The Effects of Lithium on Platelet Count

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Recently, numerous works have rekindled the interest in using lithium carbonate in hematologic oncology. It is well known that lithium can cause a neutropenia and therefore correct neutropenia [1–3]. Several authors have also pointed out the positive effects of lithium on the production of red blood cells [1, 3, 4], monocytes [5], and platelets [3, 6]. Joffe et al. [7] have recently shown that it may also cause an increase in platelets. Some authors question the validity of these experiments [5, 8]. It seems to us that these uncertainties are based on too optimistic evaluations of clinical statistics expressed in an uncritical form. Recently, Quesenberry et al. [3] have demonstrated that lithium may induce the in vitro production of stromal-derived factors acting at multiple, relatively primitive, stem-cell levels.

These studies indicated that lithium can exert these effects indirectly by acting at a multipotent stem-cell level rather than simply on granulocyte production. The results of our work have permitted us to demonstrate two aspects of the mechanisms of action of lithium. The first, or qualitative, aspect is that lithium may activate certain cellular functions in neutrophils [9], lymphocytes and macrophages [5] via a similar mechanism (control of intracellular cAMP and cGMP and ionic flow across membranes). It may be helpful to hypothesize a similar action on the progenitor cells of red blood cells, leukocytes and platelets in bone marrow as suggested by Quesenberry et al. [3].

The second, or quantitative, aspect is the increase in platelets, monocytes and granulocytes observed in some of our patients treated with lithium (900–1,200 mg/day) for at least 3 weeks [9].

In a first group of 12 patients with lymphoma treated with lithium to control myelodepression induced by chemotherapy [10], there was an increase in the following parameters: number of neutrophils [(4.970 ± 85) vs. (2.9 ± 1.83) × 10^9/μL; p < 0.005], number of monocytes [(0.364 ± 0.16) vs. (0.359 ± 0.312) × 10^9/μL; p < 0.2], number of platelets [(231 ± 84) vs. (189 ± 38) × 10^9/μL; p < 0.2].

Although the number of platelets increased, this increase is probably not very significant given the high standard deviation.

A more recent observation in 6 other patients with lymphomas and 4 patients with other neoplasias gave similar results. In particular, the number of platelets increased from (196 ± 43) × 10^9/μL to (244 ± 21) × 10^9/μL (p < 0.3). Only in 2 patients was there a significant increase in platelets (343 vs. 194 × 10^9/μL and 475 vs. 205 × 10^9/μL) concomitant with a significant increase in neutrophils and monocytes. In our experience, the only case in which lithium caused a
significant increase in red blood cells, platelets and neutrophils was in a patient with bone marrow aplasia [4]. It therefore seems as if lithium only acts on cytopenias of hemopoietic precursor cell origin. The effect of a drug should objectively be evaluated in terms of a pathological condition.

Results from hematologically normal subjects should not be compared with those from patients with myelodepressive cytopenias. The microenvironment of the bone marrow in each of these 2 populations is very different. However, since even single sporadic cases may be instructive, there is a theoretic usefulness to treat myelodepressed patients with thrombocytopenia with lithium (perhaps in association with other drugs), even though the main indication at the present time is treatment for peripheral neutropenia as due to dismyelopoiesis. It is very probable that lithium increases the numbers of all blood elements (via stimulation of multipotent stem cells). However, this effect seems to prevail, and therefore is

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statistically significant, in neutrophils. Lithium seems to selectively increase the number of neutrophils leaving the bone marrow and entering the peripheral circulation independently from an increased production [11,12].

In conclusion, our experience with lithium in patients with abnormal hemopoiesis has not, in fact, demonstrated a statistically significant increase in platelets.

References
