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Treatment of Anorexia and Weight Loss With Megestrol Acetate in Patients With Cystic Fibrosis

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Summary: Four patients with severe cystic fibrosis lung disease, anorexia and weight loss, received Megestrol Acetate (MA), as an appetite stimulant. The initial dose was 400–800 mg daily and was continued for 6–15 months. Appetite was improved, with significant weight gain in all patients and an increase in their weight for age percentile from <5% at the start of the study to approximately the 25th percentile after 6 months of use and improvement in quality of life. One patient discontinued MA after 6 months, and subsequently appetite and weight were depressed. **Pediatr Pulmonol. 1999; 28:380–382.** © 1999 Wiley-Liss, Inc.

Key words: cystic fibrosis; megestrol acetate; anorexia.

INTRODUCTION

Weight loss is a common problem in patients with advanced cystic fibrosis (CF). 24.4% of patients with CF fell below the fifth percentile of weight for age in 1996.[1] Inadequate weight gain in CF is thought to be due to energy imbalance related to the increased caloric demands of chronic respiratory disease, and possibly an elevated metabolic rate compounded by malabsorption and anorexia.[2] With progression of the pulmonary disease and anorexia, some patients may fail to gain weight despite methods of nutritional support such as enteral hyperalimentation through gastrostomy tube feedings. The suggestion has been made that nutritional intervention is likely to be beneficial when it is begun early in the development of malnutrition.[3]

Megestrol acetate (MA), is a synthetic, orally active derivative of progesterone, which is widely used to treat advanced breast cancer. A side effect of MA and progesterone derivatives in routine therapy is appetite stimulation and weight gain.[4] The mechanism by which it stimulates the appetite and causes weight gain is mostly unknown. It has been postulated that the effect is partly mediated by neuropeptide Y, a potent central appetite stimulant.[5] In animal models MA stimulates neuropeptide Y synthesis, transport and release and this may contribute to its appetite-stimulating effect.[6] Several studies were conducted to evaluate the therapeutic use of MA in adults with HIV infection and those with cancer.[7–10] As a result, MA was determined to enhance appetite, resulting in increased body weight. MA was also evaluated in children and adolescents with advanced HIV infection and severe anorexia and was found to be beneficial.[11]

We present four patients with advanced pulmonary disease, weight loss and severe anorexia. MA was initiated in these patients to stimulate their appetite. This appears to be an innovative way of treating these terminally ill patients to improve their nutritional status and decrease their pulmonary symptoms.

CASE REPORTS

Four children and adolescents with CF (3 females and 1 male) ages 10–18.5 years, received MA in an effort to stimulate their appetite and improve weight gain. These 4 patients were among the most seriously ill in our center population. Patients #1, #3 and #4 were prepubertal. Table 1 summarizes patient characteristics. All patients had severe lung disease. Three of the four patients had gastrostomy tubes (GI) placed 1–5 years prior to receiving MA, at a mean age of 13 ± 4.6 years (SD), with a range of 7.7–16 years. The fourth patient refused GT placement. Initial weight gain was noted with the GT placement and nocturnal calorie supplement. MA was started at a daily dose of 400–800 mg orally. Weight for age was less than fifth percentile for all patients at the

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TABLE 1—Patient Characteristics at Onset of Treatment With Magestrol Acetate

Patient no.	Gender (M/F)	Age (yr)	Height (cm)	Height % tile	Weight (kg)	Weight % tile	FEV_1[a] (% predicted)	CXR score[b]	Clinical score[c]
1	F	16.6	151.4	<5	43.4	<5	18	12	40
2	M	18.5	180.0	70	49.0	<5	44	15	50
3	F	13.0	142.0	<5	25.6	<5	17	14	45
4	F	10.0	121.0	<5	21.0	<5	22	12	40
Mean		14.4	150.7		34.8		25.3	13.3	43.8
SD		3.6	21.5		13.5		12.7	1.5	4.8

[a]FEV_1, Forced experatory volume at 1 second.
[b]CXR score, Brasefield CXR score for CF[12].
[c]Clinical score, Shwachman score[13].
SD, Standard Deviation.

start of MA. Three of the four patients continued MA for 6 months; it was discontinued in patient #1 following a double lung transplant, patient #2 discontinued MA due to noncompliance, and patient #3 has been on MA for 15 months, patient #4 has been on MA for 6 months.

RESULTS

All 4 patients were noted to have an increase in appetite and oral intake within days of starting MA; all patients experienced weight gain. Prior to starting MA, the first patient was receiving approximately 2,400 kcal/day mainly from enteral feeding [five cans of two cal HN]. She could not reach her daily caloric needs of 2500–2800 kcal/day secondary to anorexia. Following the start of MA, her intake increased to 4–5 meals/day plus enteral feeding and weight gain was noted.

