Oxycodone and Dexamethasone for pain management after tonsillectomy: A placebo-controlled EMG assessed clinical trial

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Summary

Background: Surface electromyographic (sEMG) study of post-tonsillectomy swallow-evoked muscular reactions was performed in order to evaluate the efficacy and safety of oxycodone and dexamethasone in pain management after tonsillectomy.

Material/Methods: 90 randomly chosen operated adults were divided into three groups. Group 1 (n=30) was treated with OxyContin (Oxycodone) injections; Group 2 (n=30) was treated with Dexamort (Dexamethasone), and Group 3 (n=30) was a placebo group. Pain assessment included visual analogue scale (VAS) pain score and the EMG data like the timing, electric amplitude and graphic patterns of muscular activity during deglutition. We investigated masseter, infrahyoid and submental-submandibular muscles. Records from trapezius muscle were used for control. The results were compared with previously established normative database. The patients were tested 24 h after surgery. The sEMG data were compared with VAS pain score with regard to changes in clinical condition of the patients.

Results: Analgesia with oxycodone smoothed the recorded sEMG swallow peaks and increases time of deglutition. Dexamethasone normalized muscular activity in deglutition in cases with edema as detected by the EMG records. Statistically significant difference in muscle reactions was detected between the two Groups and the placebo group.

Conclusions: Application of oxycodone significantly reduces the postoperative pain. Application of dexamethasone after tonsillectomy is advisable because of the reduction of postoperative morbidity while the reduction of the postoperative pain is secondary to the reduction of edema. SEMG might be used as an adjunctive measure of pain behavior via assessment of muscular reactions to pain and to analgesia.

Key words: tonsillectomy • postoperative pain • oxycodone • dexamethasone • surface electromyography

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Background

Post-operative pain is the main cause of morbidity following tonsillectomy. Despite recent efforts, it is still very difficult to provide sufficient analgesia for most patients [1,2]. Establishment of good analgesia is important in the post-operative period after adenotonsillectomy, and numerous drug comparison studies are being performed in this field [3]. Objective evaluation of analgesic activity of drugs remains an unsolved problem. Pain after tonsillectomy has two components: constant pain and swallow-evoked pain. The palatine (faucial) tonsils are closely associated with several muscles like palatopharyngeus, palatoglossus and superior constrictor of the pharynx, and surgical intervention in the site of the tonsils might affect local muscles directly or indirectly through circulus tonsillaris nervous plexus. Ligaments and muscles around the palatine tonsils are involved in deglutition and themselves are rich sources of pain receptors. While pain is subjective in general, muscular reactions to pain are objective and electromyography (EMG) can provide a practitioner with qualitative and quantitative data for their assessment. In addition to that, edema contributes substantially to the postoperative discomfort and morbidity of tonsillectomy in some patients.

Both oxycodone and dexamethasone are used as post-tonsillectomy analgesics [4–6]. The quantitative assessment of their actions was not yet performed. Subjective visual analogue scales of different variations remained the main tool for pain assessment being a weak point of many otherwise solid studies on analgesic drug comparison [5–8]. Electromyography (EMG) of swallowing, however, might supply us with data helpful for both qualitative and quantitative assessment of analgesia. EMG reactivity in relation to pain was previously studied among patients following tonsillectomy [9,10], as well as among facial pain patients [11], and in patients with myogenous temporomandibular disorders (TMD) [12–14].

The current research was designed to evaluate any changes in muscular reactions to postsurgical painful irritation that can be observed before and after administration of oxycodone or dexamethasone. We hypothesized that if these medications induce changes in muscular reactions that can be qualitatively and quantitatively assessed by the surface EMG, our understanding of analgesic effects of them might have a sound basis.

Material and Methods

Subjects

The research was designed as an ordinary randomized, double-blind, and placebo-controlled study. The patients were randomly chosen among surgical patients in the hospital across a 10-month period according to a predetermined randomization code. The surgeons, anesthesiologists, and recovery room staff members were all blinded with regard to study medications. The study was approved by the Medical Center Ethics Committee. The Group 1 of patients who undergone tonsillectomy and received Oxycontin (oxycodone) postsurgical treatment included 30 adults, 17 women and 13 men, ranging in age from 18 to 39 years (mean =21.6 years). The Group 2 of post-tonsillectomy patients received Dexacort (dexamethasone, 20mg) and included 30 adults, 16 women and 14 men, ranging in age from 18 to 34 years (mean =20.2 years). The Group 3 (n=30, 15F, 15M, mean age 21.3) was taken as a control placebo group. These groups were randomly chosen from 230 patients with recurrent tonsillitis who were scheduled for tonsillectomy.

