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Short report

Low dose megestrol acetate can abrogate cachexia in advanced tumor patients receiving systemic interferon-α and/or interleukin-2 based antineoplastic therapy

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The progression of advanced malignancies is often associated with anorexia and cachexia, especially when patients receive concomitant systemic antitumor treatment. Megestrol acetate has been reported to increase appetite and body weight, and a linear dose–response relation for doses from 160 up to 1600 mg/day has been proposed. In our study, we were able to show that megestrol acetate at doses as low as 60 mg/day was sufficient to abrogate anorexia and weight loss. In contrast to previous studies, this effect was achieved while patients continued systemic antineoplastic therapy.

Key words: Advanced malignancy, cachexia, interferon-α, interleukin-2, megestrol acetate.

Introduction

Anorexia and weight loss are common problems in advanced stage cancer patients. The precise reason for tumor associated weight loss is still unknown. The use of recombinant human cytokines such as interleukin (IL)-2 and interferon (IFN)-α in antineoplastic therapy can also cause anorexia.[1,2] Cachexia is usually associated with a poor prognosis and with deleterious effects on the patients immune system; it may also diminish quality of life for the patient.[3–5]

Several agents have been investigated to prevent further weight loss and to increase weight in these patients, such as dexamethasone and cyproheptadine. Intravenous hyperalimentation has also been employed. Megestrol acetate has been reported to abrogate anorexia and to increase body weight—most of these studies were performed in patients who were given 160–1600 mg/day of megestrol acetate and received no further antitumor treatment.[6,7]

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In this study, we report the effect of 4 weeks of 60 mg/day of megestrol acetate on the body weight of cancer patients with continuing systemic antineoplastic therapy.

Patients and methods

Fifteen patients with advanced metastatic cancer were enrolled in this study. Antineoplastic therapy consisted of subcutaneous recombinant IFN-α2b alone or in combination with IL-2 as previously described;[1] some patients received additional chemotherapy. Patient characteristics are given in Table 1.

Inclusion criteria were: (i) a decrease in body weight of at least 5% during the 4 weeks preceding initiation of megestrol treatment and (ii) continuing systemic antineoplastic therapy. Exclusion criteria were an estimated life-expectancy of less than 3 months or concomitant corticosteroid treatment.

All patients received 60 mg of oral megestrol acetate per day (30 mg in the morning, 15 mg at noon and night). Patients were carefully monitored for side effects and weight changes were recorded after 4 weeks at the end of study. Patients whose body weight was stabilized continued megestrol acetate without further evaluation.

Patient body weight at 4 weeks prior to study entry, at the time of study entry and after 4 weeks of megestrol acetate treatment was compared for statistical analysis using the Wilcoxon matched pairs test.

Results

Of 15 patients (seven female and eight male) enrolled in the study, 10 were evaluable; two patients

Table 1. Patient characteristics[a]

No.	Sex	Disease	Tumor site	Therapy
1	f	CRC	lung, liver	IFN, IL-2
2	m	RCC	lymph nodes	IFN, 5-FU
3	m	RCC	lung, lymph nodes	IFN, IL-2
4	m	RCC	lymph nodes, lymphangiosis carcinomatosa	IFN, 5-FU
5	m	RCC	lung, liver, lymph nodes	IFN, IL-2
6	m	CRC	liver	IFN, IL-2
7	f	MM	lung	IFN, IL-2, DTIC, CBDCA
8	f	RCC	lung, local relapse, lymph nodes	IFN
9	m	CRC	lung, liver, local relapse	IFN, IL-2
10	f	RCC	lymph nodes	IFN, 5-FU
11	f	MM	lung, liver	IFN, IL-2, DTIC, CBDCA
12	m	RCC	lymph nodes	IFN, IL-2
13	f	RCC	lung, liver	IFN
14	f	RCC	lung, liver, local relapse	IFN, 5-FU
15	m	MM	lung, liver, lymph nodes	IFN, IL-2, DTIC, CBDCA

[a] Abbreviations: f, female; m, male; CRC, colorectal cancer; RCC, renal cell cancer; MM, malignant melanoma; IL-2, interleukin-2; IFN, interferon-α; 5-FU, 5-fluorouracil; DTIC, dacarbazine; CBDCA, carboplatin.

were lost to follow up, one patient went off study due to concomitant corticosteroid therapy. Two patients were excluded from evaluation because weight gain occurred during off-therapy intervals.

Mean weight loss during the 4 weeks prior to megestrol treatment was 6.6% of body weight (4 kg) in evaluated patients (range, 5 to 11%).

After 4 weeks of low dose megestrol acetate, body weight was overall stabilized with a slight increase of 0.8% (range, −5 to +9%) in spite of continued systemic antineoplastic treatment (Table 2). Weight gain was nutritional and never due to fluid retention or edema.

Table 2. Weight changes in evaluable patients

No.	Body weight (kg)		
	4 weeks prior to megestrol acetate[a]	at entry into the study	after 4 weeks of megestrol acetate[b]
1	55	52	53
2	69	64	67
3	75	71	72
4	71	67	66
5	69	66	64
6	62	59	56
7	63	59	60
8	63	59	58
9	63	57	62
10	59	56	56

[a] $p < 0.01$ for weight at 4 weeks prior to megestrol acetate versus weight at study entry.
[b] Not significant for weight after 4 weeks of megestrol acetate versus weight at study entry.

Treatment with megestrol acetate was well tolerated. No major adverse effects such as thromboembolic disease, ascites or edema were observed. Evaluation of treatment related nausea and vomiting was difficult because of simultaneous antineoplastic therapy; however, megestrol acetate did not aggravate these side effects when compared with other patients who received antineoplastic therapy alone.

While statistical analysis showed a significant decrease in body weight prior to megestrol treatment ($p < 0.01$), this decrease was stopped by megestrol acetate and no further significant changes in body weight occurred over 4 weeks of concomitant megestrol plus antineoplastic therapy.

Discussion

In this study, we report the effect of low dose megestrol acetate on body weight of cancer patients during antineoplastic therapy. While the precise mechanism of action of megestrol is still unknown,

several reports show an increase in both appetite and weight.

In previous studies a linear dose–response relation has been proposed for doses from 160 up to 1600 mg/day.[8,9] In contrast, our own results suggested that megestrol acetate at doses as low as 60 mg/day can prevent further weight loss in advanced tumor patients receiving systemic antineoplastic therapy.

It should be noted that this effect was attained throughout antitumor treatment, while in previous studies patients receiving megestrol acetate had been taken off antineoplastic regimens.[6,7]

Even greater benefits of our therapy might have been achieved with a longer follow-up period. Thus, Aisner *et al.*[10] described a 4–6 week time lag between initiation of megestrol therapy and therapy related increases in body weight.

The rapid weight gain which we observed during off-therapy intervals suggested that 60 mg of megestrol are sufficient to control and reverse weight loss in cancer patients who receive only symptomatic treatment.

While the optimum dose for megestrol acetate remains to be defined, randomized studies will be needed to establish the potential benefit with regard to patient weight and overall quality of life when employing megestrol acetate at doses of 60 mg/day as used in this study.

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