Pre-Induction Dexamethasone Does Not Decrease Complications after Microvascular Decompression for Facial Spasm

Qi-Wu Fang¹*, Xiao-Yan Qian¹*, Jian-Xiong An¹, Hui Wen¹, Jian-Ping Wu¹, Doris K. Cope², and John P. Williams²

ABSTRACT

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Background: Postoperative pain, sore throat, hoarseness, early facial paralysis and pyrexia are common complications after microvascular decompression (MVD) for facial spasm. Dexamethasone (Dex) is used extensively in the perioperative setting as it is a high-potency, long-acting glucocorticoid with little mineralocorticoid effects. It may improve analgesia and decrease opioid consumption, significantly decrease the incidence and severity of sore throat and hoarseness after general anesthesia, and antagonize the inflammatory reaction in the postoperative period. We designed this study to determine the effects of Dex on these complications.

Methods: A total of 1020 adult patients with hemifacial spasm who were scheduled to receive MVD, were randomly divided into three groups: Dex-0 (N=340), Dex-1 (N=340) and Dex-2 (N=340), respectively, and were administered normal sodium, Dex 0.1 mg/kg or 0.2 mg/kg before induction of anesthesia. Incision pain, sore throat and hoarseness, early facial paralysis, and pyrexia were evaluated. Postoperative incision pain was recorded during the first and second day after surgery; sore throat and hoarseness, early facial paralysis, and pyrexia were recorded from the day after surgery and until the end of the fifth day after surgery.

Results: One thousand and fifteen patients completed this clinical trial. Within the 3 groups: Dex-0 group (N=337), Dex-1 group (N=339) and Dex-2 group (N=339), we found no significant differences concerning postoperative pain, sore throat and hoarseness, early facial paralysis and the intensity of pyrexia (P>0.05). Conclusions: Administration of Dex (0.1 mg/kg or 0.2 mg/kg) before anesthesia induction did not limit adverse outcomes after MVD.

Dexamethasone (Dex) has been extensively used in the perioperative setting because it is a high-potency, long-acting glucocorticoid with little mineralocorticoid effects. It may relieve postoperative pain (1-4), alleviate sore throat and hoarseness caused by intubation after general anesthesia (5), and reduce the inflammation reaction during the postoperative period (6). However, reports in the literatures are varied. The aim of this study was to determine whether a single-dose of Dex before induction of general anesthesia would affect postoperative pain, sore throat and hoarseness, facial paralysis and the intensity of pyrexia after microvascular decompression (MVD) for facial spasm.

MATERIALS AND METHODS

Patients

After obtaining Institutional Review
Board (IRB) approval and informed consent, 1020 American Society of Anesthesiologists (ASA) physical status I-II patients aged 40-60 years suffering with facial spasm and requiring MVD, were included in this study. They were randomly divided into three groups, Dex-0 (N=340), Dex-1 (N=340) and Dex-2 (N=340). Randomization was performed using a computer-generated randomization table. Exclusion criteria included: renal failure, active liver disease, cardiac dysfunction, pulmonary dysfunction, endocrine diseases, metabolic diseases, peptic ulcer disease, a history of postoperative nausea and vomiting (PONV), motion sickness, visual dysfunction, and auditory dysfunction. Patients were also excluded at any point if additional dosages of steroid medications were required.

**Anesthetic Protocol**

Patients were pre-medicated with scopolamine 0.3 mg intravenously (IV). Anesthesia was induced with propofol 1.5-2.5 mg/kg, sufentanil 0.3 μg/kg and cisatracurium 0.2 mg/kg. We applied reinforced tracheal tube (Safety- Flex, Mallinckrodt Medical, Ireland) with inner diameter (ID) 6.5-7.0 mm for males and ID 6.0-6.5 mm for females. Anesthesia was maintained with remifentanil 0.1-0.2 μg/kg/minute and propofol, with the propofol infusion rate titrated to maintain target bispectral index (BIS) value at 40-60. Arterial blood pressure (BP) was controlled to within 30% change of the preoperative systolic value measured on the day before surgery. If the BP went outside that target range, it was increased with phenylephrine or decreased with nitroglycerin. Heart rate (HR) was controlled to 50-80 beats per minute (BPM) using isoprenaline or esmolol. End tidal carbon dioxide (CO₂) was controlled to 30-35 mm Hg. Muscle relaxants were monitored in all groups. Intubation was performed when turnover frequency (TOF) τ=0 and cisatracurium 0.05 mg/kg was administered intraoperatively when TOF τ≥25%. Patients recovered spontaneously without administration of arousal agents or muscle relaxant antagonists. Tropisetron 2.5 mg was administered before tracheal extubation.

