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Radiofrequency denervation with or without addition of pentoxifylline or methylprednisolone for chronic lumbar zygapophysial joint pain

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Abstract:
Radiofrequency neurolysis of lumbar medial branch is currently the only proven way to treat patients with chronic lumbar zygapophysial joint pain, however, in some patients it can cause transient postoperative pain due to an inflammation caused by trauma of the electrode insertion and the thermal lesion around the target nerves. The aim of this study was to assess the effectiveness of intraoperative injection of methylprednisolone or pentoxifylline in comparison with placebo (saline) to prevent this process. 45 consecutive patients seen by one physician at one pain management clinic were included. Patients were randomly assigned to 3 groups of 15 patients treated with radiofrequency neurotomy procedure with an addition of methylprednisolone, pentoxifylline or saline, respectively, and were observed for 6 months. Pain intensity, summed pain intensity difference, minimum 50% reduction of pain intensity, Patients Satisfaction Score, and local tenderness were determined. The 50% reduction of pain intensity was achieved in 80% of patients one week after the procedure, and at 6 months such results were reported by 60% of patients. There was a significant reduction of pain intensity in all three groups at all time points compared to baseline, however, there were no differences between the three groups. There was a significant difference in local tenderness as a measure of postoperative pain indicating effectivenes of both, methylprednisolone and pentoxifylline. No other complications were noted in any of the patients. Radiofrequency neurotomy is a safe and effective method to treat patients with zygapophysial joint pain. An addition of pentoxifylline and methylprednisolone can reduce postoperative pain commonly appearing within a short time after the procedure, however, neither pentoxifylline nor methylprednisolone influences long-term follow-up results.

Key words:
zygapophysial joints, chronic pain, radiofrequency, methylprednisolone, pentoxifylline

Introduction

Zygapophysial joint pathology, also referred to as the posterior facet syndrome, can account for 16 to 94% of chronic low back pain problems as reported by various authors. However, when diagnostic blocks are used to make the adequate diagnosis the prevalence is estimated at 6–8% [4, 9, 13].

Zygapophysial joints can be a source of pain following injury and damage of the capsule or articular surfaces or in some cases, following fracture of articular processes [1, 7].

The symptoms and signs characteristic of the posterior facet syndrome are: chronic back pain that is localized to one area and to one side. Pain might be experienced in the groin and in the posterior thigh reaching as far as to the knee. The pain is relieved by rest

and made worse by movement. All movements are restricted, especially extension. Plain radiographs demonstrate enlarged posterior facets, approximation of one lamina to the next, decreased distances between the articular processes, diminished disc height, the presence of osteophytes that arise from vertebral bodies, and decreased size of the foramina [7]. Diagnosis is made on the basis of patient's history, physical examination and radiographs and then confirmed by injection of a local anesthetic into the painful joint. Relief of the back pain following such blocks can indicate that these joints are the source of pain.

Each joint is innervated by a pair of nerves: the medial branch of posterior ramus arising at the segmental level and the descending branch of the medial branch from the segment above.

In principle, facet joint pain might be treated by radiofrequency denervation of the painful joints and lumbar medial branch radiofrequency lesion is the only treatment proven to be able to relieve lumbar zygapophysial joint pain [1, 3].

Radiofrequency has the advantage that the procedure is technically simple and safe with very few complications [6], however, increased tenderness, pain and limitation of movement can be observed due to the trauma of the electrode insertion and the thermal lesion around the target nerves [2, 14]. These symptoms are due to inflammation caused by release of inflammatory mediators including proinflamatory cytokines. The use of drugs having anticytokine action such as corticosteroids or pentoxifylline administered preemptively can lead to a decrease in inflammation and alleviation of subsequent symptoms.

The aim of this study is to assess the effectiveness of intraoperative injection of methylprednisolone or pentoxifylline in comparison with placebo (saline) to prevent postoperative inflammation caused by radiofrequency lesion.

