

Curative effect research on curing intercostal neuralgia through paravertebral nerve block combined with pregabalin

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Abstract: This paper aimed to discuss the curative effect and safety of curing intercostal neuralgia through paravertebral nerve block combined with pregabalin. 90 cases of patients diagnosed as intercostal neuralgia were taken as research object. Random number method was used to divide the patients that is conforming to the inclusion criteria and exclusion criteria into 3 groups. 30 cases was in group A (oral lyrica), 30 cases was in group B (paravertebral block only) and 30 cases was in group C (paravertebral block combined with pregabalin). The clinical effect and safety of three groups was compared. The result showed that: visual analogue scale (VAS) and quality of sleep (QS) of three groups of patients after treatment all decreased obviously; group A had slow work, large amount of dosage and many adverse effects; group B had quick work, but the improvement on pain and sleep was not satisfactory; the curative effect of group C was higher than group A and B ($p < 0.05$); 3 groups all had adverse effect, among which group C had the least adverse effect. It can be concluded that paravertebral nerve block combined with pregabalin for curing intercostal neuralgia was superior than single use of pregabalin or paravertebral block and that is worth to promote.

Keywords: Paravertebral nerve block; Pregabalin; Intercostal neuralgia.

INTRODUCTOIN

Intercostal neuralgia is the inflammatory reaction produced by the damage on thoracic nerve caused by different reasons. It is the common complication after clinical thoracic surgery with a high incidence and syndrome of intercostal space or abdomen showing banded pain occurs (Simmons *et al.*, 2012; Yong *et al.*, 2013; Huan *et al.*, 2012). It brings pain not only on body and spirit but also on physiology, which affect the recovery of patients. It mainly represents to be the recurring pain occurring at one or several intercostal areas, and it is always persistent. Sometimes paroxysmal aggravation occurs. Sneezing, breathing, cough etc maybe intensify the pain. The pain sometimes is distributed in bunch of ribbon. When it is serious, dragging pain on the shoulder and back, or hyperesthesia on corresponding intercostal area of skin, rib edge tenderness, invariant skin color has no swelling generally. It is divided to be secondary and primary neuralgia (Xiangyun, 2007), primary neuralgia is extremely rare □ secondary neuralgia is mainly related with virus infection, toxins stimulation, mechanical damage and foreign oppression. Modern research sometimes considers that therapeutic effect of primary intercostal neuralgia is not very ideal (Lei *et al.*, 2013), it is mainly because of taking nerve nutrition drugs or adopting diet therapy and medicinal food. Vertebral nerve block is also a kind of effective analgesia method and could protect lung very good (Yanyan, 2012). Research of Miller V (Miller *et al.*, 2012) *et al* showed that the effect of applying paravertebral block and nimesulide tablets for treatment was more obvious than that of

applying paravertebral block only. In the Curative Effect Observation of Curing Postherpetic Neuralgia through Acusector Combined with Pregabalin, Wang Wenjuan (Wenjuan *et al.*, 2013) *et al* found that curing postherpetic neuralgia through acusector combined with pregabalin was more safe and effective. Research of Huang Renshui *et al* (2013) also showed that the curative effect of drugs connected with nerve block was superior than single use of one method. Thus this research has adopted different method to perform further treatment for 90 patients with intercostal neuralgia between 2012 June and 2014 June. Now results are concluded as following.

MATERIALS AND METHODS

General Data

90 patients who were suffered from intercostal neuralgia and hospitalized in our hospital between 2012 June and 2014 June are selected. There were 46 male patients, and 44 female patients. Their age was between 34 and 67 years old . All the disease cases were adopted with lottery approach and randomly divided into 3 groups. The number between 1 and 30 indicates it is group A, for 31~60, it is group B and for 61~90, it is group C. Inclusion criteria: (1) when all symptom disappear, the pain was still lasting for more than 3 month; (2) local skin of site of puncture of patients with paravertebral block had no ulceration, swelling and any other inflammation; (3) all patients are volunteer to participate in this research and signed the written informed consent. Exclusion criteria: (1) incompetence of liver, kidney, heart; (2) coagulation disorders were erupted simultaneously; (3) cases that occurred pneumothorax, intravascular injection of local anesthetic, no effect of block, etc in and after

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operation process; (4) cases that had language communication barriers, dysgnosis, etc and can not communicate effectively with medical staff. In addition, the weight, gender, age and involved area of patients in three groups had no statistical meaning ($P>0.05$).

