

Use of steroids for facial nerve paralysis after parotidectomy: A systematic review

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Abstract

AIM: To systematically review the literature to assess the efficacy of corticosteroids in treating post-parotidectomy facial nerve palsy (FNP).

METHODS: We searched the Cochrane library, EMBASE and MEDLINE (from inception to 2014) for studies assessing the use of corticosteroids in post-parotidectomy

FNP. Studies were assessed for inclusion and quality. Data was extracted from included studies.

RESULTS: Two randomised controlled trials met the inclusion criteria. One study assessed the use of dexamethasone and the other prednisolone. None of the studies demonstrated a significant difference in the outcome of FNP post-parotidectomy with the use of corticosteroids *vs* no therapy. The majority of FNP post-parotidectomy is transient. Preoperative factors (size of tumour and malignancy), intraoperative factors (extent of parotidectomy and integrity of facial nerve at the end of the operation) are important in determining prognosis of FNP if it does occur.

CONCLUSION: Corticosteroids do not appear to improve FNP prognosis post-parotidectomy. Further studies assessing patients by cohort and with long term follow-up are required to increase scientific evidence.

Key words: Adrenal cortex hormones; Facial paralysis; Parotid diseases; Steroids

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Core tip: Parotidectomy is a common operation performed to treat benign and malignant parotid lesions. Facial nerve palsy (FNP) is a well documented complication of parotidectomy that can significantly impair quality of life. Steroids have been proposed as a treatment option for post-parotidectomy FNP. In this systematic review of randomised controlled trials, we found minimal evidence to suggest steroids improve the prognosis of FNP after parotidectomy. However, more trials are required to assess the effectiveness of steroids in specific cohorts of patients.

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INTRODUCTION

Parotid surgery remains a key surgical intervention for the treatment of both benign and malignant parotid tumours. Facial nerve palsy (FNP) is a potential complication that can occur as a consequence of a parotidectomy.

When post-parotidectomy FNP occurs it is usually transient. The incidence of temporary FNP post-parotidectomy has a reported range of 12% to just over 40%^[1-6]. Permanent FNP is less common with a reported incidence of 0%-6%^[1-5]. Key factors linked to increased risk of postoperative FNP include: the extent of the parotidectomy^[1,3,6,7], revision surgery^[3,7], proximity of the tumour to the facial nerve^[5,7], malignancy^[6] and inflammatory conditions (e.g., sialadenitis)^[4,5,7].

FNP can significantly affect quality of life^[8], leading to distress for the patient^[9] in addition to the potential for ocular complications^[10]. Reducing the risk of FNP is therefore paramount. Intraoperatively this includes the use of key anatomical landmarks^[11] and a facial nerve monitor as an adjunct^[12].

As most cases of post-parotidectomy FNP are temporary there is a paucity of evidence assessing interventions to improve recovery of FNP. The use of corticosteroids significantly improves chance of complete recovery of FNP in Bell's palsy, with a reduction in neural oedema of the FN as a postulated mechanism^[13]. Although Bell's palsy is a distinct entity to post-parotidectomy FNP, it is thought that corticosteroids could improve FNP prognosis through a similar mechanism^[14].

To date there has been no systematic review assessing the efficacy of corticosteroids in ameliorating post-parotidectomy facial nerve paralysis. We sought to assess the effectiveness of corticosteroids versus no treatment in patients with post-parotidectomy FNP.

MATERIALS AND METHODS

Inclusion Criteria for considering studies

Types of studies: Well-designed randomised control trials that compared the use of steroids with no steroids for post-parotidectomy facial nerve paralysis were included.

Types of participants: Patients undergoing parotidectomy (superficial and deep) for benign parotid lesions and malignant parotid lesions.

Types of interventions: We included trials that

utilised corticosteroids of any type for post-parotidectomy facial nerve paralysis.