Patient-controlled intravenous analgesia (PCIA) was connected when the incision closure was completed, with sufentanil 150-200 μg and tropisetron 7.5 mg mixed in 50 ml. If the patients were older than 45 years, we administered 150 μg sufentanil; if the patients were younger than 45 years or 45 years, we administered 200 μg sufentanil. The PCIA was programmed as follows: basal infusion of 1 ml/hour, bolus dose of 0.5 ml, and lockout time of 15 minutes.

**Administration of Dex**

Dex was administrated 0.1 mg/kg (1 mg/ml) in the Dex-1 group and 0.2 mg/kg (2 mg/ml) in the Dex-2 group by IV injection in the upper extremity before the induction of anesthesia. The same volume of normal sodium was administered in the Dex-0 group. Treatment assignments were placed in sealed, opaque envelopes which were opened by the person responsible for the preparation of the trial-drug solutions. The two concentrations of Dex and normal saline were prepared in syringes; each syringe was labeled with a randomly allocated number. The doctors and nurses administering the drugs, as well as the investigators and research personnel who collected data, were blinded to the treatment assignments.

**Data Recording**

The incidence of sore throat and hoarseness, facial paralysis and postoperative incision pain intensity were recorded by specially trained nurse anesthetists who were blinded to the treatment groups. Sore throat, hoarseness and facial paralysis was recorded for five postoperative days as body temperature. Temperature limits were grouped as: 37.2°C or less, afebrile; 37.3 to 38.0°C, mild pyrexia; 38.1°C to 39.0°C, moderate pyrexia; 39.1°C to 41.0°C, severe pyrexia; and greater than 41.0°C, ultrahyperpyrexia.

**Statistical Analysis**

The primary outcome of the study showed that maximal incidence of absence of fever was 60% and the minimal incidence of absence of fever was 48% in the first and second postoperative day after reviewing the first 200 cases. We then determined that a sample size of 1000 would allow us to detect a difference with a power of 0.80 at the 0.05-significance level.
Dex has been extensively used in the perioperative setting as it is a high-potency, long-acting glucocorticoid with little mineralocorticoid effects. Many published articles have reported that Dex relieves postoperative pain, alleviates sore throat and hoarseness after general anesthesia, and reduces edema and inflammation. On the other hand, there have been opposite conclusions reported. We found that administration of Dex before induction of anesthesia did not alleviate postoperative incision pain, sore throat and hoarseness, and reduce postoperative early facial paralysis and the presence or intensity of pyrexia.

**Dex Did Not Relieve Postoperative Pain**

Unrelieved postoperative pain may result in clinical and psychological changes that increase morbidity and mortality as well as cost and decreased quality of life (7). Studies measuring the effects of Dex or other glucocorticoids on alleviating postoperative pain and reducing doses of analgesics have increased (1-5, 8, 9) since Baxendale and his colleagues (10) reported that Dex could alleviate postoperative pain in 1993. In the present study of a large population undergoing one procedure, administration of Dex did not alleviate postoperative pain. This finding was similar to the results reported by Liu et al. (11) and Lee et al. (12). The intensity of incisional pain may be one reason for this discrepancy. Dex may not be beneficial for acute surgical pain, as opposed to other models of pain such as tooth extraction. Severe pain as seen after a major surgical procedure was only slightly lessened with Dex administration as its analgesic effect tended to be minimal and unsatisfactory. Secondly, the lower doses of Dex (0.1 mg/kg or 0.2 mg/kg) were not effective for alleviating incision pain. Glucocorticoids may reduce postoperative pain through anti-inflammatory effects by changing neuronal surface structure. The analgesic effect of methylprednisolone 125 mg was similar to that of parecoxib 40 mg or ketorolac 30 mg (4, 9). The lower doses of Dex that we applied did not generate analgesic effect as compared with methylprednisolone 125 mg. In summary,
administration of a single dose of Dex before induction of anesthesia, 0.1 mg/kg or 0.2 mg/kg, did not relieve postoperative pain after MVD.

Dex Did Not Relieve Sore Throat, Hoarseness and Early Facial Paralysis
Sore throat and hoarseness are common complications after general anesthesia. They correlate with age, grade of difficulty in intubation, duration of surgery and patient's position during surgery (13), diameter of tube (14), and pressure in the cuff (15). Different technologies have been introduced to prevent sore throat and hoarseness, such as administration of topical lidocaine (16), use of special endotracheal tubes to prevent nitric oxide (NO) diffusing into cuff during tracheal intubation (17), and administration of Dex before induction of anesthesia (5).

