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 JF[1], Jin WD[2*], Jin R[3], Ma YC[2], and Ren ZB[2]

Department of Psychiatry, Tongde Hospital Affliated to Zhejiang Chinese Medical University, (Zhejiang Province Tongde Hospital, Zhejiang Province Mental Health

Department of Pharmacology, Tongde Hospital Affliated to Zhejiang Chinese Medical University, (Zhejiang Province Tongde Hospital, Zhejiang Province Mental Health

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

Introduction

Lithium carbonate and sodium valproate are the classic mood stabilizers and frequently applied in the treatment of bipolar a ective disorder. However, favorable e cacy has not been achieved in some patients undergoing treatment with one mood stabilizer or even in combination with antipsychotics [1]. erefore, combined application of mood stabilizers, especially for bipolar a ective disorder patients with type I manic episode, mixed episode or rapid cycling is necessary [2]. In our previous studies, we found the e cacy of combined application of mood stabilizers were superior to that of one mood stabilizer alone [3,4]. Recently, increasing studies have con rmed that, in not only the treatment of acute bipolar a ective disorder but the prophylactic management of the bipolar a ective disorder, the lithium carbonate together with sodium valproate has de nite e ectiveness and preventive e ects against lithium events [4,5]. To date, no evidence con rmed the mutual in uence of lithium carbonate and sodium valproate. One study showed lithium carbonate and sodium valproate could not interfere with each other, sodium valproate rarely a ected 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 e cacy 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 reby obvious psychomotor excitement were selected. e diagnosis was made based on the DSM-IV bipolar disorder, schizoa ective disorder or schizophrenia criteria and their PANSS excitement factor score >14. Among these patients, the exclusion criteria are as following: (1) e

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

 valproate at a serum were determined for 3 times.

Results: The drug concentration of lithium was 0.44 ± 0.20 m the lithium carbonate group, and 0.54 ± 0.22 mmol/L, 0.57 ± 0.29 plus sodium valproate group, suggesting no signi cant differenc 91.9 ± 20.5 mg/L, 83.8 ± 26.2 mg/L and 74.5 ± 22.7 mg/L in the ± 20.9 mg/L and 96.3 ± 31.4 mg/L in the lithium carbonate plu difference.

Conclusion: The mutual in uence of lithium carbonate and

mean: 1.6 ± 1.5) and 4 had schizophrenia (the number of episodes: 2~6; mean: 2.5 ± 2.8). ere 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: e 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). e 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.

e blood lithium and sodium valproate levels were determined when the both mood stabilizers and antipsychotics were applied at constant doses for 1st week. e 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 su ered from bipolar disorder, 3 su ered from schizoa ective and 1 su ered from schizophrenia. In the sodium valproate group, 5 su ered from bipolar disorder, 2 su ered from schizoa ective and 1 su ered from schizophrenia. In the lithium carbonate plus sodium valproate group, 5 su ered from bipolar disorder, 1 su ered from schizoa ective and 2 su ered 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). Signi cant di erence was found in the dose of quetiapine, but not in that of olanzapine. Our study was passed though by Zhejiang Tongde Hospital Ethics Committee and very patients were informed and consent for our study. e knowing 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.