6, $p=0.000$) and major depression (F=68.9, $p=0.000$), respectively, had significantly lower albumin levels than the control group after age adjustment. However, for the patients with major depression, no significant difference in serum albumin levels were found between patients who had attempted suicide and those who had not.

Conclusion: Lower serum albumin levels were noted during the acute phases of mania and major depression in Taiwanese psychiatric inpatients.
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Key words: albumin, mania, major depression, bipolar disorder, suicide attempt.

The concentration of albumin in plasma is commonly below normal during infections,⁽¹⁾ after injury (including elective surgery) and myocardial infarctions,^(2,3) in patients with malignant diseases,⁽⁴⁾ and in critically ill patients.⁽⁵⁾ The factors which determine the concentrations of circulating proteins include changes in circulating fluid volume, exchange with or loss of the extravascular tissue space, lymphatic return, catabolism, synthesis, and

outflow.⁽⁶⁾

Recently, many reports have shown that depression is accompanied by an activation of the immune/inflammatory system, including an acute phase response as indicated by changes in serum acute phase protein.⁽⁷⁻¹²⁾ Some physicians have reported that lower serum albumin (one of the negative acute phase proteins) levels were noted in patients with major depression in Western coun-

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tries.⁽¹⁵⁻²⁰⁾ However, there were no discussions concerning serum albumin levels and patients with mania except for other acute phase proteins.⁽¹²⁻¹⁴⁾ Recently, some physicians have also reported that lower serum zinc and albumin concentrations (zinc is closely bound to albumin in peripheral blood) were related to the immune/inflammatory response in patients with major depression.^(15,16) Albumin is a metal-binding protein shown to possess free radical scavenging properties, and may thus be a selective antioxidant.⁽¹⁷⁾ Therefore, the role of serum albumin in patients with psychiatric diseases is important and needs to be studied again.

In this study, the relationship between serum albumin levels and mood disorders (including mania and major depression) was investigated during the acute phases in Taiwanese psychiatric inpatients. In addition, the serum albumin levels of patients with major depression were compared between those who had attempted suicide and those who had not.

METHODS

Subjects and design

From January 1995 through December 1995, 213 patients (99 men, 114 women) admitted to the acute psychiatric inpatient unit of the Chang Gung Memorial Hospital in Kaohsiung were included in the study. All medical records were reviewed. The collected data included age, body mass index (BMI), albumin level, suicide attempts on admission, and mood disorders (including mania and major depression) in patients with no other co-morbid illnesses according to DSM-III R criteria. All subjects had normal blood test results, including complete blood count, serum sodium, potassium, blood urea nitrogen, creatinine and alanine aminotransaminase. The control group data came from 32 healthy volunteers (14 men, 18 women) who were members of the staff of the same psychiatric ward.

Laboratory data

Serum albumin levels were detected in the clinical biochemistry laboratory of the Chang Gung Memorial Hospital in Kaohsiung using the bromocresol green method, Hitachi 705 at 37 °C (Albumin Automated Analysis, Wako, Japan) after the patients had fasted for at least 9 hours the morning after admission.⁽¹⁸⁾ The data of the control group

were also collected at the same clinical biochemistry laboratory after they had fasted for at least 9 hours.

Statistical analysis

Data were evaluated using analysis of covariance (ANCOVA) after age adjustment for different sex, subtypes, and suicide attempts in mood disorders. All tests were carried out at the 5% alpha level.

RESULTS

In this study, the 213 patients included 106 with schizophrenia, 61 with mood disorders, 10 with organic disorders, 9 with delusion disorders and 11 with other disorders. Six were drug dependent and 10 were alcohol dependent. Of the 61 patients with mood disorders, 25 had mania and 36 had major depression (all patients were unipolar depression and 7 had attempted suicide before admission). The mean age, BMI, and level of serum albumin in patients with mania were 32.7 ± 15.1 years old (mean ± standard deviation, SD), 24.4 ± 3.8 kg/m², and 40.2 ± 4.0 g/L, respectively. The mean age, BMI, and level of serum albumin in patients with major depression were 43.0 ± 17.8 years old, 23.2 ± 3.9 kg/m², and 39.8 ± 2.8 g/L, respectively. The mean age, BMI and level of serum albumin in control group were 30.1 ± 4.9 years old, 22.2 ± 2.4 kg/m², and 45.8 ± 2.0 g/L, respectively.