Outcome measures: The primary outcome measure was facial nerve function monitored at increments after parotidectomy. Objective assessment of the facial nerve function is undertaken utilising the House Brackmann scale, and further classified based upon the location of the facial muscle.

Search strategy

We developed a search strategy to identify randomised controlled trials in the following databases: MEDLINE, EMBASE, Cochrane Library and NHS Evidence (from inception until August 2014). Search terms were as follows: "steroids" AND "parotidectomy", "dexamethasone" AND parotidectomy and "prednisolone" AND "parotidectomy". Relevant articles were then selected and their references screened to identify further articles.

Data collection and analysis

Study selection: Two review authors (KV and IB) assessed abstracts for relevant articles and the full text of these was obtained. The review authors (KV and IB) independently assessed these full-text articles, and any disagreements on inclusion were resolved by discussion with a third author (ND).

Data extraction: Two review authors (KV and IB) extracted data from included studies with standardised forms. Data extracted included: authors, year of publication, participants (sample size, demographics, type and extent of parotid lesion, type of parotid surgery performed, etc.), intervention (type of steroid used and duration) and results (primary and secondary outcome measures, effect size, statistical significance, adverse effects).

Quality assessment: To assess the risk of bias in included studies we utilised the Cochrane risk of bias tool^[15].

Statistical analysis

Due to a variation in the type of corticosteroids utilised in included studies (with regards to potency and duration of action) and variations in the protocol of administration, a meta-analysis was not appropriate and thus not carried out.

RESULTS

Description of studies

The original search produced 46 abstracts, from which 11 duplicate studies were excluded. The remaining 35 articles were screened for relevance. 33 articles were rejected as they did not meet the inclusion criteria. A total of two papers met the

eligibility criteria^[14,16].

Reasons for exclusion included the study having no relevance to the research question ($n = 32$) and not being a randomised controlled trial ($n = 1$). Table 1 summarises included studies.

Interventions

Of the two included studies the interventions used to assess corticosteroid efficacy in post-parotidectomy FNP were dexamethasone^[14] and prednisolone^[16].

Dexamethasone was administered in two doses intravenously (stratified based on extent of parotid surgery with superficial receiving 0.51 mg/kg and deep receiving 1.41 mg/kg) administered at 8 and 16 h postoperatively^[14].

Prednisolone was administered orally as a 10-d reducing course (50 mg/d for 5 d, 30 mg/d for 3 d and 10 mg/d for 2 d)^[16].

The control groups received intravenous saline^[14] and oral lactose^[16] administered with the same protocol as their respective interventions.

Participants

The participant cohort varied slightly between both trials. One included all patients undergoing parotid surgery^[14], whilst the other only included those who developed a postoperative FNP^[15]. Parotid operations ranged from superficial to total (or deep) parotidectomy in both trials and both studies included only adult patients^[14,16].

Outcomes and follow-up

Both trials assessed facial nerve function through clinical assessment. One assessed four facial nerve muscle groups and graded percentage function^[14]. The other utilised the House Brackmann scale^[17] [grading facial from 1 (normal function) to 6 (total paralysis)]^[16]. Duration of postoperative follow-up ranged from 6 mo^[16] to 12 mo^[14].

Risk of bias in included studies

Both included studies were assessed for quality focusing particularly on: randomisation methods, concealment of allocation, effectiveness of blinding, follow up and attrition rates, comparability of groups at baseline and adherence to treatment.

Neither trial described the methods of randomisation, but both had adequate allocation concealment and effective blinding from both the patients and clinicians^[14,16].

Both trials had some limitations with regards to comparability of control and intervention groups at baseline. Neither trial made reference to comparability with regards to tumour factors [type of tumour (malignant or benign) or size of the tumour]^[14,16]. With regards to use of a single surgeon allowing prevention of technique confounding the results, one trial utilised more than one surgeon

(including surgeons in training)^[14], whilst the other did not specify if a single surgeon undertook the operations^[16].

