Duloxetine Combined with Nerve Block for Cervical Headache with Anxiety Depression

Qing Wang; Xiangyong Li; Ya Guo; Yan Pan; Yanqing Liu

Abstract

Objective: To investigate the effect of duloxetine and nerve block in cervical headache with anxiety depression.

Methods: 60 patients with cervical headache, anxiety and depression in the pain department of our hospital were randomly divided into control group and treatment group, with 30 patients in each group. The control group was treated with a cervical nerve block, and the treatment group was treated with a cervical nerve block in combination with duloxetine. Before and after treatment, both groups used the visual analog rating scale (Visual Analogue Scale, VAS) and sleep quality (Quality of Sleep, QS) to evaluate the improvement of pain degree and anxiety and depression, evaluate the clinical treatment effect and observe adverse effects.

Results: VAS, scores and QS were lower than before treatment (P<0.05), and VAS and QS were significantly lower than the control group (P<0.05). Neither group had any serious adverse effects.

Conclusion: Duloxetine combined with nerve block can effectively treat cervical headache combined with anxiety and depression. The combined treatment has better effect than single therapy, safe and effective, and is worthy of clinical promotion and application.

Keywords: Duloxetine; Nerve block; Cervical headache; Anxiety and depression.

Introduction

Clinically, the incidence of Cervical Headache (CEH) is high, but due to the lack of understanding of the disease and not timely and effective treatment, many become chronic pain, repeated attacks and often accompanied by anxiety and depression, seriously affect the patient's mood, sleep, life and work. In the past, CEH was mostly treated by nerve block, drugs and physiotherapy, and more attention was not paid to the treatment of CEH with anxiety and depression, resulting in poor treatment effect, slow pain relief or poor curative effect. Duloxetine is a serotonin (5-HT) and Norepinephrine (NE) reuptake inhibitor recommended by the International Pain Society for treating a variety of neuropathic pain and effectively relieving the negative emotions associated with pain [1]. There are few reports of nerve block combined with duloxetine in CEH with anxiety depression. Therefore, this paper aims to explore the clinical efficacy and safety of duloxetine combined with nerve block in CEH with anxiety and depression, as reported below.
sion in the pain department of our hospital, all of which met the CEH diagnostic criteria of the International Headache Committee in 1998. All patients had the first definite diagnosis of CEH with anxiety and depression, and had no excessive loxetine combined with nerve block therapy. The patients were randomly divided into two groups: 30 controls, 13 males, 17 females; age (37±11) years, duration of disease (3.6±2.6) years; treatment group, 14 males, 16 females; age (36±11) years and duration of disease (3.3±2.5) years. There was no significant difference in age, gender and disease duration between the two groups (P>0.05), and it was comparable. The disease duration of our patients was a minimum of 3 months and a maximum of 11 years.

**Inclusion criteria:** CEH diagnosis of more than 3 months, limited neck movement, improper neck activity and/or head position or compression of the upper neck or occipital side, aggravated headache symptoms; non-radicular pain in neck, shoulder, or upper limbs with anxiety and depressive symptoms; cervical MRI examination with cervical degeneration, swelling or protrusion, but no nerve root compression and intracranial lesions. All patients were not treated with excessive loxetine and nerve block.

**Exclusion criteria:** Pregnant or lactating women; other headaches (migraine, cluster headache, sinusitis, etc.); patients with severe organic diseases such as cardiovascular, liver and kidney, tuberculosis, tumor, bone destruction, severe osteoporosis and mental illness; patients with infection and hemorrhagic diseases; patients with other hormone therapy contraindications; patients who had head and neck nerve block in the recent 3 months; patients with obvious cervical lesions or nerve root compression; patients with incomplete treatment plan or follow-up.