Patients’ flow chart is presented in the Table 1.

Before the study all subjects completed a questionnaire regarding their general health and their medical history and signed an informed consent. Subjects had no history of dysphagia or odynophagia due to reasons other than tonsillitis (exclusion criterion), and no history of medical problems or medications that might affect swallowing and drinking (exclusion criterion). All subjects had normal oral anatomical structures and complete dentition (inclusion criterion). All subjects were assessed by ENT surgeons prior to their participation to the study. All the males were well shaved.

Administration of the oxycodone, dexamethasone, and the placebo was as follows: each subject in the Group 1 received an intravenous 7-hr infusion of oxycodone 2 mg/hr (Martindale Complete Drug Reference, 35th ed., 2007) starting from 16 hours after surgery; each subject in the Group 2 received an intravenous infusion of dexamethasone (Dexacort, 20 mg) 20 hours after surgery; each subject in the Group 3 received an intravenous 7-hr infusion of normal saline (‘placebo’) (16–23 hours after surgery). The 4-hour interval for Group 2 was chosen because terminal half-time for dexamethasone is approximately 4 hours [15]. The initial surface EMG testing itself was performed 16 (Groups 1 and 3) or 20 (Group 2) hours after surgery, the final testing was performed 24 hours after surgery. After the EMG test was performed, the patients from the both groups received further analgesia at as needed basis.

Outcome measures were assessed 24 hours after surgery. These included patient rating of pain by using the visual analog pain 1–10 scale (VAS data) which was recorded by a blinded nurse observer who was unaware of the treatment, and the surface EMG investigation (EMG data). Dysphagia severity was also clinically evaluated by using the previously published rating scale (Table 2) [16]. Edema was observed clinically and was evaluated by using throat edema severity rating scale (0-5) (Table 3).

Table 1. Patients flow chart.

| Randomly assessed for eligibility (n= 104) | Excluded (n= 14) |  
|-----------------------------------------|-----------------|  
| a. Not meeting inclusion criteria (n=14) | b. Refused to participate (n=0) |  
| Total allocated (n= 90) |  
| Allocated to Group 1 (n=30) | Group 2 (n=30) | Control (n=30) |  
| Lost to follow-up (n=0) | (n=0) | (n=0) |  
| Analyzed (n=30) | (n=30) | (n=30) |
Electromyography techniques

Four muscle locations were examined: (1) m. masseter (MS location), (2) the submental-submandibular muscle group (SUB), (3) laryngeal strap muscle group (LSM), and m. trapezius (TZ). These superficial muscles are involved in the oral and pharyngeal phases of the swallow. The trapezius muscle was examined as a control muscle not involved in deglutition. All EMG recordings were made using standard surface electrodes (AE-131). The equipment used for the EMG recordings was a NeuroDyne Neuromuscular Sys/3 four channel computer based EMG unit with NeuroDyne Medical software (NeuroDyne, Cambridge, MA, USA), and AE-204 Active sensors attached to AE-131 electrodes. Each EMG record was full-wave rectified and low-passed filtered. The computer program indicates mean, SD, minimum, maximum, range of muscle activity during each trial, and its duration. Muscle activity (EMG) is quantified in microvolts. The interelectrode distance was 10 mm. Specific electrode positions were as follows (Figure 1): (1) MS location: Two bipolar stick-on surface electrodes were placed parallel to the masseter muscle fibers. (2) SUB location: Two surface electrodes were attached to the skin beneath the chin on the right or left side of midline to record submental myoelectrical activity over the platisma. (3) LSM location: Two electrodes were placed aside of the thyroid cartilage to record from the infrahyoid (laryngeal strap) muscles. The exact electrode positions (Figure 1) for each muscle group are known since the 19th century, and in addition were clarified following anatomical correlates [17]. The electrode placement technique was described in several publications [18–20]. Each pair of electrodes had a third electrode as ground. Electrical impedance at sites of electrode contact was reduced, as target areas were lightly scrubbed with alcohol gauze pads, followed by application of an electrode gel. After the four pairs of surface EMG electrodes were attached, subjects remained completely relaxed for a minute in order to establish the EMG visual pattern for resting potential of facial and neck muscles. Subjects were permitted to move chin slightly up while swallowing if needed, as we traced no changes of the graphic and numerical baseline associated with this movement. (This movement involves mm. rectus capitis posterior minor and minor, as well as some other posterior neck muscles and does not affect signals from above mentioned electrode locations.) After electrode placement, each participant performed two tasks:

1. Three trials of swallowing normal volume of tap water for a particular person. (The mean volume appeared to be 16.5 cc). Instruction given: “Make a normal single swallow”.
2. One trial of continuous drinking of 100 ml of tap water. Instruction given: “Drink this water as normal.”

