Effects of Megestrol acetate on adrenal function and survival in cancer patients

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Objectives:

Megestrol acetate (MA) has been used in various cancers as a palliative agent to treat cancer cachexia. It has glucocorticoid activity and can induce significant secondary adrenal suppression. Weakness, fatigue, hypotension and vomiting which are common in patients with adrenal insufficiency are also common in patients with metastatic cancer. Furthermore, patients receiving MA who develop asymptomatic adrenal insufficiency might have inadequate adrenal function if they become acutely ill. We designed this study to determine the extent of adrenal insufficiency in cancer patients receiving MA and find out if any predictive factor for this.

Methods:

Thirty-one patients (11 females and 20 males, aged 48–83 years) who were receiving MA took part in this study. One of the patients was receiving MA for 48 months , one of them was receiving it for 12 months. The others were not taking MA and evaluated for HPA axis; before the initiation and 1 month later. Patients who had been treated with oral corticosteroids during the 6 months preceding the study were excluded.They were evaluated at the Pamukkale University oncology and endocrinology outpatient clinic.

Serum concentrations of thyroid stimulating hormone (TSH), ACTH, free T4, cortisol were measuresd in samples obtained at 7 AM , at baseline and 1st month. Standart ACTH (250 mg) stimulation test was performed if cortisol levels were below 18 µg/dl at any time. After cosynotropin injection blood samples were obtained at 30 and 60 min for the measurement of serum cortisol concentrations.

Results:

17 of patients were died during follow up. Mean survival time was 14±2.3 months and mean follow up time was 22.16±22.1 months .

1 month after drug initiation, in 10 of 31patients (32%) basal serum cortisol levels were below 3 µg/dl and so they were accepted as adrenal insufficient. In 10 of them basal serum cortisol levels were above 18 µg/dl and so they were accepted as adrenal sufficient. In11 of them basal serum cortisol levels were between 3- 18 µg/dl and ACTH stimulation was performed. Peak serum cortisol levels following stimulation with ACTH were above 18 µg/dl for all of them.

There wasn't any correlation between the basal cortisol, ACTH levels and overall survival. There wasn't any correlation between any biochemical parameter and survival time, either. There was negative correlation between 1 month cortisol levels and survival time (p= 0,04). If cortisol levels were lower at first month of theraphy, survival was longer. Cox regression analysis showed that patients having lower cortisol levels at first month had 98% lower risk of death compared to patients having higher cortisol level (p= 0,02: OR 0,12 (0,02-0,75)). Patients in group 2 had lower cortisol levels at first month.

Conclusions:

It is important to be aware of the effects of MA on adrenal functions and evaluate adrenal functions especially during episodes of infection or after withdrawal of MA therapy since this may require prompt corticosteroid treatment.

References:

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