**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.


Sarah Mallow, Doctor of Pharmacy Candidate