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Dexamethasone in head and neck cancer patients with microvascular reconstruction: No benefit, more complications

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ABSTRACT

Objectives: Glucocorticoids are widely used in association with major surgery of the head and neck to improve postoperative rehabilitation, shorten intensive care unit and hospital stay, and reduce neck swelling. This study aimed to clarify whether peri- and postoperative use of dexamethasone in reconstructive head and neck cancer surgery is associated with any advantages or disadvantages.
Materials and methods: This prospective double-blind randomized controlled trial comprised 93 patients. A total dose of 60 mg of dexamethasone was administered to 51 patients over three days peri- and postoperatively. The remaining 42 patients served as controls. The main primary outcome variables were neck swelling, length of intensive care unit and hospital stay, duration of intubation or tracheostomy, and delay to start of possible radiotherapy. Complications were also recorded.
Results: No statistical differences emerged between the two groups in any of the main primary outcome variables. However, there were more major complications, especially infections, needing secondary surgery within three weeks of the operation in patients receiving dexamethasone than in control patients (27% vs. 7%, p = 0.012).
Conclusions: The use of dexamethasone in oral cancer patients with microvascular reconstruction did not provide a benefit. More major complications, especially infections, occurred in patients receiving dexamethasone. Our data thus do not support the use of peri- and postoperative dexamethasone in oropharyngeal cancer patients undergoing microvascular reconstruction.

Introduction

Treatment of oropharyngeal carcinoma causes major morbidity. Treatment modalities include surgery, radiation, and chemotherapy. In surgery, microvascular tissue reconstruction has become the definitive method to cover large defects after tumor resection. Reconstruction improves the healing and is essential to restore oral function and esthetics, thereby improving the quality of life after an extensive surgical procedure [1–8]. Oropharyngeal tumor surgery is associated with many postoperative problems like respiratory problems, major swelling, prolonged length of tracheostomy, and lengthened intensive care unit and hospital stay. A major goal in treatment is to achieve primary healing without delaying possible adjuvant radiotherapy.

Glucocorticoids (GCs) are widely used in association with head and neck surgery to reduce these undesirable problems due their anti-inflammatory effects [9–11]. GCs improve postoperative rehabilitation, shorten intensive care unit and hospital stay, and reduce neck swelling. However, adverse effects may follow GC use, particularly when high doses are used. Short-term GC use has been reported to increase the risk for avascular necrosis of the femoral head, steroid-induced psychosis, peptic ulcers, and gastrointestinal bleeding [12–21]. Another considerable disadvantage of steroids is impaired wound healing, which may increase postoperative infections and complications [22–24]. Despite the well-documented efficacy of systemic dexamethasone usage in surgery, no data exist regarding effects and safety of dexamethasone in oropharyngeal cancer reconstructive surgery.

We performed a prospective randomized double-blind control study to examine whether the peri- and postoperative use of dex-

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amethasone in reconstructive head and neck cancer surgery is associated with advantages or disadvantages.

Materials and methods

A prospective double-blind randomized controlled trial was conducted between December 2008 and February 2013 at the Department of Oral and Maxillofacial Surgery and the Department of Plastic Surgery, Helsinki University Hospital, Finland. The study protocol was approved by the Research Ethics Committee of Helsinki University Hospital. Written informed consent was obtained from all patients before surgery.

Consecutive patients with oropharyngeal cancer who had a microvascular reconstruction were included in the study. Exclusion criteria were history of liver or kidney dysfunction, glaucoma, peptic ulcer, psychosis from use of steroids, allergy to any constituent of the dexamethasone preparation used, and absence of written informed consent. We collected consecutive 110 patients, 55 to each group. Ninety-seven patients met the inclusion criteria. Four of these patients were subsequently excluded, three because of intraoperative cancellation of free flap reconstruction and one because he was administered additional dexamethasone. Therefore, 93 patients were included in the study, 73 from the Department of Maxillofacial Surgery and 20 from the Department of Plastic Surgery. Of the 93 patients, 51 had received dexamethasone (DEX-group) and 42 had not received dexamethasone and were the control group (NON-DEX). The discrepancy in the size of two groups is explained by the effect of luck since patients were chosen to either group by random selection.

Patients were randomly allocated into two groups. The patients in the study group received dexamethasone (Oradexon®) 10 mg intravenously (i.v.) every 8 h on the first day, every 12 h on the second day, and one dose on the third day, receiving a total dose of 60 mg (DEX). The patients in the control group received no dexamethasone (NON-DEX). The randomization was done by a nurse not participating in the study. The information about whether a patient would receive dexamethasone was given in a sealed envelope to the anesthesiologist in charge of the anesthesia of the surgery. The same anesthesiologist administered all doses to the patient if allocated during the operation and in the ICU postoperatively. Surgeons were unaware of the group to which patients were assigned.