One trial made no reference to extent of compliance and adherence to treatment^[15], whilst the other administered treatment intravenously in the immediate postoperative period allowing total compliance^[14].

Effects of interventions

Dexamethasone: A variety of analyses were undertaken due to the varying doses within the treatment protocol. Overall, no therapeutic advantage was found with the use of dexamethasone^[14]. A higher dose of dexamethasone conferred no functional advantage^[14]. Interestingly, early postoperative facial nerve function was better in the placebo group (overall and in superficial and deep parotidectomy cohorts) although not statistically significant; median time to complete recovery of facial nerve function was shorter in the placebo group (150 d in the dexamethasone group vs 60 d in the control group)^[14].

Prednisolone: There was minimal difference in extent of recovery from FNP in prednisolone vs placebo treated patients at 1, 3 and 6 mo ($P > 0.10$)^[16]. Eighty-four percent of patients with FNP had full recovery at 3 mo, increasing to 98% by 6 mo^[16]. One patient that had a total parotidectomy had a permanent FNP that persisted at 18 mo^[16].

Adverse effects: No adverse effects from short term dexamethasone therapy were noted^[14]. One patient was found to have "minor symptoms" from the use of prednisolone (although the precise symptoms were not stated)^[16].

DISCUSSION

Overall, there appears to be no benefit conferred by corticosteroids for FNP recovery post-parotidectomy. However, this systematic review demonstrates that there is a paucity of evidence assessing the use of corticosteroids in treatment of FNP post-parotidectomy.

Two corticosteroid preparations have been assessed in RCTs with slightly varying mechanisms and durations of actions^[14,16]. Prednisolone has mixed glucocorticoid and mineralocorticoid properties, whilst dexamethasone only has glucocorticoid properties (albeit much more potent than prednisolone) and a longer duration of action^[18]. This variation in the mechanisms of action allowed different dosing regimens in the two included trials. Despite the variation in types of steroids and dosing regimens, there was no evidence to demonstrate an improved chance of full recovery nor improve recovery

Table 1 Characteristics of included studies

Roh and Park ^[16]	
Methods	Randomised controlled trial
Participants	Patients undergoing parotidectomy (superficial, partial, total) ± neck dissection 44 patients Exclusion: 1 Direct FN invasion of FN requiring FN sacrifice and reconstruction 2 Incidental cutting of the facial nerve
Interventions	Started day 1 or day 2 postoperatively Reducing dose of oral prednisolone (50 mg/d for 5 d, 30 mg/d for 3 d and 10 mg/d for 2 d) Placebo group received lactose with similarly formulated doses
Outcomes	House Brackmann grading of FN by two blinded experts Assessed postoperatively: immediately, 1 wk, 1 mo, 3 mo and 6 mo
Results	Overall recovery times from FNP: At 3 mo: 84% had fully recovery At 6 mo: 98% had full recovery Prednisolone <i>vs</i> placebo recovery at 1, 3 and 6 mo (minimal difference) ($P > 0.10$)
Notes	One patient was lost to follow-up and excluded from the analysis (prednisolone group)
Risk of Bias	
Method of randomisation	Not specified
Allocation concealment	Adequate
Other confounding factors	Groups comparable demographically and extent of postoperatively FNP, however tumour size, type or type of parotid surgery not compared in between intervention and placebo groups
Lee <i>et al.</i> ^[14]	
Methods	Randomised controlled trial
Participants	Patients undergoing superficial or total parotidectomy 49 patients Exclusion criteria: Diabetes, age < 18, peptic ulcer disease, previous adverse reaction to steroids and any other contraindication to steroids Prior parotid surgery, anticipated section of FN and pre-existing FNP
Interventions	Two doses of dexamethasone (0.51 or 1.41 mg/kg) depending on type of surgery (superficial or total parotidectomy respectively) at 8 and 16 h postoperatively Placebo group received saline at the same intervals
Outcomes	Facial nerve function in the four major regions was assessed (frontal, orbital, midface, upper lip and lower lip) at a percentage 0-100 depending on extent of function Assessed postoperatively: immediately and every month for 12 mo (or until facial nerve function returned to normal)
Results	Average early postoperative facial nerve function: All patients ($n = 49$): 75.4% Overall: Dexamethasone (69.5%) <i>vs</i> placebo (81.3%) ($P = 0.239$) Dose of dexamethasone: High (63.9%) <i>vs</i> low (74.7%) ($P = 0.118$) Type of surgery: Superficial ($P = 0.637$) and deep ($P = 0.465$) Time to full recovery of facial nerve (median): Placebo (60 d) <i>vs</i> Dexamethasone (150 d) (no P value stated)
Notes	As intervention administered intravenously, total compliance can be ensured
Risk of Bias	
Method of randomisation	Not specified
Allocation concealment	Adequate
Other confounding factors	Initial power calculation required 120 patients, however a nationwide shortage of the intervention drug (dexamethasone) allowed only 52 patients to be enrolled in the trial No comparison of the type of parotid lesion excised within the trial groups (<i>i.e.</i> , malignant or benign and tumour size) Operations were conducted by more than one surgeon (including junior residents)