Materials and Methods

The study population consisted of 45 consecutive patients seen by one physician at one pain management clinic. The eligible patients had to be aged between 18 and 85, and had to have chronic low back pain not responding to conservative therapy of longer than 6 months duration. They had to present clinical features consistent with possible lumbar zygapophysial joint pain, such as pain over more than two lumbar segments unilaterally and had to have significant pain relief after two controlled diagnostic blocks. Exclusion criteria were pregnancy, prior low back surgery, compensable disability, alcohol abuse, psychiatric disorders and ongoing litigation. According to the regulations, an approval was obtained from Bioethics Commission of the Jagiellonian University.

One week after the completion of diagnostic blocks and directly before radiofrequency medial branch neurotomy, the baseline values of pain intensity were estimated using Visual Analogue Scale (VAS) – a ten centimeters long line, whose ends are labeled with descriptors of the extremes of subjective category: "least possible pain" and "worst possible pain". Pain intensity was then assessed at 3 time points during the study (1 week, 1 month and 3 months after the procedure) and at the end of the follow-up period (6 months after the procedure) and number of patients with minimum 50% reduction of pain intensity was calculated. At the end of the follow-up period, Patient Satisfaction Score – overall patient's assessment of treatment classified in one of four categories (very good, good, moderate, fair) was obtained and summed pain intensity difference (SPID) was calculated. The latter constituted the sum of pain intensity differences during a defined study period, time-weighted by multiplying by the time since the last measurement. To indicate the presence of postoperative inflammation at each time point during the study, local tenderness was measured and this was the patient's assessment of pain upon palpation in comparison to the contralateral side expressed as mild, moderate or severe.

Radiofrequency medial branch neurotomy was performed with the patient prone on fluoroscopy table. The skin over lumbar region was prepared in a sterile fashion. The skin was infiltrated over entry points with 1% lidocaine, and 10 mm pole needles were introduced unilaterally to reach target zone at L3, L4, L5 and S1 level. The correct position of the needle was checked by radiological screening in an oblique plane. With a radiofrequency generator (Neuro Therm Radio Frequency Lesion Generator model JK2 RDG Medical) on stimulation mode, the uninsulated tip of the needle was used to stimulate targeted nerves at frequency 100 Hz. After achievement of pain or strong paresthesia, frequency was changed to 2 Hz to ensure that motor contractions were not elicited. Once the needle was in a satisfactory position, 1 ml of 1%

Tab. 1. Baseline patients' characteristics

	Methylprednisolone group (n = 15)	Pentoxifylline group (n = 15)	Saline group (n = 15)	All patients (n = 45)
Male/Female: No	8/7	7/8	8/7	23/22
Age, years: mean ± SD (range)	65.87 ± 4.56 (44–81)	66.93 ± 11.74 (59–71)	66.40 ± 9.58 (44–82)	66.40 ± 8.94 (44–82)
Pain duration, years: mean ± SD	4.60 ± 2.72	4.07 ± 2.31	3.87 ± 2.39	4.18 ± 2.44
VAS score, cm: mean ± SD	6.57 ± 1.08	6.67 ± 1.23	6.37 ± 0.77	6.53 ± 1.03

Differences between groups are not significant

Tab. 2. VAS score values expressed in centimeters measured at baseline and at four time points: 1 week, 1 month, 3 months and 6 months after the procedure

	Methylprednisolone group (n = 15)	Pentoxifylline group (n = 15)	Saline group (n = 15)	All patients (n = 45)
VAS – baseline mean ± SD	6.57 ± 1.08	6.67 ± 1.23	6.37 ± 0.77	6.53 ± 1.03
VAS – 1 week mean ± SD	2.87 ± 1.06 *	3.13 ± 0.99 *	3.5 ± 1.32 *	3.17 ± 1.14 *
VAS – 1 month mean ± SD	3.5 ± 1.5 *	3.2 ± 0.88 *	3.1 ± 0.76 *	3.27 ± 1.09 *
VAS – 3 months mean ± SD	3.5 ± 1.52 *	3 ± 0.98 *	3.07 ± 0.42 *	3.19 ± 1.07 *
VAS – 6 months mean ± SD	3.9 ± 1.54 *	3.13 ± 0.99 *	3.27 ± 0.46 *	3.43 ± 1.12 *

* Differences statistically significant compared to baseline ($p < 0.001$).

