Corticosteroids for herpes zoster: what do they accomplish?
Santee J A

Authors' objectives
To examine the effectiveness and safety of corticosteroids in the treatment of herpes zoster.

Searching
MEDLINE was searched from 1966 to March 2001 for articles published in the English language; the search terms were stated. The reference lists in identified studies were checked for additional studies.

Study selection

Study designs of evaluations included in the review
Reviews, letters editorials and single case reports were excluded, but otherwise, the inclusion criteria were not explicitly defined in terms of the study design. The included studies were non-blinded and double-blinded randomised controlled clinical trials (RCTs), non-randomised controlled clinical trials, and case series.

Specific interventions included in the review
Studies that focused on the use of corticosteroids for treatment or prevention were eligible for inclusion. One study in which all patients received corticosteroids was excluded. The included studies used oral, topical and injectable corticosteroids (intralesional, intrathecal and epidural).

The included studies used the following regimens for herpes zoster: oral prednisone and prednisolone, starting dose from 35 to 60 mg/day, generally tapering over 3 to 4 weeks; oral triamcinolone, 48 mg/day and tapering; corticotropin, 1 mg thrice weekly for 7 weeks; carbamazepine, 400 mg /day for 4 weeks; aciclovir, 4,000 mg/day or 7 to 21 days; radiotherapy; prednisolone or prednisone plus aciclovir; placebo; and no treatment. Various analgesics were also used as cointerventions or controls.

The included studies used the following regimens for herpes zoster ophthalmicus: betamethasone; unspecified corticosteroid; aciclovir ointment (3%) with and without corticosteroids; and dexamethasone (0.01 to 0.1%). Treatment was generally applied five times daily.

The included studies used the following injectable corticosteroid regimens for acute herpes zoster and postherpetic neuralgia: corticotropin, 20 to 75 mg/day; triamcinolone (2 to 80 mg) plus lidocaine, procaine or saline; cortisone; methylprednisolone plus lidocaine, bupivacaine or epidural bupivacaine; intrathecal or epidural methylprednisolone (60 mg) plus lidocaine weekly for 4 weeks; intrathecal lidocaine weekly for 4 weeks; and no intrathecal injection.

Participants included in the review
Studies of people with herpes zoster, postherpetic neuralgia and/or ocular complications of herpes zoster were eligible for inclusion.

Outcomes assessed in the review
Studies that reported effectiveness and tolerability were eligible for inclusion. The included studies assessed acute pain relief, the development of postherpetic neuralgia, and the relief of postherpetic neuralgia.

How were decisions on the relevance of primary studies made?
The author did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Validity was not formally assessed, but some aspects of validity were discussed in the text: the adequacy of information on the intervention; statistical analysis; baseline comparability of the treatment groups; potential confounding by...
cointerventions; aspects of study design; and sample size.

Data extraction
The author did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Information on the study design (whether randomised or blinded), treatment and control, patient characteristics and results were tabulated.

Methods of synthesis
How were the studies combined?
The studies were grouped according to the intervention and a narrative synthesis was undertaken under the headings of oral corticosteroids, topical corticosteroids, and injectable corticosteroids.

How were differences between studies investigated?
Differences between the studies were discussed in the text with reference to aspects of study validity, but heterogeneity was not formally assessed.

Results of the review
Twenty-four studies were included (the number of patients per intervention is given in the results).

Oral corticosteroids for the prevention of postherpetic neuralgia (9 studies including 7 RCTs).
Six studies (5 RCTs with 715 patients and 1 non-randomised trial with 113 patients) found no significant difference in the rates of postherpetic neuralgia between corticosteroids and control. Three small studies (2 RCTs and 1 non-randomised study) that lacked adequate statistical analysis found that corticosteroids prevented postherpetic neuralgia.

Topical corticosteroids (5 studies: 2 RCTs with 119 people and 3 non-randomised studies with 233 patients).
Four studies found that corticosteroids increased the average duration of treatment compared with controls. Three studies found that corticosteroids increased the recurrence rate. Problems with the study quality included: non comparable groups at baseline; no baseline comparison; no information on the timing of the intervention relative to symptom onset; lack of statistical results; insufficient information on the corticosteroid regimen and whether the dose was tapered; and compliance not measured.