times^[14,16].

The use of corticosteroids is thought to reduce neural oedema, a proposed mechanism for their excellent efficacy in treating Bell's Palsy^[13]. One postulated mechanism of FNP in parotidectomy is stretch of the FN^[4,19] leading to neural degeneration^[20]. This may explain the lack of efficacy of corticosteroids in treating FNP post-parotidectomy.

There is compelling evidence to suggest that most cases of FNP post-parotidectomy are transient. Moreover, the risk of FNP is associated with a plethora of tumour and intraoperative factors (deeper parotidectomy^[1,3,6,7] revision surgery^[3,7], the facial

nerve being near the tumour^[5,7], malignancy^[6] and inflammatory conditions^[4,5,7]).

Prevention of FNP in parotidectomy is therefore largely linked to operative techniques, including the use of key anatomical landmarks to identify the FN^[11]. The use of a facial nerve monitor has been suggested as an adjunct to help prevent postoperative FNP, with reasonable efficacy demonstrated^[12,21]. Unfortunately, if FNP does occur its extent may dictate likelihood of full recovery, with a FNP preventing closure of the eyes being a predictor of permanent dysfunction^[22].

Nonetheless, when FNP does occur it can significantly reduce quality of life^[8]. It is therefore

key to ascertain interventions that can improve time to recovery. Unfortunately, both RCTs included in this trial did not account for the variety of tumour factors that can increase of postoperative FNP. The need for a high quality RCT assessing the use of corticosteroids in specific cohorts of patients is highlighted (particularly low risk patients, *e.g.*, patients with benign parotid tumours undergoing superficial parotidectomy, in whom the perceived risk of FNP should be lower).

Few adverse effects were reported by both randomised controlled trials, highlighting the relative safety of their use.

Limitations

The randomised trials included in this study had some limitations. Most importantly, statistical assessment of confounding factors in control and treatment groups did not specifically assess tumour factors^[14,16]. Moreover, one trial did not achieve the power calculation sample size^[14], limiting interpretation of its statistical analysis. The methods of randomisation were also unclear in both trials^[14,16].

Implications for practice

Based upon current best evidence the use of corticosteroids to ameliorate postoperative FNP cannot be recommended. It is likely that preoperative and intraoperative factors play a more important role in the risk of permanent FNP. Moreover, the majority of cases of FNP are likely to recover, an important factor to consider in preoperative counselling of patients.