Tab. 3. Summed pain intensity difference (SPID) – the sum of pain intensity differences during defined study period time-weighted by multiplying by the time since the last measurement

	Summed pain intensity difference mean ± SD
Methylprednisolone group	17.35 ± 6.54
Pentoxifylline group	21.42 ± 6.27
Saline group	19.07 ± 4.97
All patients	19.28 ± 6.07

Differences between groups are not significant

Tab. 4. Patient Satisfaction Score – patient's assessment of pain estimated 6 months after the radiofrequency denervation

	Methylprednisolone group n (%)	Pentoxifylline group n (%)	Saline group n (%)	All patients n (%)
4 (very good)	6 (40.0)	5 (33.3)	6 (40.0)	17 (37.8)
3 (good)	6 (40.0)	9 (60.0)	6 (40.0)	21 (46.7)
2 (moderate)	3 (20.0)	1 (6.7)	3 (20.0)	9 (15.6)
1 (poor)	0 (0)	0 (0)	0 (0)	0 (0)

Differences between groups are not significant

lidocaine was injected through the needle to anesthetize target nerve and surrounding tissue. A lesion was made by rising the temperature of the tip of the needle to 85° for 60 s. After the lesion at each level, before the needle was removed, methylprednisolone, pentoxifylline or saline was injected to protect from postoperative pain attributable to the trauma of the electrode insertion and the thermal lesion around the target nerves.

All patients were randomly divided into three groups with 15 patients in each group. Group I (n = 15) consisted of patients receiving locally 1 ml of solution of 10 mg methylprednisolone (Depo-Medrol, Jelfa, Poland) in saline. Group II (n = 15) consisted of patients receiving locally 1 ml of solution of 10 mg pentoxifylline (Polfilin, Polfarma, Poland) in saline. Group III (n = 15) consisted of patients receiving locally 1 ml of saline.

Statistical analysis

Analysis of variance (ANOVA) was performed to compare the baseline values of age, pain duration and VAS score. Scheffe test was applied for the *post hoc* analysis. The results in all groups at week 1, month 1, 3 and 6 were compared with baseline values using paired Student's *t*-test or Wilcoxon rank-sum test when appropriate. Mean VAS score reduction was calculated. Differences between groups at each time point were detected using analysis of variance (ANOVA) or chi-square test for categorical data. Statistical significance was set at the $p < 0.05$ level. All the statistical calculations were performed using the STATISTICA software.

Results

As shown in Table 1, overall gender distribution was 23 male and 22 female patients, age ranged from 44 to 82 years and the mean duration of pain (mean ± SD) was 4.18 ± 2.44 years with no statistically significant difference among the groups. All patients were included in the efficacy analysis during the whole follow-up period. There were no statistically significant differences in baseline VAS scores between the groups.

VAS score

The mean VAS score values (mean ± SD) at baseline and at four time points: 1 week, 1 month, 3 months and 6 months after the procedure are shown in Table 2. There was a significant reduction of the VAS score in all three groups at all time points compared to baseline ($p < 0.001$). However, there were no differences in pain relief between the three groups (Tab. 2).

Summed pain intensity difference

The mean values (mean ± SD) of the SPID score are shown in Table 3. There were no significant differences between the groups, however, the high values indicate a great pain relief in all three groups.

The ≥ 50% reduction of pain intensity

The ≥ 50% reduction of pain intensity was achieved in 80% of patients (n = 36) after the procedure and was observed in 60% of patients 6 months later (n = 27).

Patient Satisfaction Score

84.4% of patients obtained very good and good results in Patient Satisfaction Score. None of the patients reported poor results. There were no significant differences between the three groups of patients (Tab. 4).

Local tenderness

In saline-injected group, there were 26.7% of patients with severe local tenderness (n = 4) one week after the procedure which disappeared at the second assessment (after one month) in 3 patients and in 1 patient persisted with mild intensity. In methylprednisolone group there were no patients with severe tenderness and only 20% of patients (n = 3) reported mild tenderness which disappeared within a month ($p < 0.05$ compared to saline). In pentoxifylline group 13.3% (n = 2) of patients reported mild tenderness which also disappeared within a month ($p < 0.05$ compared to saline).