EMG record was full-wave rectified and low-passed filtered. The computer program indicates mean, SD, minimum, maximum, range of muscle activity during each trial, and its duration. Muscle activity (EMG) is quantified in microvolts.
The data were analyzed off-line by computer. All graphic recordings were initially inspected by eye. The data were statistically evaluated by one-dimensional analysis of variance, SPSS, Standard version 10.0.5 (SPSS, Chicago, IL, 1999), and correlation between pain score and sEMG data were analyzed using \( \chi^2 \) criterion with 95% confident interval and calculating of correlation coefficient. The level of significance for all analyses was set at \( p<0.05 \). Normalization procedure was performed for electric amplitude records in order to change computer-calculated range and mean ("raw" range and mean) into real range and mean (raw data minus the mean resting potential of an actual muscle group covered by skin). Further on in the results only real mean and range data are introduced.

**RESULTS**

Tables 4–6 display comparative data between Group 1 (Oxycontin group) and Group 2 (Dexacort group), and Group 3 (placebo group). It is clearly observed that Oxycontin significantly changes both VAS pain score and muscle reactions to analgesia (amplitude), dexamethasone insignificantly changes both VAS pain score and muscle reactions, while placebo changes VAS pain score and TZ muscle reaction only. Table 4 shows that both applications did not change the timing of deglutition, however, due to different reasons. It will be further explained in the Discussion. For Table 5, real mean is displayed (the mean resting potentials of an actual muscles covered by skin were 2.808 µV = for the SUB location and LSM location, 2.495 µV = for the MS location, 3.826 µV = for the TZ location). Placebo did not affect reflex movements of the tested oro-pharyngeal muscles.

For the Group 1, the EMG records showed graphic effect of oxycodone action. A typical single water swallow of a healthy individual between 18 and 70 years of age was observed graphically at the rectified and low-pass filtered sEMG as a normal wave with upward deflections and a sharp apex when recorded from the MS, SUB and LSM locations [8,9,18]. When a patient is in pain, the swallow becomes absolutely disorganized. (Figure 1). When the surface EMG record of a swallow was performed after oxycodone had been administered, it was clearly seen that the sharp apexes were gone and the swallow waves looked smooth (Figure 2). The dexamethasone group (Group 2) EMG records indicated that dexamethasone did not affect muscles the same way as oxycodone did but nevertheless improved the swallow pattern towards its normalization (Figure 3). This positive effect, however, was observed only in 43% of cases (13 out of 30).

| Test | Group1 | Group 2 | Group 3 |
|------|--------|---------|---------|
|      | Before | After | P  | Before | After | P  | Before | After | P  |
| 1    | 7.4±2.7 | 4.2±2.2 | <0.05 | 7.7±2.5 | 5.1±2.1 | <0.05 | 7.5±2.5 | 6.6±2.3 | >0.05 |
| 2    | 7.3±2.9 | 4.0±1.8 | <0.05 | 7.7±2.5 | 4.3±1.7 | <0.05 | 7.4±2.7 | 6.2±2.2 | <0.05 |

**Intergroup comparison**

| Test | Group1 vs. Group 2 | P  | Group 1 vs. Group 3 | P  | Group 2 vs. Group 3 | P  |
|------|-------------------|----|--------------------|----|-------------------|----|
| 1    | Gr. 1 vs. Gr. 2   | <0.05 | Gr. 1 vs. Gr. 3    | >0.05 | Gr. 2 vs. Gr. 3   | <0.05 |
| 2    | Gr. 1 vs. Gr. 2   | >0.05 | Gr. 1 vs. Gr. 3    | >0.05 | Gr. 2 vs. Gr. 3   | >0.05 |

**Table 4.** Pain scores (VAS 10-points pain scale, mean ± standard deviation) in two tests after surgery before (“before”) and after (“after”) administering the medications and the placebo. Intergroup comparison was performed using data after drug/placebo administration. The time period was calculated by the software program from the beginning of the MS activity and to the end of LSM activity.