For patients with mania, the mean serum albumin levels in men and women were 40.1 ± 5.0 g/L and 40.3 ± 2.7 g/L, respectively. Analysis of covariance after age adjustment revealed no significant difference in mean serum albumin levels between men and women with mania ($F=0.42$, $p=0.523$). For patients with major depression, the mean serum albumin levels in men and women were 39.8 ± 3.0 g/L and 39.8 ± 2.7 g/L, respectively. Analysis of covariance after age adjustment revealed no significant differences in mean serum albumin levels between men and women with major depression ($F=0.05$, $p=0.830$).

Analysis of covariance after age adjustment revealed significant difference in the mean serum albumin levels between patients with mania and control subjects ($F=64.6$, $p=0.000$). Analysis of covariance after age adjustment also revealed significant difference in mean serum albumin levels between patients with major depression and control subjects

($F=68.9, p=0.000$).

In addition, for those who had attempted suicide, analysis of covariance after age adjustment revealed no significant difference in the mean serum albumin levels between patients with major depression who had attempted suicide and those who had not. ($F=2.6, p=0.117$).

DISCUSSION

The results of this retrospective study showed that there were lower serum albumin levels in psychiatric inpatients with mood disorders compared with the control group using analysis of covariance after age adjustment. This suggests that psychiatric inpatients with mood disorders in Taiwan may also suffer systemic responses similar to those noted in Western countries during the acute phase of illness.^(7-12,14) It has been suggested that mania or major depression might be accompanied by an immunological or acute-phase protein response.⁽⁷⁻¹²⁾

Gabay and Kushner (1999) described conditions that commonly lead to severe changes in the plasma concentration of acute-phase proteins including those found during infection, trauma, surgery, burns, tissue infarction and advanced stage cancer.⁽¹⁹⁾ Moderate changes occur after strenuous exercise, heat stroke, and childbirth.^(20,21) Small changes occur after psychological stress and in patients with several types of psychiatric illnesses.^(12,19,21,22) Furthermore, no significant difference was noted in the mean serum albumin levels between those with major depression who attempted suicide and those with major depression who did not attempt suicide. This suggests that acute phase proteins results in only small changes in patients with major depression who had attempted suicide, although suicide attempts are thought to be severe behavior in those with psychiatric diseases.

Due to the retrospective nature of this study, severity ratings and nutritional conditions were not available for analysis. The records of intake and course of illness after the first episode were not complete and were therefore not included in this analysis.

There have been reports showing a significant negative correlation between albumin concentrations and severity of illness⁽¹⁰⁾ and lower albumin levels in patients with treatment-resistant depression in Western countries.⁽²³⁾ However, no discussions about the serum albumin levels and patients with mania

were included except for other acute phase proteins.⁽¹²⁻¹⁴⁾ The finding that serum albumin levels were lower in patients with mania than those in the control subjects in this study may be the first time it has been reported. According to recent studies, interleukin-6 and interleukin-2 are the chief stimulators of the production of most acute-phase proteins.^(24,25) The research showed the levels of both soluble interleukin-2 receptor (sIL-2R) and soluble interleukin-6 receptor (sIL-6R) were elevated in patients with major depression. However, Tsai et al. found that Taiwanese patients with manic episodes had increased levels of sIL-2R but not sIL-6R.⁽²⁶⁾

It has been demonstrated that the serum albumin concentration may be a prognostic marker for mortality in elderly hospitalized patients,⁽²⁷⁾ survival in human immunodeficiency virus-infected women,⁽²⁸⁾ and prognosis of disease in patients with injury or inflammation.⁽²¹⁾ Therefore, the level of serum albumin might apply to be a predictive marker for the discussion of the prognosis of drug responses and clinical courses in patients with mood disorders.