Injectable corticosteroids (2 RCTs with 295 patients and 8 case series with 408 patients).
Acute herpes zoster: 3 case series (125 patients) found that corticosteroid injection improved pain within 24 hours in 40 to 100% of the patients with acute herpes zoster, but none assessed the subsequent return of pain. One case series (13 patients) found that after the initial 24 hours, pain returned within 48 hours. Four case series (150 people) found that corticosteroid injection relieved pain in most patients with acute herpes zoster within 35 days, but none of the studies systematically assessed postherpetic neuralgia.

Postherpetic neuralgia: 4 case series found that corticosteroids were less effective in treating postherpetic neuralgia than acute herpes zoster.

Adverse events for injectable corticosteroids: none of the 6 case series noting adverse events reported cases of herpes zoster dissemination. The adverse events reported included: flushing; weight gain; increase in blood-pressure with epidural injection; and haemorrhage, abscesses, moon face and thrombophlebitis with intralesional corticosteroid injection.

Intrathecal corticosteroids for postherpetic neuralgia (2 RCTs, 295 patients): one RCT (25 patients) found that intrathecal steroids significantly reduced pain at 1 and 24 weeks compared with epidural steroid (pain assessed on visual analogue scale, P<0.005). One RCT (270 patients) found that intrathecal methylprednisolone plus lidocaine significantly reduced pain at 4 weeks and 1 and 2 years compared with lidocaine alone and no treatment (difference in
pain assessed on visual analogue scale was about 4 cm on a 10-cm scale, P<0.001).

Adverse events for intrathecal corticosteroids: neither RCT found evidence of biochemical alterations in cerebrospinal fluid. One RCT found no evidence of complications on a magnetic resonance imaging scan. No other adverse events were mentioned.

**Authors’ conclusions**
Most studies of topical and injectable corticosteroids were of a low quality. Findings from two blinded RCTs suggested that intrathecal corticosteroids significantly reduce pain in postherpetic neuralgia, but other authors have suggested that this intervention may have serious adverse events. Injectable corticosteroids should only be used as a last resort and should only be administered by experienced professional.

**CRD commentary**
The review question was clear in terms of the intervention, participants and outcomes, but the inclusion criteria were not defined in terms of the study design. By limiting the literature search to studies published in English and listed in only one database, some other relevant studies may have been omitted. The methods used to select the studies, assess validity and extract the data were not described; hence, the adequacy of the methods used cannot be judged. Validity was not formally assessed, but some of the limitations of the included studies were mentioned in the text: for example, lack of a control group, potential confounding by co-administration of local anaesthetics, lack of information on concurrent medical treatments, and small sample sizes. Some relevant information on the included studies was tabulated, but the design of the included studies and the mode by which the injectable corticosteroids were administered were not stated clearly for all studies. A narrative synthesis was appropriate given the small number of studies. However, in the narration, attention was not drawn to higher quality studies though the deficiencies in the evidence base were discussed. No comment was made on the likelihood that studies reporting no significant difference could be underpowered. The evidence presented appears to support the author’s conclusions although, as the author correctly acknowledged, the evidence base is weak.

**Implications of the review for practice and research**
Practice: The author stated that there is no evidence that corticosteroids prevent postherpetic neuralgia. Any small reduction in pain from oral corticosteroids may be outweighed by harm in people with medical conditions that could be made worse by corticosteroids. The author also stated that topical corticosteroids should be avoided where possible in herpes zoster ophthalmicus. The use of epidural, intramuscular or subcutaneous corticosteroids was not recommended. However, it was recommended that intrathecal corticosteroids be used only for people with postherpetic neuralgia who have not responded to adequate trials of other treatments, and that only trained personnel should perform the injection.

Research: The author did not state any implications for further research.

**Bibliographic details**

**PubMedID**
12358552

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Administration, Oral; Administration, Topical; Adrenal Cortex Hormones /adverse effects /therapeutic use; Clinical Trials as Topic; Drug Administration Schedule; Herpes Zoster /complications /drug therapy; Humans; Injections /methods; Neuralgia /prevention & control; Pain /drug therapy /etiology; Treatment Outcome
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.