The main cause of sore throat and hoarseness is injury of the mucous membrane after intubation (14). Al-Qahtani et al. (18) also found that using a smaller tube in tracheal intubation dramatically minimized the incidence of postoperative hoarseness and sore throat. Computerized tomography (CT) scans have demonstrated that Dex could not reduce upper airway edema after intubation in adult undergoing endarterectomy (19). In this research, small tubes, ID 6.5-7.0 mm for male and ID 6.0-6.5 mm for female, were used for these patients. Mucous membrane injury was minor and administration of Dex did not affect upper airway complications.

Early facial paralysis after surgery has been correlated with inflammatory edema of the facial nerve. The best way to reduce early facial paralysis is by operative approach and good exposure of the surgical field (20). In the past prior to this study, we empirically administered Dex to prevent facial paralysis, but lacked evidence-based medicine (EBM). Although Dex had the effect of anti-inflammatory action in periphery, it did not possess the effect of anti-inflammator action in the central nervous system, possibly because it is a synthetic corticosteroid and is limited in ability to penetrate the blood-brain barrier (21).

Dex Did Not Affect Pyrexia after Operation
Postoperative pyrexia is associated with increased length of patient stay and patients' medical cost. Some published articles showed that administration of Dex could reduce the incidence of pyrexia (22-25). On the contrary, several other studies have shown that administration of Dex did not affect the incidence of pyrexia after surgery (6, 26). In this investigation, we also found that administration of Dex did not affect the incidence of pyrexia after surgery. That the dose of Dex employed may have been inadequate to inhibit the release of pyrexin was our hypothesis.

Advantages and Limitations
In this study all participants had a single diagnosis of facial spasm, experienced the same surgical procedure, as well as, a nearly identical anesthetic technique with postoperative PCIA. We believe that the differences in the three groups with respect to incision pain, sore throat, hoarseness, facial paralysis and fever were directly related to the dose of Dex.

However, this study has several limitations worth noting. Side effects of Dex, such as increasing blood glucose, impairing wound heal-

### Table 1. Demographic Data of Three Groups (Mean ± SD or Number of Cases).

| Item                        | Dex-0 (N=337) | Dex-1 (N=339) | Dex-2 (N=339) | P value |
|-----------------------------|---------------|---------------|---------------|---------|
| Gender (male/female)        | 128/209       | 139/200       | 127/212       | 0.594   |
| Age (year)                  | 48.0±5.77     | 48.9±5.35     | 48.0±5.60     | 0.085   |
| No-smoking status, N (%)    | 260 (77.2)    | 276 (81.4)    | 274 (80.8)    | 0.327   |
| Degree of intubation (1/2/3/4) | 280/39/13/5 | 266/36/29/8 | 279/44/13/3 | 0.154 |
| Number of intubation (1/2/3) | 270/60/7     | 266/70/3      | 279/57/3      | 0.457   |

### Table 2. Visual Analogue Scores (VAS) for All the Patients on the 1st and 2nd Day after Surgery (Mean ± SD).

| Item                        | Dex-0 (N=337) | Dex-1 (N=339) | Dex-2 (N=339) | P value |
|-----------------------------|---------------|---------------|---------------|---------|
| VAS-1*                      | 1.09±2.00     | 1.05±1.92     | 1.20±2.08     | 0.347†  |
| VAS-2#                      | 0.87±1.58     | 0.78±1.46     | 0.83±1.45     | 0.737†  |

*1st day after surgery; †2nd day after surgery; †The P values were calculated with the use of the Kruskal-Wallis nonparametric test.
ing, and gastric mucosa injury were not observed. In future studies, the side effects of single dose of Dex before anesthesia induction should be further studied.

## CONCLUSION

Administration of Dex (0.1 mg/kg or 0.2 mg/kg) before anesthesia induction did not affect the outcomes of MVD for facial spasm. Dex should not be routinely administered due to lack of demonstrated benefit and risk of untoward side effects.

