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Greater occipital nerve injection in primary headache syndromes – prolonged effects from a single injection

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Abstract

Most patients with primary headache syndromes who have frequent attacks of pain have tenderness in the sub-occipital region. Injection of the greater occipital nerve (GON) with local anesthetic and corticosteroids has been widely used in clinical practice for many years, yet there is no clear understanding of its mechanisms of action. Moreover, there is no current gold-standard of practice regarding GON injections in the management of headache. We audited of our practice to generate hypotheses about the range of primary headaches that might benefit, to determine response rates to power future studies, and to assess whether we should continue to do this procedure. Twenty-six of fifty-seven injections in 54 migraineurs yielded a complete or partial response that lasted for the partial response a median of 30 days. For cluster headache 13 of 22 injections yielded a complete or partial response lasting for a median of 21 days for the partial response. Tenderness over the GON was strongly predictive of outcome, although local anesthesia after the injection was not. The presence or absence of medication overuse did not predict outcome. Apart from two patients with a small patch of alopecia the injection was well tolerated. GON injection is a useful tool in some patients that provides interim relief while other approaches are explored. It is remarkable that in all conditions in which an effect is observed the response time so much exceeds the local anesthetic effect that the mechanism of action may well be through changes in brain nociceptive pathways.

Keywords: Migraine; Cluster headache; Greater occipital nerve

1. Introduction

Patients with primary headaches, such as migraine, complain of pain affecting both the trigeminally innervated anterior regions of the head and the posterior region innervated by the C_2 spinal root. This is thought to be a consequence of the overlap of processing of nociceptive information at the level of the second order neurons as both trigeminal afferents and C_1 to C_2 spinal afferents have been shown to converge upon the trigeminal nucleus caudalis and dorsal horn nuclei of the upper cervical spinal cord (Kerr, 1961; Goadsby and Hoskin, 1997; Bartsch and Goadsby, 2002). Occipital nerve zone tenderness has long been associated with headache syndromes and consequently local anesthetic with or without a steroid has been injected into the region in an attempt to alleviate headache (Hadden, 1940).

The greater occipital nerve (GON), which derives most of its fibres from the C_2 dorsal root, is the main sensory nerve of the occipital area (Bogduk, 1982). The indications for the use of the GON injection are not clear. It has been used for a range of headaches including cervicogenic headache, occipital neuralgia, migraine and cluster headache (Anthony, 1992, 2000; Bovim and Sand, 1992; Peres et al., 2002). We wished to determine the efficacy of the treatment in our practice, examine any features which may predict a response and

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assess whether there were any systematic complications that patients should be warned of as part of the process of informed consent. We had also noted that the positive clinical effect of GON injection seemed to exceed very considerably the half-life of the local anesthetic, and wished to study this issue prospectively. When we noted local alopecia, we immediately reported that effect separately taking the view this was an important finding that patients and doctors should be aware of (Shields et al., 2004). Those patients are also included in the total group in this report.

2. Methods

All patients attending the National Hospital for Neurology and Neurosurgery, London, for a GON injection over a 16-month period were assessed. Two clinicians were involved in administering the injections throughout the period. The injection was offered to patients with various forms of primary Chronic Daily Headache, meaning headache on 15 days or more per month (Welch and Goadsby, 2002), that was relatively treatment-refractory. For our patients this meant failing to respond to at least three preventive classes for a reasonable trial of treatment using standard approaches (Matharu et al., 2003; Lance and Goadsby, 2005).

Patients were asked to fill in a headache diary for one week prior to and four weeks following the injection. On the day of the injection it was noted whether there was any tenderness in the region of the greater occipital nerve and what medications the patients were taking, in particular whether there was any medication overuse. This is defined by the International Headache Society (Headache Classification Committee of The International Headache Society, 2004) as "the use of a triptan or ergotamine on 10 days or more per month and/or the use of analgesics on 15 days or more per month for longer than three months".

A mixture of 3 ml of 2% lidocaine and 80 mg of methylprednisolone was injected 1–2 cm below the midpoint between the occipital tubercle and mastoid process unilaterally in all cases. The injection site was then massaged to spread the solution. The side of injection was determined by clinical symptoms. Sensation to pinprick was noted immediately before and 20 min following the injection. Patients were followed up with a telephone call after four weeks and asked to return their headache diaries.