Other complications

Patients were evaluated for various types of complications, including infections, rash reaction, subarachnoid blockade, and weight gain. No complications were noted in any of the patients in any one of the three groups.

Discussion

Radiofrequency neurotomy has been proven to be an effective procedure in a number of clinical trials. First study was conducted by North et al. in 1994 where in a retrospective way 42 patients were included and 45% of them reported at least 50% reduction of pain intensity. Also in 1994 Gallagher et al. conducted the first prospective controlled study in which he proved the superiority of radiofrequency neurotomy over placebo assessed at 1 and 6 months after the procedure [5, 11]. The results were confirmed by van Kleef in 1999 in a randomized controlled trial on 31 patients, where radiofrequency neurotomy resulted in a significant alleviation of pain and reduction of functional disability both on a short-term and long-term basis [15]. Dryfuss et al. stated that approximately 60% of patients can expect at least 80% relief of their pain at 12 months and 80% of patients obtain at least 60% relief [3].

As reported by other authors, radiofrequency appears to be a safe procedure. One study found the overall serious complication rate to be 0.4 per cent [6]. However, many patients complain of a transient increase in lumbar pain after radiofrequency lesioning of the medial branch [16]. It is manifested as a local tenderness and increase in pain intensity reported to appear in 10–20% of patients [2, 14]. Local tenderness in the area of the denervation with or without protective muscle spasm is transient but may last a few weeks [18]. It is believed that thermal nerve damage can lead to a subsequent neural inflammation where mediators responsible for pain and hyperalgesia are released. These include proinflamatory cytokines, nitric oxide, cyclooxygenase-2, phospholipase A2, tromboxanes and others [17]. There are multiple sites and situations where immune system-derived proteins – tumor necrosis factor, interleukin-1, interleukin-6 are correlated with and probably causative of neuropathic pain conditions. There have been few approaches to cope with this problem. Some advocate the use of corticosteroid injections to decrease postoperative pain [12, 16]. In another study, patients were provided with 20 tablets of 5 mg hydrocodone (1–2 tablets every 8 h) for relief of pain [3]. In our study, to prevent this process we locally injected methylprednisolone or pentoxifylline as both of these drugs have an anti-inflammatory action [10, 19]. The influence of pre-injury pentoxifylline on the development of post-injury nociception in animals and patients was already assessed by Wordliczek et al. [19]. Those results confirm the hypothesis suggesting that it is possible to modulate nociception through preemptive administration of a non-specific cytokine inhibitor – pentoxifylline [19].

In our investigation there was no difference between the groups of patients receiving methylprednisolone, pentoxifylline or saline intraoperatively on pain intensity after the procedure, however, Manchikanti showed in a group of 180 consecutive patients that methylprednisolone added to local anesthetics in nerve blockade of the medial branch led to longer pain alleviation [8]. This could suggest that intraoperative administration of methylprednisolone or pentoxifylline can improve the overall effect of radiofrequency. However, in our study only SPID score indicated that the results tended to be better in pentoxifylline group, but the difference was not statistically significant.

Our investigation shows that the highest number of patients with severe local tenderness was in saline-injected group, but only in 1 patient it persisted longer than one month. The results correspond with those described by other authors [2, 14]. Regardless of small sizes of the groups in the population examined in this study, it appears that administration of not only methylprednisolone but also pentoxifylline reduces the occurrence of postoperative pain that might indicate the role of proinflamatory cytokines in the development of post-injury nociception.

In conclusion, our study confirmed previous results and demonstrated that radiofrequency medial branch neurotomy was an effective method to treat low back pain originating from the zygapophysial joints. Intraoperative local injection of both methylprednisolone and pentoxifylline did not significantly influence the outcomes of the procedure, however, it tended to decrease the frequency of postoperative pain that manifested as local tenderness and soreness. Nevertheless, the small number of patients in the groups under study does not allow to draw definite conclusions.

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