

Dexamethasone for Treatment of Cancer-Related Fatigue

BACKGROUND:

- Cancer-related fatigue (CRF) is a common issue in advanced cancer patients, yet little research has been conducted in this area. In a recent survey, 23-33% of oncologists indicated that they frequently utilize steroids to treat CRF.
- No double-blinded, randomized, placebo-controlled studies of the efficacy of steroids for CRF have been performed.

OBJECTIVE:

- The primary purpose of this study was to compare the effects of dexamethasone and placebo on CRF using a validated tool.
- Secondary objectives were to determine the effects of dexamethasone on anorexia, anxiety, depression, and symptoms-distress scores.

METHODS:

- *Design:* randomized, double-blind, parallel, controlled experimental
- *Duration:* 14 days
- *Inclusion criteria:* diagnosis of advanced cancer; ≥ 3 symptoms during the previous 24 hours with average intensity of ≥ 4 on the ESAS; normal cognition, no infections, hemoglobin ≥ 9 within 1 week of enrollment, life expectancy ≥ 4 weeks, no history of AIDS, ANC ≥ 750 within 1 week of enrollment, and no diabetes or surgery within 2 weeks of enrollment
- *Enrolled:* 132 patients; 65 (placebo) and 67 (dexamethasone)
- *Drug regimens/dosages:* dexamethasone 4 mg or placebo orally twice daily
- *Outcome measures:* The primary endpoint was the change in FACIT-F fatigue subscale score from baseline to day 15. The authors also examined differences in scores between treatment groups at baseline and on days 8 and 15 for the FAACT subscale, HADS, and ESAS individual symptoms as well as ESAS physical distress, psychological distress, and symptom distress scores; difference in adverse event frequency between groups was analyzed.
- *Power:* 80% assuming 50 evaluable patients per treatment group; alpha 0.05; effect size 7 points
- *Data-handling:* per-protocol

RESULTS:

- 84 patients completed the study: 43 (dexamethasone) and 41 (placebo)
- There was a statistically significant improvement in the primary endpoint (FACIT-F fatigue subscale) in the dexamethasone group compared to the placebo group at days 15 (mean difference=5.9 points; $p=.008$) and 8 (mean difference=4.95 points; $p=.005$). This improvement continued to be statistically significant at days 15 and 8 after controlling for sex using a generalized linear model.
- The following were also statistically improved with dexamethasone compared to placebo: FACIT-F total quality of life score at day 15 ($p=.03$), FACIT physical well-being score at days 8 and 15 ($p=.007$; $p=.002$), ESAS physical distress score at days 8 and 15 ($p=.009$; $p=.013$), FAACT score at day 15 ($p=.013$), and ESAS pain score at day 8 ($p=.014$). There were no significant differences in the improvement of ESAS individual symptoms, psychological distress, HADS anxiety, or HADS depression scores.
- The authors concluded that dexamethasone was more effective than placebo in reducing CRF in patients with advanced cancer. They also determined that there was significant improvement in physical well-being, physical distress, and quality of life.

STRENGTHS:

- No conflicts of interest
- Gold-standard study design
- Validated instruments used for measured outcomes
- Appropriate statistical tests utilized (t-test and Chi square)

LIMITATIONS:

- Potential differences existed between the treatment groups (other medications, environmental factors)
- Inclusion criteria of advanced disease was not defined
- Compliance was not assessed
- Patients were not stratified by type/severity of cancer (stage/grade), which might affect therapy response
- Unknown when/how adverse effects were assessed
- Severity and type of adverse effects were not statistically analyzed
- Power was not sufficient for multiple secondary endpoints
- Study duration was too short to observe long-term adverse effects
- Confidence intervals were not reported

CONCLUSIONS:

- Dexamethasone showed promising results for treatment of CRF in advanced cancer patients with ≥ 3 symptoms of ≥ 4 severity on the ESAS scale (among other inclusion criteria).
- There is currently no standard treatment for CRF. Dexamethasone is inexpensive and appears to be an effective therapeutic option.
- Further research is needed. Larger, long-term studies are necessary to establish the safety and efficacy of dexamethasone for treating CRF associated with specific type of cancers.

Yennurajalingam S, Frisbee-Hume S, Palmer JL, et al. Reduction of Cancer-Related Fatigue With Dexamethasone: A Double-Blind, Randomized, Placebo-Controlled Trial in Patients With Advanced Cancer. *J Clin Oncol*; 31(25):3076-3082.

Sarah Mallow, Doctor of Pharmacy Candidate