Anorexia Evaluation Table 2023: Ghrelin

Systematic Review

Citation	Design/Method Sample/Setting	Variables and Intervention	Outcome Measures	Results/Analysis	Limitations	Quality and Nursing Implications
Khatib, M.N., Shankar, A.H., Kirubakaran, R., Gaidhane, A., Gaidhane, S., Simkhada, P., & Quazi Syed, Z. (2018). Ghrelin for the management of cachexia associated with cancer. *The Cochrane Database of Systematic Reviews, 2*(2), CD012229. https://doi.org/10.1002/14651858.CD012229.pub2	**Design:** Systematic review of randomized controlled trials (RCTs) **Method** Database search of Cochrane, Medline®, Embase®, and various clinical trials platforms was conducted, as well as citation searching. Dual screening and review were performed. **Sample:** 3 RCTs (2 crossover and 1 parallel design) of participants with cancer experiencing weight loss and anorexia were included. Initial total sample consisted of 59 patients (37 men, 22 women) with age range of 54–78 years. **Setting**: Sweden, Switzerland, United Kingdom	**Independent Variable(s):** Ghrelin **Dependent Variable(s):** Primary: food intake, body weight changes from baseline, adverse events Secondary: survival, body composition including lean body and fat mass, plasma ghrelin levels, quality of life (QOL) **Interventions**: Use of ghrelin versus placebo or use of ghrelin at low doses compared with high doses. Route of administration, dosage, and frequency varied between studies.	Food intake: food diary Body weight: Not measured in any studies Body composition Adverse events (AEs) Plasma ghrelin levels QOL: Hospital Anxiety Depression Scale (HADS)	47 of 59 enrolled patients completed the study treatment. 1 study (n = 7) had 31% increase in food intake after ghrelin was administered intravenously (mean intake = 9,270 kJ, 95% CI [3,249, 15,290] compared to placebo (mean intake = 6,854 kJ, 95% CI [3,634, 10,070]) (p = 0.09). Food intake was greater in higher-dose ghrelin (n = 11) participants as compared to lower-dose ghrelin (n = 9) participants compared with baseline in one study with daily monitoring and did not differ in another (high dose n = 12 versus low dose n = 10). Lean body mass measured by one study reported greater lean body mass improvement over time with higher-dose compared to lower-dose ghrelin. Mean whole body fat loss was less in the high-dose (–1.3 kg, SD = 0.7) versus the low-dose (–3.7 kg, SD = 0.8) group (p < 0.04). In the study that measured QOL using the HADS, baseline differences were noted on the anxiety and mental health components between the high- and low-dose ghrelin groups. Health-related QOL did not change over time for either group, The higher-dose ghrelin group reported less anxiety and scored better for mental health on the HADS compared to the lower-dose ghrelin group. Plasma ghrelin level measurement had missing data; authors noted that plasma ghrelin was higher compared to placebo after infusion in a small study (n = 7). In another study, plasma ghrelin levels increased after 8 weeks in the high- and low-dose groups. No AEs were reported in the use of higher- versus lower-dose ghrelin in 1 study. 1 study reported 17 AEs in 11 participants in the higher-dose ghrelin group, including increased bowel activity, abdominal pain, dry mouth, neuropathy worsening, asthenia, diarrhea, and nausea, compared to 7 AEs in 9 participants in the lower-dose ghrelin group, including increased bowel activity, shortness of breath, sweating, and vomiting.	All three studies had attrition greater than 10%. Small sample size in all three studies Evidence was rated as very low quality and insufficient to draw conclusions on effectiveness and safety of ghrelin as an intervention for people with cancer who experienced anorexia or cachexia.	Authors noted insufficient evidence to perform meta-analysis. Narrative summary was included and comprehensive. Conclusions are difficult to draw because of lack of evidence on efficacy and high risk of bias. Findings in this review can be used to guide additional research into the efficacy of ghrelin for treatment of cancer- or cancer treatment–related anorexia/cachexia. Quality and amount of evidence indicate treatment recommendations that include ghrelin are based on clinical expertise. AE findings were inconclusive.

Clinical Practice Guidelines

Citation	Design/Method Sample/Setting	Variables and Intervention	Outcome Measures	Results/Analysis	Limitations Quality and Nursing Implications
Arends, J., Strasser, F., Gonella, S., Solheim, T.S., Madeddu, C., Ravasco, P., . . . Ripamonti, C.I. (2021). Cancer cachexia in adult patients: ESMO Clinical Practice Guidelines☆. *ESM O Open, 6*(3), 100092. https://doi.org/10.1016/j.esmoop.2021.100092	To provide answers to questions regarding the diagnosis and treatment of cachexia-related physical and psychological problems, relying on evidence-based information whenever possible.	Adult patients with cancer cachexia	1. Regular nutritional screening and nutritional support is recommended based on expected survival (weighing burden to patient). Screen and assess nutritional metabolic status and risk. Rescreen for those not at risk every 3 months. 2. Anorexia/cachexia interventions include: • Ensuring adequate intake for energy, protein requirements, and muscle training; • Using pharmacological agents to increase appetite; and • Engaging in psychosocial interactions to alleviate distress. 3. Pharmacologic interventions include: • Corticosteroids and progestins may improve appetite for brief periods of time and must be weighed against potential risk. • There is moderate evidence for olanzapine use. • Cannabinoids showed no significant effect on appetite or QOL, and safety data is lacking. • There is insufficient evidence to support use of NSAIDs. • Ghrelin receptor agonist anamorelin is approved in Japan but showed only modest effects in the ROMANO study in Europe and is not currently recommended. 4. Cachexia care should be delivered using a combination of nutrition; physical activity; psychological, oncologic, and palliative/supportive/rehabilitative care; and oncologist competencies. 5. Comprehensive assessment and patient-centered approach to care includes consideration of cost effectiveness, availability, multitargeted and multimodality treatment options.	1. Level and strength of evidence not reported for each article. 2. Search strategy not defined. 3. Adults only 4. Overall aim of the guideline was cachexia, therefore limited focus was given to anorexia.	Search strategy per European Society for Medical Oncology standard operating procedures for clinical practice guidelines. Findings and recommendations are feasible and relevant for cancer-related anorexia. Strong evidence is provided with numerous recommendations for cachexia, of which anorexia is one subjective component. Care must be multimodal, interprofessional, and patient- and family-centered. Pharmacologic interventions such as corticosteroids and progestins may improve appetite for brief periods of time and must be weighed against potential risk. There is moderate evidence for olanzapine use. Nursing education regarding the management of patients considering pharmacologic interventions is necessary and should include financial review.