Follow-Up of Superoxide Production by Phagocytes in Whole Blood of Leukaemic Patients during Therapy

Giuseppe Todeschini, Lucia Zeni, Paolo Bellavite

Cattedra di Ematologia, Istituto di Patologia Medica, e Istituto di Patologia Generale, Università di Verona, Italia

Key Words. Leukaemia treatment · Phagocyte metabolism · Phagocytosis · Superoxide production

Abstract. The phagocyte function of granulocytes and monocytes of whole blood was measured as superoxide production in patients treated for acute nonlymphoblastic leukaemia. The results indicate that the antileukaemic protocol used in this study did not cause a decrease of the oxidative metabolism triggered by phagocytosis and by phorbol esters.

Introduction

One of the parameters that are usually followed during the treatment of cancer patients is the leucocyte count. However, it would be also relevant for the clinician to know the functional capacity of the leucocytes during therapy. It has been reported that drugs used in cancer patients such as prednisone or methotrexate inhibit leucocyte function [1-3]. Concomitantly with neutropenia, such an effect is expected to markedly increase the risk of infection.

We have utilized a quantitative assay of superoxide (O_2^-) production in whole blood [4-6] of patients with acute nonlymphoblastic leukaemia (ANLL) in order to verify whether the protocol of cytostatic agents used in our patients affected the phagocyte function. By using whole blood the need of isolating the leucocytes was eliminated. This reduced the amount of blood and the time necessary for the assay and, more important, allowed the measurement of phagocyte function without washing the cells, i.e., in conditions very similar to those occurring in vivo.

Patients and Methods

Studies were done on patients affected by ANLL, before and during polychemotherapy. The induction treatment was based on two repeated cycles of adriamycin (ADM, 35 mg/m^2/day, days 1 + 2), cytosine arabinoside (ARA-C; 200 mg/m^2/day, days 1-7), 6-thioguanine (6-TG; 200 mg/m^2/day, days 1-7), alternated with a cycle consisting of ADM (50 mg/m^2/day, day 1), vincristine (VCR; 1.3 mg/m^2/day, day 2) and ARA-C (1 mg/m^2/day, days 1-6). After three cycles, also amsacrine (AMSA, 100 mg/m^2/day, days 1-5) and etoposide (VP16, 100 mg/m^2/day, days 1-5) were given as consolidation chemotherapy.

The phagocyte function was measured as O_2^- production according to the method of Bellavite et al. [6]: 1-2 ml of heparinized (20 U/ml) venous blood were withdrawn and utilized for the assay within 2 h; for each blood sample duplicate assays of O_2^- production in the absence and in the presence of opsonized zymosan (1 mg/ml) and of phorbol 12-myristate 13-acetate (PMA; 1 μg/ml) as stimulatory agents were done. On the same blood sample the leucocyte count and formula were done and the number of phagocytes was reported as the sum of mature granulocytes plus half of mature monocytes, because monocytes have about half the capacity of superoxide production with respect to granulocytes [6]. The patients considered in this study had small numbers of circulating immature myeloid precursors (less than 5,000/mm^3 before therapy, less than 1,200 during therapy). The presence of blasts did not affect the assay of O_2^- production because it is known that in these cells the respiratory burst is almost totally absent [3, 7, 8].

Results and Discussion

Figure 1 shows the course of the phagocyte numbers and superoxide-producing capacity of whole blood in two ANLL patients during the first three months of therapy. It can be seen that the initial chemotherapeutic cycle induced a rapid decrease of both phagocyte number and superoxide production.
Superoxide Production in Leukaemic Patients

Superoxide production in whole blood of ANLL patients before and during therapy

<table>
<thead>
<tr>
<th></th>
<th>O₂, nmol/15 min/10⁶ phagocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>unstimulated</td>
</tr>
<tr>
<td>Patients</td>
<td></td>
</tr>
<tr>
<td>before therapy</td>
<td>8.6 ± 5.7</td>
</tr>
<tr>
<td>during therapy</td>
<td>12.0 ± 9.9</td>
</tr>
<tr>
<td>Healthy controls</td>
<td>4.9 ± 2.7</td>
</tr>
</tbody>
</table>

The data are means ± SD of the values from 5 patients and 5 controls. The differences between patients before and during therapy and between patients and controls are not statistically significant.

host defences. This accounts for the common clinical observation that in the course of infections associated with drug-induced bone marrow aplasia, even a small increase of blood neutrophils could cause a dramatic improvement. From the results here reported it can be also concluded that in the course of the chemotherapy with ARA-C, 6-TG and ADM the monitoring of leukocyte count and formula is a reliable and probably sufficient parameter for the evaluation of nonspecific immunity.

Acknowledgements

This work was supported by grants from Italian National Research Council (Special project 'Oncologia', No. 86.00557.44) and from Associazione Italiana per la Ricerca sul Cancro.

References