The results of this study only provided the preliminary data. The relationship of serum albumin levels and mood disorders needs to be further explored in controlled prospective studies that include larger numbers of patients.

REFERENCES

1. Grossman J, Yalow AA, Weston RE. Albumin degradation and synthesis as influenced by hydrocortisone, corticotrophin and infection. *Metabolism* 1960;9:528-50.
2. Ballantyne FC, Fleck A. The effects of environmental temperature (20 and 30 °C) after injury on the concentration of serum proteins in man. *Clin Chim Acta* 1973;44:341-7.
3. Fleck A. The influence of the nature, severity and environmental temperature on the response to injury. In: Wilkinson AW, Cuthbertson D, eds. *Metabolism and the Response to Injury*. London: Pitman Medical, 1976:44-8.
4. Waterhouse C, Fenninger LD, Keutmann EH. Nitrogen exchange and caloric expenditure in patients with malignant neoplasias. *Cancer* 1951;4:500-14.
5. Bradly JA, Cunningham KJ, Jackson VJ, Halmiton DNH, Ledingham IA. Serum protein levels in critically ill surgical patients. *Intensive Care Med* 1981;7:291-5.
6. Fleck A. Computer models for metabolic studies on plasma proteins. *Ann Clin Biochem* 1985;22:33-49.
7. Swartz CM. Albumin decrement in depression and cholesterol decrement in mania. *J Affect Disord* 1990;19:173-6.