The second patient's calorie intake/day was 2,250 kcal from enteral feeding of 4 cans of 2 Cal/min HN formula plus polycose; his oral intake was negligible. Following the start of MA his appetite had improved. He continued to receive enteral feeds, this exceeded his daily requirement of 3,300–3,500 kcal.

The third patient was receiving 1920–2400 kcal/day, mainly through enteral feeding of 4–5 cans of 2 Cal/min HN. Even though her estimated calorie needs were 2100–2300 kcal/day, she continued to lose weight. Her appetite improved after MA was started. She continued enteral feeding along with 3 meals and 5 snacks/day.

The fourth patient's calorie intake was 990 kcal/day prior to starting MA. She did not have a gastrostomy tube. Her daily requirement was 2,200–2,400 kcal. Following the initiation of MA her calorie intake increased to exceed her daily requirement. Two months following MA initiation, she was receiving 2400–2600 kcal/day.

ABBREVIATIONS

CF	Cystic fibrosis
FEV_1	Forced expired volume in 1 sec
HN	High nutrition
MA	Megestrol acetate

Table 2 summarizes the weight gain over 6 months of therapy. All patients were less than the fifth percentile weight for age at the time of starting MA. Six months later they were at approximately the 25th percentile weight for age (patient #1 = 25–50%, patient #2 and #3 = 10–25%, and patient #4 = 25% weight for age). Patient 3 who has been on MA for 15 months, has continued to maintain 10–25% weight for age.

By self report, the well being and quality of life of the patients improved with the use of MA with decreased frequency of coughing, decreased sputum production and increased energy level. Moreover, there were decreases in the number of pulmonary exacerbations, antibiotic use and the number of hospitalizations during the study period. Pulmonary function testing, chest radiograph scoring[12] and clinical scoring[13] remained stable with no further deterioration. Serum glucose level and glycosylated hemoglobin were stable with no increase during the study period.

DISCUSSION

Anorexia and weight loss in advanced CF disease are due to bronchiectasis, chronic infection and advanced lung disease. Severe lung disease results in respiratory failure and accounts for over 90 percent of fatalities.[14] Chronic bacterial endobronchitis is associated with an intense inflammatory response which damages the airway and impairs local host-defense mechanisms, resulting in progressive lung damage and respiratory failure.[15] Weight loss can have significant impact on the physical and psychological well being of CF patients and can lead to increased mortality. Dietary intervention through high calorie diet and supplemental gastrostomy tube feedings have been widely used in CF patients. However, it is our observation that with advanced lung disease, some patients become anorexic and increasing supplemental tube feedings do not compensate for the increased calorie requirement.

Appetite stimulation can improve the chance that anorexic CF patients will increase oral intake to meet their

TABLE 2—Summary of Results of Therapy

Patient No.	Before treatment			2 months			6 months		
	Weight (kg)	Height (cm)	FEV_1 (% predicted)	Weight (kg)	Height (cm)	FEV_1 (% predicted)	Weight (kg)	Height (cm)	FEV_1 (% predicted)
1	43.4	151.4	18	48.4	155.0	20	52.2	159.0	17
2	49.0	180.0	44	56.9	180.0	41	59.5	180.0	37
3	25.6	142.0	17	31.5	146.0	17	38.9	149.0	25
4	21.0	121.0	22	27.2	123.0	32	29.8	125.0	32
Mean	34.8	148.6	25.3	41.0	151.0	27.5	45.1	153.3	27.8
SD	13.5	24.4	12.7	14.0	23.6	11.1	13.3	22.8	8.7

nutritional requirements. MA has been shown to stimulate appetite in HIV and cancer patients.[5–11] We, therefore, initiated MA in four patients once they had exhibited acute weight loss (patients #1, #2, and #3) or prolonged poor weight gain (patient #4 who refused gastrostomy tube placement). The general well being for these patients improved significantly and the respiratory symptoms (cough, shortness of breath and sputum production) decreased with the use of MA, which in turn, lead to weight gain in all patients. MA was well tolerated by all patients. Side effects reported with MA include hypertension, hyperglycemia, carpal tunnel syndrome, alopecia, edema, depression and clinical adrenal insufficiency (fatigue and hypotension).[16] None of these side effects were noted in our patients. However, the number of subjects in this report is clearly insufficient to draw conclusions about the likelihood of adverse effects, or the potential consequences of long term use. To our knowledge, this is the first report of the use of MA in CF patients for treatment of anorexia and weight loss.

Based on our initial experience, we believe a carefully designed randomized trial is warranted to establish the benefits and potential side effects of MA in patients with advanced CF disease and compromised nutritional status.

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