3. Results

A total of 116 injections were recorded with 101 patients. The breakdown of headache diagnosis (Headache Classification Committee of The International Headache Society, 2004) is shown with caveat that migraine indicates definite (1.1) and probable migraine (1.6; Table 1). The four main groups were migraine (49%), cluster headache (19%), new daily persistent headache (14%) and hemicrania continua (9%).

3.1. Efficacy

The efficacy of response was determined on the basis of the followup phone call and diary. Response was grouped into complete response (pain free), partial response (reduction in severity or frequency of headache by >30%), or no response. Patients were informed that the response to the injection would be variable and unpredictable. Of the 116 injections, 62 (53%) showed some response in the form of pain relief. Twenty-six (22%) resulted in a complete response and 36 (31%) in a partial response (Table 1).

The mean latency of response was 2 days. The mean duration of complete response was 20 days and the median was 7 days (range 1–90 days). The mean duration of partial response was 45 days and the median was 20 days (range 3–420 days).

3.1.1. Migraine

Looking at the migraine group separately, the mean duration of complete response in the group was 9 days with a median of 6-day response. The mean and median duration of partial response was 61 and 30 days, respectively.

3.1.2. Cluster headache

In the cluster headache group, the mean duration of complete response was 17 days with a median of 12 days. The mean and median partial response was 52 and 21 days, respectively.

Table 1
Response of various headache types in 101 patients to greater occipital nerve injections ($n = 116$)

	Migraine[a]	Cluster headache	NDPH	HC	Other
Number of patients	54	19	10	7	11
Number of injections	57	22	16	10	11
Number with complete response	9	10	4	1	2[b]
Number with partial response	17	3	6	5	5[c]

Abbreviations: HC, hemicrania continua; NDPH, new daily persistent headache.
Other: SUNCT-3, Chronic Paroxysmal Hemicrania-3, Chronic post-traumatic headache 2, Cervicogenic headache-2, Low CSF volume headache-1.
[a] *Migraine:* International Headache Society 1.1 and 1.6 (Headache Classification Committee of The International Headache Society, 2004).
[b] SUNCT, 1; CPH, 1.
[c] Cervicogenic, 2; post-traumatic, 2; low CSF pressure, 1.

3.2. Predictive factors

Decrease to pin-prick sensation in the distribution of the GON occurred following 12 of the 23 injections which led to a complete response and 20 of the 35 with a partial response. There was no significant association between response and presence of anesthesia in the distribution of the GON ($\chi^2 = 2$, $P = 0.15$).

All but one of the patients who had some response to the injection were found to have moderate or severe tenderness around the GON prior to injection. There was a significant relationship between tenderness around the GON region and response ($\chi^2 = 3.8$, $P = 0.05$).

Thirty-one of the migraine patients were overusing analgesics or triptans. Twenty of these had a response to the injection. There was no significant relationship between response to injection and medication overuse ($\chi^2 = 1.9$, $P = 0.17$).

3.3. Adverse effects

Relatively few adverse effects were reported. One patient had a vaso-vagal syncopal attack during the procedure. Three patients reported transient dizziness following the injection lasting less than an hour in two patients but lasting 2 days in the third patient. Two cases of alopecia around the injection site were reported (Shields et al., 2004). A typical headache was triggered immediately by the injection in three patients: two with migraine and one with SUNCT. Two patients also felt that their migraines were worse for one to two weeks following the injection.

4. Discussion

Overall 53% of our patients demonstrated a response to the injection. It appears that, compared to the other headache groups, a relatively greater proportion of the cluster headache patients had a complete response although it must be noted that the number of cluster patients was much smaller than the number of migraine patients. The duration of partial response was greater than the duration of complete response for both cluster and migraine groups. Remarkably the time to onset of effect and the duration of effect for all responders, irrespective of diagnosis, and the lack of a correlation between local anesthesia and response, each suggest that any response seen was not simply dependent on the direct local anesthetic effect of the injection.

