Case Report

Decrease in the haemoglobin level in haemodialysis patients undergoing antiandrogen therapy


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Key words: haemodialysis; antiandrogen therapy; leuprolide; haemoglobin

Introduction

There are several known haematopoietic growth factors and cytokines. Among them, erythropoietin is an essential hormone for the regulation of red blood cell production. Clinical evidence suggests that androgens also play a role in erythropoiesis. Men and women exhibit differences in haemoglobin concentration and during puberty, haemoglobin levels increase only in males. Moreover, it has been shown that haemoglobin levels decline after castration or antiandrogen therapy [1–3]. Levels of erythropoietin are similar in both men and women, and therefore it is assumed that testosterone is responsible for the observed differences in haemoglobin levels.

Anaemia in uraemic patients is a consequence of inappropriately low erythropoietin production. Generally, it is most severe in women and children, suggesting that erythropoiesis in end-stage renal failure is also influenced by androgens [4]. A role for androgens in erythropoiesis is supported by the fact that pharmacological doses of androgens have been used to treat anaemia successfully. However, male end-stage renal failure patients frequently have low testosterone levels [5] and it remains to be determined whether testosterone contributes to erythropoiesis in uraemic male patients.

We observed a profound decrease in the haemoglobin levels of three male haemodialysis patients undergoing antiandrogen therapy. This clinical observation supports the notion that even low levels of testosterone may have a positive influence on erythropoiesis in chronic renal failure.

Case reports

Three Caucasian haemodialysis patients were diagnosed with prostatic cancer. The clinical and biochemical data at the time of diagnosis are shown in Table 1. During the 12 months prior to diagnosis, stable haemoglobin levels were maintained with monthly doses of 62.5 mg of elemental iron in the form of sodium ferric gluconate i.v. None of the patients was administered human recombinant erythropoietin.

Prostatic carcinoma was treated with antiandrogen therapy which consisted of a depot preparation of leuprolide acetate (7.5 mg every 4 weeks by i.m. injection) and 250 mg flutamide t.i.d. Androgen blockade was very effective; serum testosterone, luteinizing hormone, and prostate-specific antigen levels decreased in all patients and reached undetectable levels after the 3rd month of antiandrogen treatment.

Figure 1 shows the haemoglobin levels 6 months before, and after the initiation of antiandrogen treatment. Haemoglobin levels were decreased 1 month post-treatment and the three patients required recombinant human erythropoietin therapy to control anaemia at 3, 4 and 5 months respectively post-antiandrogen treatment. The patients remained

| Table 1. Clinical and biochemical data at the time of diagnosis of prostatic carcinoma |
|-----------------------------------------------|-----------------|-----------------|-----------------|
| Aetiology of renal disease                   | Patient 1       | Patient 2       | Patient 3       |
| (Polycystic disease)                         | (Polycystic disease) | (Polycystic disease) | (Interstitial nephropathy) |
| Months on haemodialysis                      | 24              | 29              | 130             |
| Age                                           | 48              | 69              | 79              |
| Prostate-specific antigen (ng/ml) (normal <4) | 16              | 24              | 31              |
| Testosterone (ng/ml) (normal range 3–11)     | 1.5             | 2.8             | 2.1             |
| Prostatic carcinoma staging                  | D1              | C1              | C2              |

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The combination of these two substances results in total androgen blockade [7]. We observed a sharp decline in the haemoglobin levels of the three male haemodialysis patients with prostatic carcinoma who were treated with these two drugs. A mild, but statistically significant decrease in haemoglobin was also observed in male patients with normal renal function treated with a similar androgen blockade regimen [3].

Before antiandrogen therapy, the haemoglobin levels of all three patients with hypogonadism were maintained with intravenous iron supplementation. One month following testosterone blockade, there was a profound decline in haemoglobin concentration not associated with changes in erythropoietin levels. This fall in haemoglobin concentrations cannot be attributed to malignancy since it coincided with the initiation of antiandrogen therapy and did not improve with the decrease in prostatic specific antigen concentration.

Our data suggest that the low testosterone levels in these patients were necessary to maintain haemoglobin concentrations through a mechanism independent of the erythropoietin level. Therefore, testosterone appears to be involved in the regulation of erythropoiesis in male patients with chronic renal failure. The mechanism of action of androgenic steroids may be an increase in the sensitivity of erythroid progenitors to erythropoietin.

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References


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Discussion

The influence of testosterone on erythropoiesis in humans with normal renal function may account for the differences in haemoglobin concentrations observed between healthy women and men and explain the decline in haemoglobin levels seen after androgen blockade. Chronic renal failure patients commonly suffer from anaemia secondary to erythropoietin deficit. The possible effects of other growth factors such as androgen steroids on erythropoiesis in end-stage renal failure have not been extensively studied. Many male patients with end-stage renal disease have hypogonadism and low levels of testosterone and it is unclear how this affects the regulation of erythropoiesis. However, it has been shown that exogenous androgens potentiate the effects of recombinant erythropoietin in uraemic patients [6].

Leuprolide is an analogue of luteinizing hormone-releasing factor and flutamide is a synthetic antiandrogen drug competing with androgens at the receptor level. The combination of these two substances results in total androgen blockade [7]. We observed a sharp decline in the haemoglobin levels of the three male haemodialysis patients with prostatic carcinoma who were treated with these two drugs. A mild, but statistically significant decrease in haemoglobin was also observed in male patients with normal renal function treated with a similar androgen blockade regimen [3].

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