

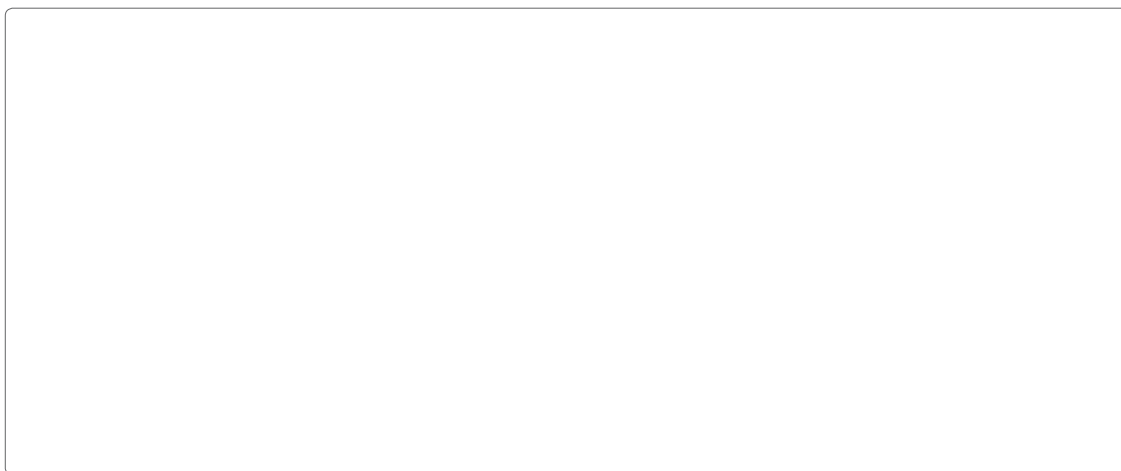
Comparison of Lithium and Valproate Concentration in Serum During Three Different Patients Treated by Lithium Carbonate, Sodium Valproate and Their Combination: A Preliminary Study

Zhu JF¹, Jin WD^{2*}, Jin R³, Ma YC², and Ren ZB²

¹Zhejiang Chinese Medical University, Hangzhou, China, 310053

²Department of Psychiatry, Tongde Hospital Affiliated to Zhejiang Chinese Medical University, (Zhejiang Province Tongde Hospital, Zhejiang Province Mental Health Institute), Hangzhou, China, 310012

³Department of Pharmacology, Tongde Hospital Affiliated to Zhejiang Chinese Medical University, (Zhejiang Province Tongde Hospital, Zhejiang Province Mental Health Institute), Hangzhou, China, 310012



Keywords: Lithium carbonate; Sodium valproate; Drug concentration; Mutual influence; Bipolar disorder

Introduction

Lithium carbonate and sodium valproate are the classic mood stabilizers and frequently applied in the treatment of bipolar affective disorder. However, favorable efficacy has not been achieved in some patients undergoing treatment with one mood stabilizer or even in combination with antipsychotics [1]. Therefore, combined application of mood stabilizers, especially for bipolar affective disorder patients with type I manic episode, mixed episode or rapid cycling is necessary [2]. In our previous studies, we found the efficacy of combined application of mood stabilizers were superior to that of one mood stabilizer alone [3,4]. Recently, increasing studies have confirmed that, in not only the treatment of acute bipolar affective disorder but the prophylactic management of the bipolar affective disorder, the lithium carbonate together with sodium valproate has definite effectiveness and preventive effects against lithium events [4,5]. To date, no evidence confirmed the mutual influence of lithium carbonate and sodium valproate. One study showed lithium carbonate and sodium valproate could not interfere with each other, sodium valproate rarely affected the pharmacokinetics of lithium carbonate, and the AUC, C_{MAX} and C_{MIN} were only slightly increased [6]. Although the combination therapy with lithium carbonate and sodium valproate can improve the efficacy and is suitable for rapid cycling bipolar disorder [7]. Sometimes this therapy should be performed with other antipsychotics [8]. In our previous study, lithium carbonate and sodium valproate were used in a rat model and results did not reveal obvious psychomotor excitement were selected. made based on the DSM-IV bipolar disorder, schizoaffective disorder or schizophrenia criteria and their PANSS excitement factor score >14. Among these patients, the exclusion criteria are as following: (1) effective

*Corresponding author: Jin Weidong, Tongde Hospital Affiliated to Zhejiang Chinese Medical University, (Zhejiang Province Tongde Hospital, Zhejiang Province Mental Health Institute), Hangzhou, China., 310012, Tel: 86-13588480677; E-mail: wjjin@163.com

Received January 25, 2018; Accepted May 05, 2018; Published May 15, 2018

Citation: Zhu JF, Jin WD, Jin R, Ma YC, Ren ZB (2018) Comparison of Lithium and Valproate Concentration in Serum During Three Different Patients Treated by Lithium Carbonate, Sodium Valproate and Their Combination: A Preliminary Study. *Neurosci Psychiatry* 1: 102.