Previous studies have looked at the response to an injection of steroid and local anesthetic into the occipital nerve region. Saadah and Taylor (1987) performed injections of 1% lidocaine and 12 mg betamethasone into multiple tender points in the vicinity of the occipital nerves in 112 patients with a variety of headaches: tension-type, vascular, post-infection and post-traumatic. They noted a response of prolonged relief in 65% of patients. Anthony looked at methylprednisolone (160 mg) injection into 50 patients with "migraine with unilateral GON irritation" and 86 with occipital neuralgia (Anthony, 1992). Of the migraineurs 88%, and of the occipital neuralgia patients 87%, had a headache response for a mean duration of 32 and 31 days, respectively. Interestingly, Anthony administered an intramuscular injection of 160 mg methylprednisolone and a GON injection of lidocaine to 20 migraineurs and 20 occipital neuralgia patients in order to determine whether local anesthetic alone or systemic steroids are capable of producing a response. Neither measure produced a response for longer than 3 days. In a later study, he found similar results for cervicogenic headache and described a response in all 20 subjects with chronic cluster headache following injection of 160 mg methylprednisolone into the occipital nerve with a mean duration of relief of 32 days (Anthony, 2000). Other studies have also shown a response in cluster headache (Bigo et al., 1989; Peres et al., 2002). Ambrosini and colleagues compared local anesthetic with saline or long-acting local corticosteroid in a double-blind study in episodic ($n = 16$) and chronic ($n = 7$) cluster headache. Ninety percent of the corticosteroid group and only one of the saline patients had a reduction in headache frequency (Ambrosini et al., 2003). These data suggest that the corticosteroid has an important role at least in patients with cluster headache.

Local anesthetic alone injected into GON was used as early as 1940 with documentation of headache relief (Hadden, 1940). More recently, Bovim used lidocaine alone and looked at immediate pain relief which was much more significant in cervicogenic headache than in migraine and tension-type headache (Bovim and Sand, 1992). Bovim also looked at the response to a saline injection into the GON in 16 subjects with cervicogenic headache and found 12 responded but only for 20 min. Caputi demonstrated some response to bupivicaine injected into both GON and supraorbital nerves repeated on alternate days (total of 5–10 injections) in 11 migraineurs (Caputi and Firetto, 1997). It is worth noting that our group of patients included those with intractable headache often resistant to prophylactic medications.

4.1. Predictive factors

It is interesting to note that in our patient group there was no significant association between response and level of anesthesia following injection. There are two possible explanations for this. It may be that

due to the slight degree of anatomical variability we were not injecting exactly into the GON but when the area was rubbed following the injection the steroid dissipated sufficiently enough to reach the GON; we should have detected that during pin-prick testing. Another possibility which we cannot exclude without further placebo-controlled studies is that in those without anesthesia the response is a placebo response. However, consistent with the dissociation between anesthesia and outcome, the effect times far exceeded what would be predicted from the effect of the local anesthetic. Tenderness around the region of the GON was significantly associated with a positive response to the injection. This suggests that tenderness may be useful in selecting out patients who are more likely to respond. It was also interesting to note that analgesia or triptan overuse did not appear to have any affect on response to the GON injection in the migraine group. This suggests that GON injections are a potential treatment for patients who overuse medication and may be particularly helpful during withdrawal of medication.

4.2. Recommendations

It is clear that a placebo-controlled study is required in order to answer some of the questions posed by our findings, and confirm and extend those of Ambrosini and colleagues in cluster headache (Ambrosini et al., 2003). Our practice might be improved by the use of a nerve stimulator, as used by Anthony (2000), to locate the GON which would take into account the degree of anatomical variation of the nerve. We could also consider altering the dose of the steroid component of the injection following results from a suitable study. It is interesting to note that Anthony used a steroid dose twice as large as we do. As mentioned above, we can improve our selection of patients by assessing tenderness in the region of the GON. Our results suggest that GON injection has a place in the management of primary headache and its use is worthy of exploration. Moreover, the data converge in a number of ways to suggest that the effect of the injection is not direct but through an alteration of nociceptive processing and neuroplastic mechanisms within pathways, such as the trigeminocervical relay (Bartsch and Goadsby, 2005), that form an important substrate for each of the primary headaches studied.

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