**Treatment methods**

Control group: According to the pain using pillow, small, ear nerve block: patients sit, arms cross on the pillow, neck, forehead on the forearm, fully expose the pillow and neck, occipital and ear breast connection inside 1/3 (occipital nerve), 1/3 (small occipital nerve) and 2 cm (ear nerve) after needle point, marking and conventional disinfection, towel, wear sterile gloves. After puncture to the bone with 5 ml syringe, it was slightly reduced to induce anaesthesia as much as possible. After rebleeding, anti-inflammatory and analgesic complex [1 ml of lidocaine hydrochloride, 1 ml of compound betamethasone injection (1 ml/dose, Belgium Schering-Plough Labo N.V.), Dilate to 5 ml with normal saline], injected 2.5 ml of each site, press locally after needle extraction, and instructed the patient to keep the injection site clean for 48 h. Once every 2 weeks for 1 month.

**Observation group:** in addition to the same nerve block, oral duloxetine (specification: 60 mg/pill, imported drug registration number: H20110320, manufacturer: Eli Lilly and Company), administration method: 60 mg 1 time/d, a course of 4 weeks, then the dose was gradually reduced to withdrawal.

**Observational indicators:** All patients were assessed by VAS score 1 week before, 2 weeks and 1 month after treatment (0: no pain, 1-3: mild pain, 4-6 points: moderate pain, 7-9: severe pain, 10: unbearable pain); sleep quality assessed by sleep quality (QS) score (0: no effect on sleep, 5: no sleep at all); also, observed and recorded adverse reactions, such as dizziness, drowsiness, gastrointestinal reaction, constipation and perih-

**Results**

1. **Comparison of the VAS scores between the two groups before and after treatment**

There was no significant difference VAS scores between the two groups in pretreatment (P>0.05). The VAS scores of two groups at 2 weeks and 1 month after treatment were significantly lower than before treatment (P<0.05). The VAS score of the treatment group was significantly lower than the control group at 2 weeks and 1 month after treatment (P<0.05). Results are shown in Table 1.

2. **Comparison of the QS scores between the two groups before and after treatment**

There was no significant difference in pre-treatment QS scores between the two groups (P>0.05). Group 2 was significantly lower than before treatment (P<0.05); and the treatment group was significantly lower than the control group (P<0.05). Results are shown in Table 2.

3. **The occurrence of adverse reactions of the two groups**

The adverse effects in both groups were very mild, and two cases in the control group had transient dizziness after the first treatment, rested for half an hour, and the symptoms disappeared. In the treatment group, 2 cases had dizziness and nausea at the beginning of treatment, and 1 case showed dry stool. With the passage of treatment time, the adverse reactions gradually decreased or disappeared, without affecting the normal life and work, and without corresponding treatment.

**Discussion**

At present, with the change of people’s living and working style, the occurrence of CEH has increased significantly, and it

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**Table 1:** Comparison of the VAS between the two groups before and after treatment.

<table>
<thead>
<tr>
<th>Time</th>
<th>Control Group</th>
<th>Treatment Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pretherapy</td>
<td>6.30±1.03</td>
<td>6.55±0.96</td>
</tr>
<tr>
<td>Two weeks after treatment</td>
<td>2.60±0.60*</td>
<td>2.05±0.58△*</td>
</tr>
<tr>
<td>Four weeks after treatment</td>
<td>1.05±0.60*</td>
<td>0.55±0.51△*</td>
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</tbody>
</table>

P<0.05, compared with pretreatment; △P<0.05, compared with the control group.

<table>
<thead>
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<th>Time</th>
<th>Control Group</th>
<th>Treatment Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>pretherapy</td>
<td>3.50±0.76</td>
<td>3.50±0.67</td>
</tr>
<tr>
<td>Two weeks after treatment</td>
<td>1.50±1.0*</td>
<td>0.82±0.73△*</td>
</tr>
<tr>
<td>Four weeks after treatment</td>
<td>1.10±0.91*</td>
<td>0.55±0.51△*</td>
</tr>
</tbody>
</table>

P<0.05, compared with pretreatment; △P<0.05, compared with the control group.