Preoperative and predictive data in DEX and NON-DEX groups are given in Table 1. The majority (92%) of tumors were squamous cell carcinomas. The oral tongue and mandible were the most common sites of malignancy, each affected in 29% of cases. These were followed by the maxilla (16%), floor of the mouth (12%), buccal mucosa (10%), tonsilla (3%), palate (1%), and larynx – hypopharynx (1%). There were 83 fasciocutaneous and 10 osseofasciocutaneous reconstructions. The radial forearm (RFF) was the most frequently performed flap (31 in DEX, 20 in NON-DEX), followed by the anterolateral thigh (ALT) perforator flap (15 in DEX, 18 in NON-DEX). The other flap types included the deep circumflex iliac artery (DCIA) bone flap, fibula free flap, latissimus dorsi (LD) muscle flap, and scapula or parascapular flaps. The surgical data are given in Table 2 and TNM classifications in Table 5. We classified surgical complications according to Dindo et al. so that all major complications were included to complication group IIIb or worse and received secondary surgery within three weeks [25,26].

All patients received standard, balanced anesthesia. Patients received cefuroxime 1.5 g × 3 i.v. and metronidazole 500 mg 1 × 3 i.v. over an average of 7 days, starting from induction of general anesthesia. Patients with allergies were given clindamycin 300 mg × 4 i.v. In the postoperative period, patients were given paracetamol 1 g × 3 i.v. No non-steroidal anti-inflammatory drugs were used. Postoperatively, oxycodone 0.2–0.4 mg/10 kg i.v. was administered if the patient scored more than 4 on a Visual Analog Scale (VAS) or when requested by the patient. Postoperative nausea was treated with ondansetron as needed. One physician (SK) collected and sorted the data from the follow-up forms and hospital database.

Statistical analysis

Significance of associations between groups and categorical variables was evaluated by Chi-square tests. Differences in mean values between groups and continuous variables were evaluated by Student's *t*-tests for normally distributed variables and by Wilcoxon two-sample test for variables with skewed distributions. To indicate overall recovery from the surgery, a score was formed that included the following 12 continuous variables: change in neck circumference, start of using Heat and Moisture Exchanger (HME), time of decannulation of tracheostomy/extubation, neck drainage removal time, start of communication, sitting, standing, walking, drinking fluids, transferring to the hospital ward and home, and change in patient's weight during hospital stay. Each variable was at first categorized according to median value (-1 if $\leqslant$ median and +1 if > median). A sum score of these was calculated and further dichotomized according to median value (median $\geqslant 7$; 1 indicating shorter/better recovery, median $\geqslant 7$; 0 indicating longer/poorer recovery, median < 7) to serve as an outcome in logistic regression analysis. Explanatory variables included group (NON-DEX or DEX), age as continuous, sex, Body Mass Index (BMI), history of alcohol use (major, moderate, or none), length of surgery, American Society of Anesthesiologists (ASA) score, and major complications. We did a power analysis to evaluate the statistical reliability of the present study.

Results

No statistical differences existed between the DEX and NON-DEX groups regarding preoperative demographic data or preoperative treatments given to patients, except that there were more heavy alcohol users in the NON-DEX group (DEX n = 8 (16%), NON-DEX n = 13 (31%), p = 0.113). Localizations of the tumors, TNM classifications, and surgical defects were similar between the groups. The flap types used as well as the neck dissection types and operation times were also similar between DEX and NON-DEX groups. In the NON-DEX group, more patients were tracheostomized at the beginning the operation than in the DEX group (60% vs. 33%, p = 0.034). Postoperative adjuvant treatments were similar in both groups. There were more diabetics in the DEX group, however this difference was not statistically significant (Tables 1 and 2).

The main primary outcome variables were neck swelling, length of intensive care unit stay and hospital stay, duration of intubation or tracheostomy, and delay to start of radiotherapy. No statistical differences existed between the two groups in any of these variables. Patients' neck swelling was measured daily from the highest point of the neck for seven days postoperatively, and the highest increase in neck circumference (cm) relative to the preoperative circumference was used in analysis. Length of tracheostomy was three days shorter (23%) in the DEX group, but the difference was not significant. Four primarily intubated patients in the DEX group and one patient in the NON-DEX group were tracheostomized postoperatively due to prolonged need for mechanically assisted ventilation. Therefore, the total number of tracheostomies was 21/51 patients (41%) in the DEX group and 26/42 patients (62%) in the NON-DEX group (Table 3).

The DEX group had more major complications during the postoperative period (27% in DEX vs. 7% in NON-DEX, p = 0.012). The