PART XXI

POSTERS ON NEPHROLOGY
PERIPHERAL HAEMATOCRIT MODULATES ERYTHROPOIETIN PRODUCTION AND KINETICS OF RETICULOCYTES IN CHRONIC URAEMIC PATIENTS

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Summary

Determination of reticulocytes (RETI), haematocrit (HCT) and serum erythropoietin (by radioimmunoassay = EP-RIA) before and after transfusions of 500ml red blood cells (RBC) into 15 chronic uraemic patients demonstrated that there was a converse relation between both of these, EP-RIA and RETI, and the HCT. The same conditions were found in cases of spontaneous bleeding. This pattern of reaction of RETI, EP-RIA and HCT suggested a feedback circuit, operative between these three parameters in chronic uraemic patients.

Introduction

Anaemia in patients with chronic renal failure is thought to be in part due to a lack of erythropoietin (EP), since the diseased kidneys are no longer able to supply the required amounts of EP to the bone marrow, which is under the influence of a variety of uraemic toxins. In order to recognise whether or not EP had a regulatory role in these uraemic conditions, we stimulated (by low haematocrit values) and suppressed (by transfusing 500ml of RBC) erythropoietic bone marrow activity (Figure 1).

Materials and methods

Fifteen patients with various kidney diseases, who were kept on a chronic intermittent haemodialysis programme (four hours thrice weekly), took part in the study. Residual diuresis varied between 10 and 700ml/day, (mean 105ml). Clinical pretransfusion parameters were quantified as follows: body weights, mean 61.3 ± 6.8kg; haemoglobin values, mean 4.9 ± 0.7g/dl; serum iron, mean 143.2 ± 86.4µg/dl; serum creatinine, mean 7.8 ± 1.9mg/dl; reticulocyte (RETI) counts, mean 31.9 ± 19.2 expressed as number of reticulocytes per 1000 red cells; EP-RIA, mean 75.7mU/ml of serum. RETI were stained on blood smears with brilliant cresyl blue.
Figure 1. Schematic outline of the haematocrit-erythropoietin feedback control

Figure 2. Relation between haemoglobin concentration in the blood (HGB), reticulocyte count (RC), and radioimmunoassayed erythropoietin (EP-RIA) of 3 representative patients. Increase in HGB effected by transfusions of 500ml red blood cells into each of the patients
Figure 3. Mean values of 15 patients for HGB, reticulocytes and EP-RIA before and after transfusions of 500ml red blood cells.
Serum EP-RIA was measured by a recently published method [1], normal value was 22mU/ml. 500ml packed red blood cells (RBC) were transfused into each of the patients.

Results

Figure 2 shows three representative examples of HGB, RC and EP-RIA curves after transfusions of 500ml RBC into each of three patients. The transfusions induced a decrease in RC and EP-RIA levels.

Figure 3 shows the mean values for the three parameters HGB, RC and EP-RIA of 15 chronic uraemic patients after 500ml RBC transfusions into each of them: on days two to three, the HGB was raised to 164 per cent, the EP-RIA was suppressed to 45 per cent, and the RC was suppressed to 39 per cent of the pre-transfusion levels, respectively.

Figure 4 shows the values in cases of spontaneous bleeding.

Figure 4. Two representative examples of spontaneous bleeding episodes in previously trans-fused (T) patients. Note the inverse relation between HGB on the one hand and the reticulocytes and erythropoietin on the other hand after both transfusions and haemorrhages. The short-lasting EP-RIA peaks immediately after the transfusions remain unexplained by present data.
Discussion

One of the commonly acknowledged causes in the pathogenesis of the anaemia of chronic renal failure is a lack of erythropoietin, since an anaemia of 40 or 60 per cent of the normal value should result in an enormous rise in EP activity. Mostly, however, as is the case with normal healthy people, the EP activities in sera of chronic uraemic patients are below the level of detectability of the commonly used posthypoxic polycythaemic mouse bioassay. The advent of the very specific and sensitive radioimmunoassay for erythropoietin [1] made it possible to recognise, in these studies, that both decrease as well as increase in the peripheral HCT were well able to modulate the serum EP levels and the reticulocyte counts. These facts suggested that the normally existing feedback circuit [2, 3] between HCT and erythropoiesis might be operative in chronic renal failure. Hence, a lack of EP does not appear to range amongst the major causes for the usually low HCT values in anaemic uraemic patients.

References

1 Garcia JF, Sherwood J, Goldwasser E. Blood Cells 1979; 5: 405
2 Adamson JW. Blood 1968; 32: 597
3 Alexanian RJ. J Lab Clin Med 1973; 82: 438