| Test | Group1 | Group 2 | Group 3 |
|------|--------|---------|---------|
|      | Before | After | P  | Before | After | P  | Before | After | P  |
| 1    | 5.834  | 6.365  | >0.05 | 5.81   | 6.23   | >0.05 | 5.782  | 5.871  | >0.05 |
| 2    | 24.769 | 23.833 | >0.05 | 24.7   | 23.7   | >0.05 | 25.543 | 23.67  | >0.05 |

**Intergroup comparison**

| Test | Group1 vs. Group 2 | P  | Group 1 vs. Group 3 | P  | Group 2 vs. Group 3 | P  |
|------|-------------------|----|--------------------|----|-------------------|----|
| 1    | Gr. 1 vs. Gr. 2   | >0.05 | Gr. 1 vs. Gr. 3    | >0.05 | Gr. 2 vs. Gr. 3   | >0.05 |
| 2    | Gr. 1 vs. Gr. 2   | >0.05 | Gr. 1 vs. Gr. 3    | >0.05 | Gr. 2 vs. Gr. 3   | >0.05 |

**Table 5.** The duration of muscle activity (normal range and patients’ mean) in seconds in swallow tests after the operation of tonsillectomy before (“before”) and after (“after”) administering the medication and the placebo. Intergroup comparison was performed using data after drug/placebo administration.

Test 1 – normal swallow; test 2 – drinking.
Clinical data of these 13 patients indicated significant edema around the operated site that was reduced after dexamethasone was administered. For these patients, the throat edema severity rating scale (Table 3) indicated mean 4.1 before and 2.3 after the treatment (p<0.05). The records taken from the patients of the placebo group (Group 3) did not show even these changes (Figure 4).

Changes toward improvement in dysphagia severity rating scale were significant for Group 1, and insignificant for Group 3. For Group 2, these changes were significant for patients with edema (the same 43% of cases) and insignificant for the others.

There were no significant differences between the three study groups with respect to age, sex, height, weight, or duration of surgery. There was no significant difference in

| Muscle       | Group 1 Before | Group 1 After | P     | Group 2 Before | Group 2 After | P     | Group 3 Before | Group 3 After | P     |
|--------------|----------------|---------------|-------|----------------|---------------|-------|----------------|---------------|-------|
| Single swallow |                |               |       |                |               |       |                |               |       |
| MS           | 14.04          | 8.74          | <0.05 | 14.04          | 12.71         | >0.05 | 14.12          | 13.93         | >0.05 |
| (Normative mean: 6.041) |               |               |       |                |               |       |                |               |       |
| SUB          | 7.42           | 8.22          | >0.05 | 7.42           | 7.30          | >0.05 | 7.38           | 7.95          | >0.05 |
| (Normative mean: 10.781) |               |               |       |                |               |       |                |               |       |
| LSM          | 11.77          | 6.18          | <0.05 | 11.77          | 7.55          | <0.05 | 10.63          | 11.85         | >0.05 |
| (Normative mean: 4.530) |               |               |       |                |               |       |                |               |       |
| TZ           | 18.38          | 4.25          | <0.01 | 18.38          | 8.25          | <0.01 | 20.01          | 8.21          | <0.05 |
| Drinking     |                |               |       |                |               |       |                |               |       |
| MS           | 15.34          | 5.38          | <0.01 | 15.34          | 8.35          | <0.01 | 15.62          | 16.38         | >0.05 |
| (Normative range: 3.63±2.3) |               |               |       |                |               |       |                |               |       |
| SUB          | 14.58          | 11.27         | <0.05 | 14.58          | 12.87         | >0.05 | 13.60          | 12.73         | >0.05 |
| (Normative range: 7.43±2.2) |               |               |       |                |               |       |                |               |       |
| LSM          | 15.55          | 4.96          | <0.01 | 15.55          | 8.90          | <0.01 | 16.14          | 15.04         | >0.05 |
| (Normative range: 3.2±1.7) |               |               |       |                |               |       |                |               |       |
| TZ           | 18.38          | 4.25          | <0.01 | 18.38          | 8.56          | <0.01 | 20.01          | 8.21          | <0.05 |

Figure 2. A typical single swallow of a patient 24 hours after tonsillectomy after Oxycontin was administered. Green line – MS location, blue line – SUB location, red line – LSM location, yellow line – TZ location. Normal sharp apexes are gone, m. trapezius is absolutely relaxed. X-axis (horizontal) – time in ms, Y-axis (vertical) – electrical amplitude in µV.

