Lithium versus Rubidium in Chemiluminescence

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It is known that some granulocyte functions such as phagocytosis and killing are closely related to the respiratory burst. Once the respiratory burst has been activated, it may be evaluated by monitoring the chemiluminescence. Chemiluminescence tests have thus been used to quantify granulocyte activation and to evaluate drug interference [1, 3]. We have been recently involved in studying the roles of some oligoelements on polymorphonucleate activities. Evidence has been given that lithium inhibits the adherence as well the bactericidal activity of granulocytes [7,4].

Moreover, it has been suggested that Li is able to reduce chemotaxis depending on the concentration, whereas rubidium appears to increase this function [2]. The aim of the present paper was to evaluate, by means of chemiluminescence measurements, the effects of Li and Rb on polymorphonucleate activity induced by different stimuli.

Leukocytes were isolated from blood of healthy donors by density-gradient centrifugation. The cells were resuspended in MEM for the chemiluminescence experiments. Chemiluminescence was induced in 2×10^5 cells by adding either 0.5 mg/ml of opsonized zymosan or 10^{-6} M FMLP. Luminal (2×10^{-6} M) was used as an amplifier of light emission. The chemiluminescence signal was detected using a Packard Pico-lite chemiluminometer thermostated at 37°C . The two oligoelements were tested at three different concentrations (0.5, 1 and 1.5 mEq/l). Results were expressed as the integrated area of the chemiluminescence curve of experiments repeated 6 times. Statistical analysis of the integrated area was performed by Student's t test.

When the tests were performed by activating the cells with zymosan, Li showed a significant inhibitory effect at the higher concentrations (controls: 0.552 ± 0.089 ; Li 1.5 mEq/l: 0.407 ± 0.085 ; $p < 0.01$), whereas Rb significantly increased the chemiluminescence both at concentrations of 1 mEq/l (0.715 ± 0.129 ; $p < 0.01$) and of 1.5 mEq/l (0.760 ± 0.176 ; $p < 0.01$) but not at a concentration of 0.5 mEq/l. When the two oligoelements were added together, both at 1 mEq/l, the potentiating effect of Rb still prevailed. On the contrary, the two metals did not modify the chemiluminescence induced by FLMP.

Thus the activation induced by zymosan could be mediated by Li- and Rb-sensitive processes, whereas the activation by the chemotactic peptide FMLP is probably mediated by Li- and Rb-insensitive processes, at least at the concentrations assayed. These results confirm those of previous papers showing opposite actions of Li and Rb on chemotaxis [2].

A Rb, 1.5 mEq/i Δ Rb, 1 mEq/i
 • OZ, 0.5 mg/ml □ Li, 1 mEq/l ■ Li, 1.5 mEq/i
 Time, min

Fig. 1. Chemiluminescence induced by opsonized zymosan (OZ) in the presence or absence of Li or Rb.

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Li and Rb are used in different phases of the treatment of cyclothymic psychiatric patients: Li is given as an antimaniac drug and Rb as an antidepressant; on the basis of this opposite action, Rb has been called an 'anti-Li drug' [8, 9]. The Na-like effects of Li and the K-like effects of Rb on the nerve membrane [9] suggest opposite roles of the two metals. The opposite actions on cyclic nucleotides [5] and the role on o-methylations [10, 6] appear to confirm the Rb appellation of 'anti-Li'.

In conclusion, in spite of the difficulty in evaluating the precise action mechanism, the present data indicate that Rb has an action on some granulocyte functions which is opposite to that of Li. We believe that these results should be kept in mind when using Li in neutropenias and suggest the validity of a clinical use of Rb in hematology.

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