Copyright: © 2018 Zhu JF, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Results: The drug concentration of lithium was 0.44 ± 0.20 mmol/L in the lithium carbonate group, and 0.54 ± 0.22 mmol/L, 0.57 ± 0.29 mmol/L in the lithium carbonate plus sodium valproate group, suggesting no significant difference between the two groups. The concentration of sodium valproate was 91.9 ± 20.5 mg/L, 83.8 ± 26.2 mg/L and 74.5 ± 22.7 mg/L in the lithium carbonate group, 96.3 ± 31.4 mg/L in the lithium carbonate plus sodium valproate group. There was no significant difference between the two groups. Volume 1 • Issue 1 • 1000102

Conclusion: The mutual influence of lithium carbonate and sodium valproate was not significant.

mean: 1.6 ± 1.5) and 4 had schizophrenia (the number of episodes: 2~6; mean: 2.5 ± 2.8). There were 16 males and 8 females with a mean age of 37 ± 13 years (range: 19~60 years). All the patients were randomly assigned into 3 groups (n=8 per group) according to a table of random numbers and received randomly treatment with lithium carbonate, sodium valproate and lithium carbonate plus sodium valproate and their atypical antipsychotics.

Methods

Dosage and administration: The lithium carbonate was purchased from Hunan Qianjin Xiangjiang Pharmaceutical Co Ltd (Lot number: 050702) and sustained release sodium valproate (Depakine) from Sano Pharmaceutical Co Ltd (Lot number: H20010259). Patients were treated with lithium carbonate (1 g/d), sodium valproate (1 g/d) and lithium carbonate plus sodium valproate (1 g/d for each drug). The therapeutic doses of both drugs were achieved at day 4. In addition, atypical antipsychotics were also applied and their therapeutic doses were achieved within 1 week.

The blood lithium and sodium valproate levels were determined when the both mood stabilizers and antipsychotics were applied at constant doses for 1st week. The antipsychotics included quetiapine (400~800 mg/d) and olanzapine (10~25 mg/d), and the doses of these antipsychotics increased according to the disease condition. In the lithium carbonate group, 4 patients suffered from bipolar disorder, 3 suffered from schizoaffective and 1 suffered from schizophrenia. In the sodium valproate group, 5 suffered from bipolar disorder, 2 suffered from schizoaffective and 1 suffered from schizophrenia. In the lithium carbonate plus sodium valproate group, 5 suffered from bipolar disorder, 1 suffered from schizoaffective and 2 suffered from schizophrenia. In respect of the antipsychotics, the mean dose of quetiapine was 660 ± 160 mg/d (range: 600~1000 mg/d) and that of olanzapine was 16.8 ± 5.0 mg/d (range: 15~20 mg/d) in the lithium carbonate group. In the sodium valproate group, the mean dose of quetiapine was 640 ± 150 mg/d (range: 600~800 mg/d) and that of olanzapine was 13.5 ± 9.0 mg/d (range: 10~25 mg/d). In the lithium carbonate plus sodium valproate group, the mean dose of quetiapine was 540 ± 180 mg/d (range: 400~800 mg/d) and that of olanzapine was 11.1 ± 4.5 mg/d (range: 10~20 mg/d). Significant difference was found in the dose of quetiapine, but not in that of olanzapine. Our study was passed through by Zhejiang Tongde Hospital Ethics Committee and every patient was informed and consent for our study. The informed approval document were signed by their guardian.

5. Geddes JR, Goodwin GM, Rendell J, Azorin JM (2010) Lithium plus valproate combination therapy versus monotherapy for relapse prevention in bipolar I disorder (BALANCE): a randomised open-label trial. *Lancet* 375: 385-395.