Implications for research

Given the extensive effect of FNP on quality of life, it is in the interest of patients to ascertain methods of improving recovery times. Future research should focus on assessing the cohort of patients in whom permanent FNP is more likely, allowing better preoperative counselling. Moreover, well-designed randomised controlled trials that assess the use of corticosteroids in more statistically comparable groups (*i.e.*, with regards to the type of parotid operation and tumour factors), that will allow assessment of specific cohorts of patients in whom corticosteroids may provide benefit.

COMMENTS

Background

Facial nerve palsy (FNP) is a potential complication that can occur after parotidectomy. FNP can be temporary or permanent, and can significantly affect quality of life. Corticosteroids have been proposed as a treatment for post-parotidectomy FNP. A systematic review of clinical trials is needed to provide scientific evidence for the efficacy of the use of corticosteroids for post-parotidectomy FNP.

Research frontiers

Parotidectomy, facial nerve palsy.

Innovations and breakthroughs

Both studies in this systematic review demonstrated no evidence that corticosteroids improve the prognosis of FNP after parotidectomy. Preoperative factors including the size of tumour and presence of malignancy, as well as intraoperative factors including the extent of parotidectomy (superficial or deep) and facial nerve integrity at the end of the operation are key in determining prognosis of FNP when it occurs.

Applications

There is no convincing evidence to propose the routine use of corticosteroids for post-parotidectomy FNP. Further clinical trials are needed to assess the efficacy of corticosteroids in ameliorating FNP in specific cohorts of patients.

Terminology

Parotidectomy is a commonly performed operation for the treatment of both benign and malignant parotid gland pathology. The facial nerve is at risk during parotidectomy.

Peer review

This study is well conducted and written.

REFERENCES

- 1 Upton DC, McNamar JP, Connor NP, Harari PM, Hartig GK. Parotidectomy: ten-year review of 237 cases at a single institution. *Otolaryngol Head Neck Surg* 2007; **136**: 788-792 [PMID: 17478217 DOI: 10.1016/j.otohns.2006.11.037]
- 2 Witt RL. Facial nerve function after partial superficial parotidectomy: An 11-year review (1987-1997). *Otolaryngol Head Neck Surg* 1999; **121**: 210-213 [PMID: 10471859]
- 3 Guntinas-Lichius O, Klusmann JP, Wittekindt C, Stennert E. Parotidectomy for benign parotid disease at a university teaching hospital: outcome of 963 operations. *Laryngoscope* 2006; **116**: 534-540 [PMID: 16585855 DOI: 10.1097/01.mlg.0000200741.37460.ea]
- 4 Nouraei SA, Ismail Y, Ferguson MS, McLean NR, Milner RH, Thomson PJ, Welch AR. Analysis of complications following surgical treatment of benign parotid disease. *ANZ J Surg* 2008; **78**: 134-138 [PMID: 18269474 DOI: 10.1111/j.1445-2197.2007.04388.x]
- 5 Gaillard C, Périé S, Susini B, St Guily JL. Facial nerve dysfunction after parotidectomy: the role of local factors. *Laryngoscope* 2005; **115**: 287-291 [PMID: 15689752 DOI: 10.1097/01.mlg.0000154735.61775.cd]
- 6 Meier JD, Wenig BL, Manders EC, Nenonen EK. Continuous intraoperative facial nerve monitoring in predicting postoperative injury during parotidectomy. *Laryngoscope* 2006; **116**: 1569-1572 [PMID: 16954980 DOI: 10.1097/01.mlg.0000231266.84401.55]
- 7 Bron LP, O'Brien CJ. Facial nerve function after parotidectomy. *Arch Otolaryngol Head Neck Surg* 1997; **123**: 1091-1096 [PMID: 9339986 DOI: 10.1001/archotol.1997.01900100065009]
- 8 Coulson SE, O'dwyer NJ, Adams RD, Croxson GR. Expression of emotion and quality of life after facial nerve paralysis. *Otol Neurotol* 2004; **25**: 1014-1019 [PMID: 15547436 DOI: 10.1097/00129492-200411000-00026]
- 9 Cross T, Sheard CE, Garrud P, Nikolopoulos TP, O'Donoghue GM. Impact of facial paralysis on patients with acoustic neuroma. *Laryngoscope* 2000; **110**: 1539-1542 [PMID: 10983957 DOI: 10.1097/00005537-200009000-00024]
- 10 Bhamra P, Bhargava AD. Ocular protection in facial paralysis. *Curr Opin Otolaryngol Head Neck Surg* 2013; **21**: 353-357 [PMID: 23689596 DOI: 10.1097/MOO.0b013e32836239cf]
- 11 Pather N, Osman M. Landmarks of the facial nerve: implications for parotidectomy. *Surg Radiol Anat* 2006; **28**: 170-175 [PMID: 16636775 DOI: 10.1007/s00276-005-0070-z]
- 12 Eisele DW, Wang SJ, Orloff LA. Electrophysiologic facial nerve monitoring during parotidectomy. *Head Neck* 2010; **32**: 399-405 [PMID: 19672866 DOI: 10.1002/hed.21190]
- 13 Sullivan FM, Swan IR, Donnan PT, Morrison JM, Smith BH, McKinstry B, Davenport RJ, Vale LD, Clarkson JE, Hammersley V, Hayavi S, McAteer A, Stewart K, Daly F. Early treatment with