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### References

1. Bogaard T, Klarskov B, Kehlet H, Rosenberg J. Perioperative dexamethasone improves surgical outcome after laparoscopic cholecystectomy: a randomized double-blind placebo-controlled trial. Ann Surg 2003; 238: 451-60.
2. Kardash KJ, Sarrain F, Teleser MJ, Velly AM. Single-dose dexamethasone reduces dynamic pain after total hip arthroplasty. Anesth Analg 2008; 106: 1257-7.
3. Karst M, Kegel T, Lukas A, Lidemann W, Husein S, Peppisnick E. Effect of cefuroxim and dexamethasone on postoperative pain after lumbar disc surgery. Neurosurgery 2003; 53: 331-6.
4. Romundstad L, Breivik H, Roald H, Skolleborg M. Methylprednisolone 125 mg, salin, and placebo. Anesth Analg 2008; 107: 1814-8.
5. Park SH, Han SH, Do SH, Kim JW, Rhee KY, Kim JH. Prophylactic dexamethasone decreases the incidence of sore throat and hoarseness after tracheal extubation with a double-lumen endobronchial tube. Anesth Analg 2008; 107: 1814-8.
6. Holte K, Kehlet H. Perioperative single-dose glucocorticoid administration: pathophysiologic effects and clinical implications. J Am Coll Surg 2002; 195: 694-712.
7. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. Anesth Analg 2003; 97: 534-40.
8. Gan TJ, Meyer T, Apfel CC, Chung F, Davis PJ, Eubanks S, et al. Consensus guidelines for managing postoperative nausea and vomiting. Anesth Analg 2003; 97: 62-71.
9. Romundstad L, Breivik H, Niemi G, Helle A, Stubhaug A. Methylprednisolone intravenously 1 day after surgery has sustained anesthetic and opioid-sparing effects. Acta Anaesthesiol Scand 2004; 48: 1223-31.
10. Baxendale BR, Yater M, Lavermy KM. Dexamethasone reduces pain and swelling following extraction of third molar teeth. Anesthesiology 1993; 79: 961-4.
11. Liu K, Hsu CC, Chia YY. Effect of dexamethasone on postoperative emesis and pain. Br J Anaesth 1999; 80: 85-6.
12. Lee Y, Lai HY, Lin YS, Huang SJ, Sby MH. A dose ranging study of dexamethasone for preventing patient-controlled analgesia-related nausea and vomiting: a comparison of droperidol with saline. Anesth Analg 2004; 98: 1066-71.
13. Ahmed A, Abbassi S, Ghafour HR, Ihsaq M. Postoperative sore throat after elective surgical procedures. J Ayub Med Coll Abbottabad 2007; 19: 12-4.
14. Stout DM, Bishop MJ, Dweirseg J, Cullen BF. Correlation of endotracheal tube size with sore throat. Augmentation of facial paralysis following general anesthesia. Anesthesiology 1997; 87: 419-21.
15. McHardy FE, Chung F. Postoperative sore throat: cause, prevention and treatment. Anesthesiology 1999; 54: 444-53.
16. Tanaka Y, Nakayama T, Nishimori M, Sato Y, Furuya H. Lidocaine for preventing postoperative sore throat. Cochrane Database Syst Rev 2009; 3: CD004081.

### Table 3. Incidence of Sore Throat, Hoarseness and Early Facial Paralysis (Number of Case, %).

| Item                  | Dex-0 (N=337)   | Dex-1 (N=339)   | Dex-2 (N=339) | P value |
|-----------------------|-----------------|-----------------|---------------|---------|
| Sore throat (N, %)    | 53 (15.7)       | 38 (11.2)       | 37 (10.9)     | 0.108   |
| Hoarseness (N, %)     | 18 (5.34)       | 17 (5.01)       | 12 (3.54)     | 0.494   |
| Early facial paralysis (N, %) | 5 (1.48)     | 5 (1.47)       | 10 (2.95)     | 0.283   |

### Table 4. Body Temperature from 1st to 5th Day after Surgery (Number of Case).

| Time  | Dex-0 (≤37.2℃ /37.3~38.0℃ /38.1℃) | Dex-1 (≤37.2℃ /37.3~38.0℃ /38.1℃) | Dex-2 (≤37.2℃ /37.3~38.0℃ /38.1℃) | P value |
|-------|----------------------------------|----------------------------------|----------------------------------|---------|
| 1st day | 173/155/9                        | 196/135/8                        | 165/165/9                        | 0.196   |
| 2nd day | 174/155/9                        | 195/137/7                        | 209/122/8                        | 0.126   |
| 3rd day | 236/99/2                         | 238/100/1                       | 246/92/1                         | 0.891   |
| 4th day | 250/85/2                         | 270/65/4                        | 269/68/2                        | 0.271   |
| 5th day | 293/44/0                         | 290/48/1                        | 306/33/0                        | 0.252   |

Note: All statistics were calculated using the Fisher exact test.