

A phase II dose titration study of thalidomide for cancer-associated anorexia

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Abstract:

Context. Sixty-five percent of people with advanced cancer suffer from loss of appetite. Several inflammatory cytokines appear to cause appetite loss in animal models. Thalidomide is an immunomodulatory drug that has been associated with improved appetite in those with HIV infections and cancer.

Objective. We completed a two-stage Phase II dose titration study of thalidomide, the primary purpose of which was to assess appetite response to thalidomide in cancer-associated anorexia.

Methods. Individuals older than 18 years of age with **active cancer**, loss of appetite by numerical rating scale (NRS), life expectancy of at least four weeks, and Eastern Cooperative Oncology Group performance status of 0-3 were entered into the study. Pretreatment screening included medical history, neurologic examination, and symptoms by NRS and categorical scale (CAT). Patients received **50 mg of thalidomide** by mouth at bedtime for **two weeks**. Individuals who did not respond were **dose escalated to 100 mg** at night for two weeks. **Assessment of appetite, early satiety, fatigue, insomnia, night sweats, pain, and quality of life (QOL)** occurred at two-week intervals. Toxicity also was assessed. The primary outcome was appetite response defined as a two-point reduction in the NRS or a one-point improvement in the CAT.

Results. Thirty-five patients entered the study; 33 completed 14 days of therapy and were analyzed for efficacy and toxicity. **Sixty-four percent who completed at least two weeks of thalidomide had improved appetite.** The CAT scores for appetite, insomnia, and QOL improved significantly. The 95% confidence intervals did not overlap. Five participants dropped out because of toxicity: two before two weeks and three later.

Conclusions. **Thalidomide reduced multiple symptoms commonly associated with cancer-related anorexia** and improved QOL. Our findings confirmed and validated a previously published single arm trial. A recent randomized trial demonstrated greater benefits when thalidomide is used combined with other agents to treat cancer-associated anorexia and cachexia. Thalidomide helped cancer-associated anorexia in most patients. It also improved insomnia and QOL in advanced cancer.

Strengths:

- Despite years of evidence suggesting a possible benefit of thalidomide for anorexia, this is one of the only studies looking at its potential uses in palliative care

- Study population generally reflective of palliative patient population
- Use of multiple outcome measures
- Very thorough follow-up during the study for possible side effects
- Rigorous protocol to ensure patient safety

Weaknesses:

- Single arm study with no control group, therefore it is impossible to ascertain whether positive changes on thalidomide were from the drug itself or merely a placebo effect
- The study is not powered to make conclusions about any of the secondary outcome measures
- The 2 patients that dropped out of the study before 2 weeks were not included in the analysis
- The study excludes patients receiving concurrent radiation or chemotherapy

Relevance to palliative care:

Cancer-related anorexia is a common and often distressing symptom in the palliative population. Limited research with thalidomide suggests a possible benefit for appetite and perhaps even insomnia and quality of life. While this study is promising, further research including randomized control trials are needed to explore the benefits and risks of treatment.