- prednisolone or acyclovir in Bell's palsy. *N Engl J Med* 2007; **357**: 1598-1607 [PMID: 17942873 DOI: 10.1056/NEJMoa072006]
- 14 **Lee KJ**, Fee WE, Terris DJ. The efficacy of corticosteroids in postparotidectomy facial nerve paresis. *Laryngoscope* 2002; **112**: 1958-1963 [PMID: 12439162 DOI: 10.1097/00005537-200211000-00009]
 - 15 **Higgins JPT**, Altman DG: Chapter 8: assessing risk of bias in included studies. In *Cochrane Handbook for Systematic Reviews of Interventions*. In: Higgins JPT, Green S, editors. Chichester: John Wiley & Sons Ltd, 2008: 187-241
 - 16 **Roh JL**, Park CI. A prospective, randomized trial for use of prednisolone in patients with facial nerve paralysis after parotidectomy. *Am J Surg* 2008; **196**: 746-750 [PMID: 18757050 DOI: 10.1016/j.amjsurg.2008.04.010]
 - 17 **House JW**, Brackmann DE. Facial nerve grading system. *Otolaryngol Head Neck Surg* 1985; **93**: 146-147 [PMID: 3921901]
 - 18 **Livertox®**. Corticosteroids. Available from: URL: <http://livertox.nih.gov/Corticosteroids.htm>
 - 19 **Dulguerov P**, Marchal F, Lehmann W. Postparotidectomy facial nerve paralysis: possible etiologic factors and results with routine facial nerve monitoring. *Laryngoscope* 1999; **109**: 754-762 [PMID: 10334226 DOI: 10.1097/00005537-199905000-00014]
 - 20 **Wang Z**, Dai CF, Chi F. Retrograde degeneration of the facial nerve after acute traction on parotid gland: an experimental investigation. *Otolaryngol Head Neck Surg* 2002; **127**: 55-59 [PMID: 12161731 DOI: 10.1067/mhn.2002.126720]
 - 21 **Acevedo JL**, Brietzke SE and Coppit GL. Facial Nerve Monitors and Parotidectomy: A Systematic Review. *Otolaryngol Head Neck Surg* 2006; **135**: 63 [DOI: 10.1016/j.otohns.2006.06.329]
 - 22 **Tung BK**, Chu PY, Tai SK, Wang YF, Tsai TL, Lee TL, Hsu YB. Predictors and timing of recovery in patients with immediate facial nerve dysfunction after parotidectomy. *Head Neck* 2014; **36**: 247-251 [PMID: 23766022 DOI: 10.1002/hed.23287]

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