Figure 3. A typical single swallow of a patient 24 hours after tonsillectomy after dexamethasone was administered. Green line – MS location, blue line – SUB location, red line – LSM location, yellow line – TZ location. The swallow is clearly seen as a good high wave (mark 20–40) but uncoordinated aftereffect follows (mark 40–70). MS activity is slightly ahead of SUM activity that is normal. LSM activity is low as normal. Trapesius is relaxed. X-axis (horizontal) – time in ms, Y-axis (vertical) – electrical amplitude in µV.

Table 6. Mean of electric activity of masseter (MS), submental (SUB), laryngeal strap (LSM), and trapezius (TZ) muscles in swallow and drinking tests, in µV, after the operation of tonsillectomy before (“before”) and after (“after”) administering the medication and the placebo.
blood loss between the oxycodone group (2.3±1.6 mL/kg), the dexamethasone group (2.5±1.6 mL/kg), and the placebo group (1.9±0.9 mL/kg).

**Discussion**

Anesthesia and following analgesia affect muscular reactions of the swallowing cycle. The reflex muscle reactions express themselves via EMG most vividly. Numerous reflexes, like glottic closure reflex, gag reflex, jaw reflex, are associated with the oral-pharyngeal area. Even the pharyngeal phase of swallowing itself is defined as “the most complex reflex elicited by the nervous system” [21]. It is important for a placebo-controlled study, because a medication can change the true involuntary reflex response and a placebo cannot [22,23].

The current study clearly shows that oxycodone changes deglutition pattern and that this change can be well observed on the sEMG records (Figure 1 vs. Figure 2). In addition to graphic changes, quantitative amplitude changes also were well detected and the difference between Group 1 and Group 3 (placebo) was clearly seen. Dexamethasone also might change deglutition pattern while not as vividly as oxycodone, and this change is observed on the sEMG records (Figure 1 vs. Figure 3). Thus, we might suggest that sEMG is a valid technique to study drugs like analgesics that affect muscular reactions.

While oxycodone reduces pain due to its effect on opioid receptors, that affect muscles as well, dexamethasone does not affect muscles. Steroids have a multiplicity of physiological actions: effects on metabolism, electrolyte and water balance, skeletal muscle, the cardiovascular system, the central nervous system, formed blood elements, and anti-inflammatory and immunosuppressive actions but otolaryngologists use them mainly because of their anti-inflammatory actions. In the present study, it appears that the use of the steroid dexamethasone reduced pain significantly in some patients but only slightly in other patients. The statistics was performed for the whole cohort of 30 patients and the mean data were obtained. If, however, only 43% of cases (15 patients) with visible EMG changes are examined, the results of dexamethasone administration appear more impressive. While these 15 patients had significant clinically proven postoperative edema, we may think that the primary action of dexamethasone was the reduction of the edema and the reduction of pain was secondary to this effect.

The absence of statistically significant changes of timing patterns of deglutition might have an explanation. It is known that postsurgical dysphagia/odynophagia increases time needed for a single swallow [10,19]. It could be suggested (an additional study on healthy subjects is needed to prove this) that oxycodone due its opioid nature affects temporal relationships of the events of the swallowing cycle the same way. Thus, despite the fact that a patient is relieved from pain, his/her swallowing remains slow. In case of dexamethasone the swallow remains slow because the pain even was being reduced, still exists. Timing of dexamethasone administration is essential for good results [24].

The sEMG test was set 24 hours after surgery because 12 hours after surgery or earlier, the majority of the patients were unable to drink and presented a spasm of submental-submandibular muscles recorded from the SUB location. This fact, perhaps, might indicate a weakness of the sEMG method in cases when rapid 1–2 hours after surgery evaluation is needed. Otherwise, for the research purposes in drug comparison it seems to be very suitable and convenient technique.

**Conclusions**

Application of oxycodone significantly reduces the postoperative pain. Application of dexamethasone after tonsillectomy is advisable because of the reduction of postoperative morbidity while the reduction of the postoperative pain is secondary to the reduction of edema. SEMG might be used as an adjunctive measure of pain behavior via assessment of muscular reactions to pain and to analgesia.

**Declaration of interest**

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