Use of Orexigenic Medications in Geriatric Patients

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ABSTRACT

Background: The loss of appetite, anorexia, is commonly observed in older persons and associated with adverse outcomes. It is becoming increasingly apparent that anorexia is the chief factor in producing weight loss in older adults. Although common and expected in acute illness, anorexia is also frequently associated with chronic diseases and leads to inadequate nutrient intake.

Objective: The aim of this paper was to review clinical studies on the use of orexigenic drugs to stimulate appetite.

Methods: Clinical trials were identified related to improving appetite and/or weight gain in older persons. Articles were identified by Ovid search using terms nutrition, anorexia, cachexia, weight loss, orexigenic drugs, and by searching references from retrieved papers.

Results: Environmental and nutritional interventions to improve intake should be the first intervention. When these fail to produce adequate intake, orexigenic drugs should be considered. No drug has received approval from the US Food and Drug Administration for geriatric anorexia.

Conclusions: In the presence of adequate food, weight loss most often is due to cytokine-associated cachexia and anorexia. Assessment of changes in appetite is essential to evaluating older persons with weight loss. When anorexia is identified, a search for reversible causes should be instituted. Intervention should first be aimed at the provision of adequate calories and protein, often in the form of high-density nutritional supplements. Failure to respond to adequate nutrition or supplements should trigger a concern for cachexia. Orexigenic drugs have been reported to improve appetite and produce weight gain. The mechanism is unknown, but it may relate to suppression of proinflammatory cytokines. (*Am J Geriatr Pharmacother*. 2011;9:97–108)

Key words: anorexia, cachexia, malnutrition, orexigenic drugs, weight loss.

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INTRODUCTION

The loss of appetite, anorexia, is commonly observed in older persons and is associated with adverse outcomes. Appetite is associated with seeking food for the enjoyment of food itself, rather than for physiological need, and is conditioned by sensory perception, visual stimuli, and both social and cultural factors. Anorexia is distinct from hunger, which is the physiological drive to find food. Hunger often results in aggressive food-seeking and in ingestion of nutrients which would otherwise be revolting. Remarkably, hunger seems to be suppressed in acute illness and in end-stage starvation even in the face of availability of food and weight loss.[1]

Involuntary weight loss in older persons may result from several conditions, including inadequate availability of protein/calories (starvation), decrease in appetite leading to inadequate ingestion of protein/calories (anorexia), disuse atrophy or hormonal deficiencies (sarcopenia), the effects of disease (cachexia), or a combination of these factors. The hallmark of starvation is a positive response to provision of nutrients, except in the very late stages when the drive to find food lessens.[2]

It is becoming increasingly apparent that anorexia is the chief factor in producing weight loss in older adults. During an acute illness, a voluntary suppression of food intake is common to most species,[3] although this response seems paradoxical in the face of a need for increased nutrients during healing.[1] Clinicians routinely observe that a return of appetite and the ingestion of food is a sign of patient recovery. Although common and expected in acute illness, anorexia is also frequently associated with chronic diseases and leads to inadequate nutrient intake.

This anorexia/cachexia syndrome was first described in cancer patients. Up to 65% of patients with cancer report anorexia with or without weight loss, which is independent of active cancer treatment.[4] Cardiac cachexia occurs in 10% to 15% of patients with New York Heart Association Class II–III heart failure. The 18-month mortality rate in patients with cardiac cachexia approaches 50% and is 17% in patients with heart failure without cachexia (P for trend < 0.001).[5] Anorexia and protein-energy wasting ranges from 18% to 75% of patients with chronic kidney disease undergoing maintenance dialysis therapy.[6] Other chronic illnesses have been associated with the anorexia/cachexia syndrome, which includes chronic pulmonary disease, end-stage dementia, rheumatoid arthritis, liver disease, non-dialysis chronic kidney disease, chronic infections, and AIDS.[2] Anorexia may also occur as a component of normal aging and is frequently observed in community-dwelling adults.[7] By direct observation, older persons consume less food than younger persons. On average, persons aged >70 years consume one-third less calories than younger persons. Energy intake of men 40 to 74 years old ranges from 2100 to 2300 calories/d compared with 2700 calories per day in men 24 to 34 years old.[8]

A population-based cross-sectional study of persons >70 years old found a 30% prevalence of self-reported anorexia (37% in women and 18% in men). Loss of appetite was related to higher risk of undernutrition (41% in anorexic vs 27% in non-anorexic persons), lower muscular strength and poorer functional capacity.[9] In persons admitted to a geriatric acute care or rehabilitation ward, the prevalence of anorexia was 33% in women and 27% in men.[10]

Cachexia is a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat mass. The prominent clinical feature of cachexia is weight loss in adults. Anorexia, inflammation, insulin resistance, and increased muscle protein breakdown produce a wasting syndrome. Cachexia is distinct from starvation, age-related loss of muscle mass, primary depression, malabsorption, and hyperthyroidism and is associated with increased morbidity.[11]

Physiological Regulation of Appetite

Appetite is carefully regulated by a combination of a central feeding drive and a peripheral satiation system. The interplay of these two systems is modulated by a hormonal feedback system that determines the nutrient status of the organism.

Centrally, the arcuate nucleus releases neuropeptide Y, the most common and potent appetite stimulator, and another hunger mediator, an agouti-related peptide. These mediators inhibit the ventromedial hypothalamus, a "satiety center." Stimulation of the lateral hypothalamic area produces a "hunger" effect, mediated by alpha-melanocortin precursors released in the arcuate nucleus. Cocaine-amphetamine–related peptide and melanocortin stimulating hormone are inhibited by neuropeptide Y.

Peripheral mediators (such as leptin, produced by the adipose tissue, and insulin, from the pancreas) inhibit neuropeptide Y and agouti-related peptide expression and stimulate pro-opiomelacortin expression, resulting in satiety. Gut hormones produced in response to meals by the upper and lower intestine, including cholecystokinin and peptide YY, produce a short-term signal of satiety by inhibition of neuropeptide Y and agouti-related peptide. Ghrelin, the only peripheral hormone known to stimulate appetite, is produced by the stomach during fasting and stimulates hunger and eating through