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Myeloprotective Effect of Medroxyprogesterone Acetate (MPA)

Paolo Pedrazzoli

IN A RECENT paper published in *The European Journal of Cancer* Amadori *et al.* [1] evaluate the myeloprotective effect of medroxyprogesterone acetate (MPA) by looking at bone marrow granulocyte–macrophage progenitor cell (CFU-GM) growth in patients with head and neck cancer receiving chemotherapy alone or in combination with the progestin. They conclude that "the myeloprotective effect of MPA is due to its capability to induce mitotic rest in the stem cells which are thus protected from the action of chemotherapeutic drugs", but what they state is not clearly supported by data presented.

Their conclusion relies mainly on results comparing the number of progenitors before and after 2 weeks of MPA treatment; a reduction in CFU-GM growth was observed at day 14 in 7 out of 10 cases. Despite the fact that no statistical significance is reached, they do not give an explanation on the 3 cases in which the number of progenitors increases on day 14. In addition, their conclusion is not supported by any cell cycle analysis.

Further support for a protective role of MPA on bone marrow progenitors comes, in this study, from results comparing CFU-GM growth before and 14 days after chemotherapy. In 8 out of 10 cases of the MPA-treated group an increase of CFU-GM was observed on day 14, while in chemotherapy-alone group there was a reduction of CFU-GM at the same time. However, the authors did not point out and discuss that before chemotherapy the number of progenitors was significantly lower in MPA-treated patients and it was very close in the two groups—101.3 (6.0–187.2) vs. 95.0 (36.7–178.5)—on day 14.

As far as clinical results are concerned, they report 3 cases of grade 1 leukopenia and thrombocytopenia in MPA-treated patients as compared to 4 cases of grade 1 leukopenia and 3 cases of grade 2–3 thrombocytopenia in chemotherapy-alone group. This is, in my opinion, too little to state that "we observed lower haematological toxicity in the peripheral blood stream in arm B" (MPA). Furthermore they did not specify whether the two groups were matched for age, sex, previous myelotoxic therapy, etc.

Our and other experiences [2, 3] have failed to demonstrate a direct *in vitro* effect of MPA on bone marrow progenitor cells. Amadori *et al.* [1] have used a different and interesting approach to study this issue, but their data are not sufficient to draw any conclusions.

In the era of haemopoietic growth factors, the use of MPA to reduce chemotherapy-related myelotoxicity seems unrealistic, although the drug clearly remains an important tool in other oncological settings.

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Myeloprotective Effect of Medroxyprogesterone Acetate (MPA)

D. Amadori

PEDRAZZOLI'S CRITICISM of our paper [1] stems from the statement that the authors' conclusions "rely mainly on results comparing the number of progenitors before and after 2 weeks of medroxyprogesterone acetate (MPA) treatment".

Our conclusions were, on the contrary, based on the comparison of the behaviour of bone marrow activity in each subject, evaluated by counting the colony forming unit granulocyte–macrophage (CFU-GM) before and after a cycle of chemotherapy (CT), in patients treated with MPA (arm B) and in those not treated with MPA (arm A).

Pedrazzoli's main criticism is based on the observation that "before chemotherapy the number of progenitors was significantly lower in MPA-treated patients and it was very close in the two groups −101.3 (6.0–187.2) vs. 95.0 (36.7–178.5) — on day 14". We cannot accept this criticism for the following reasons:

(a) The two randomised groups are comparable in terms of absolute number of CFU-GM before each treatment (day 0 in cases not treated with MPA and day −14 in those treated with MPA). The number of progenitors in the two groups was not, in fact, statistically different at that time

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