8. Roos RP, Davis K, Meltzer HY. Immunoglobulin studies in patients with psychiatric diseases. *Arch Gen Psychiatry* 1985;42:124-8.
9. Maes M, Vandewoude M, Scharp'e S, DeClercq L, Stevens W, Lepoutre L, Schotte C. Anthropometric and biochemical assessment of the nutritional state in depression: evidence for lower visceral protein plasma levels in depression. *J Affect Disord* 1991;23:25-33.
10. Maes M, Wauters A, Neels H, Scharp'e S, Van Gastel A, D'Hondt P, Peeters D, Cosyns P, Desnyder R. Total serum protein and serum protein fractions in depression: relationships to depressive symptoms and glucocorticoid activity. *J Affect Disord* 1995;34:61-9.
11. Song C, Dinan T, Leonard BE. Changes in immunoglobulin, complement and acute phase protein levels in the depressed patients and normal controls. *J Affect Disord* 1994;30:283-8.
12. Maes M, Delange J, Ranjan R, Meltzer HY, Desnyder R, Cooremans W, Scharp'e S. Acute phase proteins in schizophrenia, mania and major depression: modulation by psychotropic drugs. *Psychiatry Res* 1997;66:1-11.
13. Hornig-Rohan M, Van Bell CT, Kuhn P, Amsterdam JD. Acute phase proteins in affective illness. *Biol Psychiatry* 1995;37:607.
14. Hornig M, Goodman DBP, Kamoun M, Amsterdam JD. Positive and negative acute phase proteins in affective subtypes. *J Affect Disord* 1998;49:9-18.
15. Maes M, Vandoolaeghe E, Neels H, Demedts P, Annick Wauters, Meltzer HY, Aitamura C, Desnyder R. Lower serum zinc in major depression is a sensitive marker of treatment resistance and of the immune/inflammatory response in that illness. *Biol Psychiatry* 1997;42:349-58.
16. Maes M, De Vos N, Demedts P, Annick Wauters, Neels H. Lower serum zinc in major depression in relation to changes in serum acute phase proteins. *J Affect Disord* 1999;56:189-94.
17. Yao JK, Reddy R, van Kammen DP. Abnormal age-related changes of plasma antioxidant proteins in schizophrenia. *Psychiatry Res* 2000;97:137-51.
18. Dumas BT, Watson WA, Biggs HG. Albumin standards and the measurement of serum albumin with bromocresol green. *Clin Chim Acta* 1971;31:87-96.
19. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. *N Engl J Med* 1999;340:448-54.
20. Maes M, Bosman E, Calabrese J, Meltzer HY. Plasma interleukin-2 and -6 in schizophrenia and mania: effects of neuroleptics and mood stabilizers. *J Psychiatr Res* 1995;29:141-52.
21. Fleck A. Clinical and nutritional aspects of changes in acute-phase proteins during inflammation. *Proc Nutr Soc* 1989;48:347-54.
22. Van Hunsel A, Van Gastel A, Neels H, Wauters A, Demedts P, Bruyland K, DeMeeter I, Scharp'e S, Janca A, Song C, Maes M. The influence of psychological stress on total serum protein and patterns obtained in serum protein electrophoresis. *Psychol Med* 1998;28:301-9.
23. Van Hunsel A, Wauters A, Vandoolaeghe E, Neels H, Demedts P, Maes M. Lower total serum protein, albumin, and beta- and gamma-globulin in major and treatment-resistant depression: effects of antidepressant treatment. *Psychiatry Res* 1996;65:159-69.
24. Maes M, Bosman E, Meltzer HY, Scharp'e S, Suy E, Calabrese J, Cosyns P. Relationships between interleukin-6 activity, acute phase proteins and HPA-axis function in severe depression. *Psychiatry Res* 1993;49:11-27.
25. Maes M, Meltzer HY, Bosman E, Vandoolaeghe E, Ranjan R, Desnyder R. Increased plasma concentrations of interleukin-6, soluble interleukin-6, soluble interleukin-2, and transferrin receptor in major depression. *J Affect Disord* 1995;34:301-9.
26. Tsai SY, Chen KP, Yang YY, Chen CC, Lee JC, Leu SJC. Activation of cell-mediated immunity during manic episodes in bipolar disorder. *Taiwanese J Psychiatry* 1998;12:207-17.
27. Hermann FR, Safran C, Levkoff SE, Minaker KL. Serum albumin level on admission as a predictor of death, length of stay, and readmission. *Arch Intern Med* 1992;152:125-30.
28. Feldman JG, Burns DN, Gange SJ, Bacchetti P, Cohen M, Anastos K, Nowicki M, Delapena R, Miotti P. Serum albumin as a predictor of survival in HIV-infected women in the Women's Interagency HIV study. *AIDS* 2000;14:863-70.

情感性疾病患者之血清白蛋白濃度

黃條來

背景： 在西方國家已有許多報告指出曾有較低的血清白蛋白和情感性疾病有關。本研究將調查是否在台灣的精神科住院病人其血清白蛋白在疾病急性發作期亦有較低的現象。

方法： 回顧南部某醫學中心其精神科在某一年213位急性住院病人中含有61位情感性疾病。記錄其年紀、體重、身高、有無自殺行為、血中白蛋白濃度、血中常見的生化檢查等資料。對照組資料來自病房32位健康的工作同仁。並利用共變異分析等統計方法分析比較情感性疾病患者的血中白蛋白濃度與32位精神科工作同仁的資料是否有差異。

結果： 25位躁症患者血中平均白蛋白濃度為 40.2 ± 4.0 克/升。36位重憂鬱症患者血中平均白蛋白濃度為 39.8 ± 2.8 克/升。而正常組其血中平均白蛋白濃度為 45.8 ± 2.0 克/升。統計的結果，躁症患者及重憂鬱症患者其血中平均白蛋白濃度皆較正常組為低，有顯著的差異。但在重憂鬱症患者中，有無自殺行為其血中平均白蛋白濃度並無統計上顯著的差異。

結論： 在台灣的情感性疾病住院病人其血清白蛋白濃度在急性發作期亦有較低的現象。
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關鍵字： 白蛋白，躁症，重憂鬱症，自殺。