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**Discussion**

All statistical analysis was performed by SPSS 16.0 statistical software, measurement data were expressed as mean ± SD, group comparisons were performed by t-test, and P<0.05 indicates a statistically significant difference.
has attracted more and more attention from the medical community. Since all head and facial structures are innervated by the trigeminal and C1-4 spinal nerves, most headaches may be associated to pathological changes in the cervical spine. Peng Baogang, et al. [2]. The degenerated intervertebral disc can produce phospholipase A2, interleukin 1 and 6, tumor necrosis factor, and many other inflammatory mediators. The inflammatory mediators can directly stimulate nerve pain, also can lead to the nerve innervation area of muscle, blood vessels and other soft tissue inflammation, cause neck soft tissue spasm, ischemia, hypoxia and the release of inflammatory mediators, these inflammatory mediators and in turn stimulate nerve endings, lead to a vicious cycle of pain-inflammatory mediators-pain [3-6]. In addition, long-term desk work or improper use of the pillow makes the neck muscles in a long-term tension, cervical spine dynamic balance system disorder, resulting in abnormal physiological radian of the cervical spine, so that the posterior occipital tendons arch tension contracture, resulting in increased internal pressure of the bone-fiber tube, at the same time, the neck muscle, fascia strain, so that aseptic inflammation of the neck. CEH recurrent attacks, leading to patients with anxiety and depression, such as emotional disorders, clinical CEH, often accompanied by anxiety and depression. Therefore, in this group, duloxetine combined with nerve block therapy achieved satisfactory efficacy, and no obvious adverse reactions occurred.

Currently, nerve block is the most common treatment for CEH in the world, including large occipital nerve, small occipital nerve, large auricular nerve and high paracervical block. Nerve block drugs mainly include local anesthetics and glucocorticoids [7]. Glucocorticoids can not only eliminate aseptic inflammation, inhibit the production of prostaglandins, but also can eliminate edema, improve local blood circulation and metabolic disorders, thus blocking the vicious cycle of pain. Local anesthetics can not only quickly relieve muscle tension, but also effectively relieve pain. Duloxetine [8-10]. It is a potent inhibitor of 5-HT and NE reuptake (SNRIs) recommended by IASP for a variety of pain, such as trigeminal neuralgia, diabetic peripheral neuralgia and chronic musculoskeletal pain. Numerous studies have proved that the optimal analgesic dose of duloxetine is 60 mg/d, with high patient compliance. Its analgesic mechanism may be to enhance neurotransmitter transmission by inhibiting the reuptake of 5-HT and NE by neurons in the brain and spinal cord, enhance the function of descending inhibitory pathway, restore the balance of downward inhibition and facilitation system, and reduce the upload of spinal pain signals and increase the body’s tolerance to pain. Duloxetine also improves sleep quality and improves affective disorders such as anxiety and depression. Clinical trials have shown that duloxetine can break the vicious cycle of "pain-anxiety-depression-pain", with more severe pain levels in patients [11,12].

In this study, the VAS score decreased and sleep time was prolonged in the control group compared with before treatment, indicating that the application of nerve block alone can effectively relieve pain, and the treatment effect is positive, which is consistent with previous reports [6,7]. However, compared with the control group, the VAS and QS scores decreased more significantly after the treatment. In addition, the patient’s anxiety and negative mood were also significantly improved, indicating that nerve block combined with duloxetine in CEH combined with anxiety and depression is better than a single nerve block. The combination of multiple methods for treating CEH is the current treatment trend. The effect of duloxetine combined with nerve block in CEH combined with anxiety and depression is satisfactory, and the sleep quality of patients is significantly improved, which can effectively prevent and reduce the recurrence of neuropathic pain, and improve negative emotions such as depression and anxiety, which is similar to previous reports in China [9,10].

Conclusion

In conclusion, the treatment of CEH with duloxetine and anxiety and depression is better than nerve block alone, which improves the clinical treatment effect, has good patient tolerance, high safety, and does not increase the incidence of adverse reactions. It is an effective clinical treatment method, which is worthy of further promotion and application.

Conflict of interest: All the authors declare that there is no conflict of interest.

References