Effects of Lithium on the Platelet Count in Neoplastic Patients Treated with Polychemotherapy

G.	Giovanni	Carulli
A.	Antonio	Azzarà
A.	Alessandra	Marini
M.	Mario	Petrini
F.	Fabio	Ambrogi

Pisa

Giovanni Carulli, MD, Antonio Azzarà, MD, Alessandra Marini, MD, Mario Petrini, MD, Fabio Ambrogi, MD, Medical Clinic I, University of Pisa, I-56100 Pisa (Italy)

The ability of lithium to induce neutrophil leuko-cytosis [1] has made it possible to use this drug to attenuate and to control myelodepression induced by chemotherapy in neoplastic patients [2–4].

Furthermore, the effectiveness of lithium has been clinically demonstrated in rare forms of chronic neu-tropenia [5] and neutropathy [6], and experiments have indicated that this drug is capable of modulating the microtubular system of human neutrophils [7, 8].

It has recently been shown that lithium is also able to increase the platelet count [9] and to stimulate CFU-Meg [10]. These effects are in good agreement with recent findings about the action mechanism of the drug on haematopoiesis: lithium appears to be capable of stimulating stem cells, with an effect mediated by stromal cells [11]. In this way, the drug might cause hematopoiesis to be oriented in various directions besides the granulopoiesis.

As a result of these considerations, modifications in the platelet count were evaluated in 19 patients affected by lymphomas and other neoplasias, who had been treated with lithium carbonate (900 mg/day for 21 days), in an attempt to control myelodepression which had arisen during polychemotherapy.

In the group of 11 patients with neutropenia and monocytopenia the neutrophil count was normalised ($3.6 \pm 1.0 \times 10^9/l$ vs. $1.3 \pm 0.2 \times 10^9/l$; $p < 0.001$) and monocytes increased significantly ($0.323 \pm 0.056 \times 10^9/l$ vs. $0.132 \pm 0.064 \times 10^9/l$; $p < 0.001$) though there was no modification in the platelet count ($248 \pm 73.3 \times 10^9/l$ vs. $244 \pm 60.9 \times 10^9/l$; $p = \text{NS}$).

In the second group, made up of 8 patients with thrombocytopenia (platelets $< 150 \times 10^9/l$) together with neutropenia and monocytopenia, there was a normalisation of the number of platelets in 5 out of 8 patients. The results, which are illustrated in table I, show that 2 out of the 5 patients whose platelet count

was normalised by lithium did not exhibit a satisfactory neutrophil response (neutrophils $> 2 \times 10^9/l$). On the other hand, 2 of the 3 patients whose platelet count did not increase revealed a good neutrophil response.

Monocytes showed a significant increase in 6 out of the 8 patients ($0.253 \pm 0.102 \times 10^9/l$ vs. $0.165 \pm 0.082 \times 10^9/l$; $p < 0.025$).

In a control group, made up of 9 patients with thrombocytopenia caused by polychemotherapy, the platelet count did not increase during the same period of observation ($76.8 \pm 24.5 \times 10^9/l$ vs. $97.2 \pm 17.4 \times 10^9/l$; $p = NS$).

The present results, which are not in agreement with those reported by Ricevuti et al. [12], indicate that in a certain number of patients affected by

Table I. Effects of lithium carbonate on platelet and neutrophil counts in patients suffering from neoplasia

Effects of Lithium on the Platelet Count in Neoplastic Patients Treated with Polychemotherapy 243

thrombocytopenia caused by antineoplastic treatment, lithium was able to bring about the normalization of the platelet count. This effect may be separated from the neutrophil response. The effect of lithium can only be seen clearly when thrombocytopenic patients are distinguished from non-thrombocytopenic ones: the latter do not reveal any modification in the platelet count, while the neutrophil response is excellent in all patients.

It is the authors' belief that lithium may well act on the stem cells, orienting them towards more than one evolutionary line. It is furthermore possible that, when the bone marrow damage is particularly serious, the differentiating lines may enter into competition [13].

References

- Shopsin, S.; Friedman, R.; Gershon, S.: Lithium and leukocyto-sis. *Clin. Pharmacol. Ther.* 12: 923–938 (1971).
- Catane, R.; Kaufman, J.; Mittleman, A.; Murphy, G.R.: Attenuation of myelodepression with lithium. *New Engl. J. Med.* 297: 452–453 (1977).
- Stein, R.S.; Beaman, C.; Ali, M.Y.; Hansen, R.; Jenkins, D.D.; Jume'an, H.G.: Lithium carbonate attenuation of chemotherapy-induced neutropenia. *New Engl. J. Med.* 297: 430–431 (1977).
- Lyman, G.H.; Williams, C.C.; Preston, D.: The use of lithium carbonate to reduce infection and leukopenia during systemic chemotherapy. *New Engl. J. Med.* 302: 257–260 (1980).
- Carulli, G.; Azzarà, A.; Polidori, R.; Marini, A.; Grassi, B.; Ambrogi, F.: Effects of lithium carbonate on leukocyte functions in chronic benign neutropenia. *Acta haemat.* 72: 408–412 (1984).
- Perez, D.H.; Kaplan, H.B.; Goldstein, I.M.; Shenkman, L.; Bor-kowsky, W.: Reversal of an abnormality of polymorphonuclear leukocyte chemotaxis with lithium. *Clin. Immunol. Immunopathol.* 16: 308–315 (1980).
- Carulli, G.; Marini, A.; Azzarà, A.; Petrini, M.; Ruocco, L.; Ambrogi, F.: Modifications in the phagocytosis of human neutrophils induced by vinblastine and cytochalasin B: the effects of lithium. *Acta haemat.* 74: 81–85 (1985).
- Azzarà, A.; Petrini, M.; Carulli, G.; Polidori, R.; Vaglini, F.; Trombi, L.; Mian, M.; Bertelli, A.; Ambrogi, F.: The effects of lithium and rubidium on human leukocyte functions. *Int. J. Immunotherapy* (in press).
- Joffe, R.T.; Kellner, C.H.; Post, R.M.; Unde, T.W.: Lithium increases platelet count. *New Engl. J. Med.* 311: 674–675 (1984).
- Joyce, R.A.: Sequential effects of lithium on hematopoiesis. *Br. J. Haemat.* 56: 307–321 (1984).

Quesenberry, P.J.; Coppola, A.M.; Gualtier, R.J.; Wade, P.M.; Song, Z.; Doudas, M.A.; Schideller, C.E.; Baker, D.G.; McGrathe, H.: Lithium stimulation of murine hematopoiesis in liquid culture: an effect mediated by marrow stroma cells. *Blood* 63: 121–127(1984).
Ricevuti, G.; Mazzone, A.; Rizzo, S.C.: The effects of lithium on platelet count. *Acta haemat.* 74: 118–119(1985).
Hellman, S.; Grate, H.E.: Hematopoietic stem-cell: evidence for competing proliferative demands. *Nature* 216: 65–66 (1967).