Bipolar disorder (BD) is a common, chronic and sometimes a debilitating mental illness, characterized by an episodic course with life time prevalence of 1-6% [1,2]. The morbidity is rather high and mortality rate, mostly due to suicide, is estimated to be three times higher than the general population. Thus, the prevention of manic and depressive recurrences in bipolar disorder is a hallmark of the long-term treatment of BD. Drugs which may treat mania and/or depression without causing switch to one another state while preventing the emergence of a new episode could be defined as mood stabilizers. In general, this definition is based on either anti-manic, anti-depressant or prophylactic properties to varying degrees and they usually require two of the three effects. When applied such a definition to the agents in the market, Lithium remains as the golden standard. After the introduction of lithium or first anti-psychotic drugs (i.e. chlorpromazine) about 40-50 years ago, the major steps in the pharmacological treatment of BD have started. Two decades ago, lithium carbonate was the only drug in the mood stabilizer category. Carbamazepine was used in refractory cases and in a small number of specialty clinics and valproate was emerging as a novel and an effective mood stabilizer. Since then, it seems that every new anticonvulsant is evaluated for its mood-stabilizing properties (3). Yet, lithium, still, remains to be the most important drug in the treatment of BD, being effective both for acute states and prevention. Lithium is absorbed by intestinal membranes and eliminated exclusively by the kidneys. Its levels should be monitored carefully during follow-up treatment because of narrow therapeutic index. Drugs that alter renal function can increase the risk for chronic lithium toxicity. Anorexia, cystic fibrosis, decreased effective circulating volume (e.g. cirrhosis, congestive heart failure, nephrotic syndrome), decreased dietary sodium intake, diabetes insipidus, diabetes mellitus, gastroenteritis, infections, medications (e.g. angiotensin-converting enzyme inhibitors, cyclosporine, diuretics: loop diuretics and thiazides, non-steroidal anti-inflammatory drugs, tetracycline), overdose, renal insufficiency, schizophrenia, surgery and volume depletion are among the factors that increase the risk for toxicity in previously stable patients (4).

Though lithium remains as one of the most widely used medications for the treatment of BD, it has long been known to cause problems in three aspects: kidneys, appetite and thyroid. Firstly, there are four well-known ways to have kidney problems due to lithium. Fortunately, only one of them is very common and the rest are rare. The most common side-effect is the ability of the kidney to concentrate urine (i.e. “distal tubule” effect). The rest are failure to excrete acids, glomerular and interstitial changes. Secondly, weight gain, the epidemic side-effect of our era, which also happens without lithium for a lot of people. Unlike valproate, which causes weight gain by increasing appetite to obvious extremes, lithium causes a slow but steady accumulation. Women, those who are heavier to start, young patients and patients who have hypothyroidism can gain weight. Third and probably the most important side-effect is thyroid dysfunction (5). Different studies have produced very different numbers of prevalence, ranging from 23 to 100% of all patients taking lithium while women are more vulnerable than men, it appears. Lithium effects thyroid function in many ways. First of all, lithium interferes with the iodination right at the beginning of the process and this is reversible. Then, lithium inhibits the release of fully-formed thyroid hormone from the thyroid gland into the bloodstream. Finally, it affects the conversion of T4 to T3 out in the cells to which the T4 travels in the blood. Recent treatment guidelines suggest the presence of thyroid function abnormalities should not constitute a direct contraindication to lithium treatment (8).

In this era, many new agents are being proposed by the pharmaceutical industry as mood stabilizers but, as Schou and many others pointed out, the prophylactic effect of them remains either weak or controversial. Our old lithium still remains as the gold standard among others. If a drug which has efficacy in treating acute manic and depressive episodes while preventing new mood events is to be considered as a mood stabilizer, only lithium fulfills this criteria, for now.

References

Timuçin Oral M.D.
Yazışma Adresi/Correspondence Address:
İstanbul Commerce University, Department of Psychology, Istanbul, Turkey
E-mail: etoral@hotmail.com