Therapeutic method

Group A: Pregabalin is taken orally at the first day (trade name is Le Ruika, Pfizer pharmaceutical Co., LTD.), its dose is 75mg each time, 2 times a day, then it will be increased to 150mg each time, 2 times a day according to efficacy and tolerability within one week. For these patients whose pain is not fully eased after 2~4 weeks, if they are tolerant to this product, its dose should be increased to 300mg each time, 2 times a day, or 200 mg each time, three times a day (600mg). If drug withdrawal is needed, it should be performed one week before withdrawal. Group B: According to affected nerve localization, paravertebral nerve block is performed under the guidance of peripheral nerve stimulator. Drug formulations: 0.75% Ropivacaine (Commodity name Naropin, Astrazeneca PLC) 5ml+compound betamethasone (Commodity name: Diprospan, Schering plough) 1ml + vitamin B12 1mg, it is diluted to 20ml with physiological saline. Intrathecal injection about 4~6ml is performed for each segment, once a week. Diprospan would reduce into half gradually from the second week; one course contains 3 times. Group C: Paravertebral block method is applied as group B. Stating from the day of block, pregabalin tablet is taken every day, and its dosage will be increased according to the condition of pain. Nerve block operation in group B and C is accomplished by the same physician alone.

Observational indexes

Evaluation for pain degree: Visual analogue scale method (VAS) is adopted for all patients after 1, 3, 6 weeks treatment during referral, pain self-report is performed by patients themselves, the degree of pain ease is recorded (the score is around 0~10, 0 indicates there is no pain, 10 refers to the unbearable pain).

α Patients' sleep quality is evaluated (0 indicates that sleep is not influenced, 5 score indicates that sleep is unavailable completely). Adverse reactions related to medicine in the course of therapeutic process are observed at the same time: dizziness, drowsiness nausea, peripheral edema. Total number of cases that represent adverse reactions is recorded in statistics within six weeks.

Clinical curative effect

Comprehensive evaluation is performed for patients' pain and visual analogue scale (VAS), sleep quality scale (QS), patients' clinical curative effect is determined. Among these patients, their VAS has dropped to 0~3 score or their QS has dropped to 0~1 score, then it is considered to be excellence treatment. That patients' VAS drops to

4~6 score or their QS drops to 2 score indicate that the treatment is effective. $VAS \geq 7$ score or $QS \geq 3$ score indicate that the treatment has no effect. The writer in this research think that the treatment is always effective = (the number of excellence cases + the number of effective cases) / total number of treatment medical history $\times 100\%$.

STATISTICAL ANALYSIS

SPSS 13.0 software is adopted to perform statistic analysis, measurement data is denoted with mean \pm standard deviation ($\bar{x}\pm s$), comparison among groups adopts group t test. Comparison for count data is performed through adopting χ^2 test, comparison among groups adopts variance analysis, $P \leq 0.05$ indicates it has statistical significance.

RESULTS

VAS evaluation score and comparison in three groups

Comparison within group, $*P \leq 0.05$; comparison between groups: comparing with group A, $\#P \leq 0.05$, $\square P \leq 0.01$, comparing with group B, $\blacktriangle P \leq 0.01$ As it is shown in table 1, VAS score evaluation in three groups after treatment is lower than it before treatment. On the sixth week of treatment, VAS of patients in group C is significantly lower than that of patients in group B and group A after treatment, VAS in group B is the highest. It demonstrates that under the treatment method of using single means, using pregabalin could decrease visual analogue scale (VAS) more than applying vertebral nerve block, the difference has statistical significance ($P < 0.0050$).

QS comparison among three groups

Compared with the condition before treatment, $*P \leq 0.05$; comparison among groups: comparison with group A, $\#P \leq 0.01$, comparison with group B, $\square P \leq 0.01$ As it is shown in table 2, QS score evaluation of three groups after treatment is lower than that before treatment. On the sixth week of treatment, QS of patients in group C is significantly lower than that of group B and A, QS in group B is the highest. It illustrates that under the treatment method of using single means, using pregabalin could decrease sleep quality scale (QS) more than applying vertebral nerve block, the difference has statistical significance ($P < 0.005$).

Comparison of dosage in pregabalin treatment group A and C

Comparison with group A, $*P < 0.01$ As it is shown in table 3, dosage in group A is significantly more than group C and dosage of group A has increased gradually, dosage of group C first represents increase and then decrease.

Table 1: VAS evaluation score before and after treatment among three groups of patients

Group	N	Before treatment	After treatment		
			1 week	3 weeks	6 weeks
A group	30	94.58±0.02	47.56±0.73*	31.74±0.27*	26.46±0.71*#
B group	30	91.93±0.69	43.16±0.29*#	36.56±0.73*#	34.48±0.72*
C group	30	94.35±0.91	26.46±0.27*□▲	20.29±0.06*□▲	12.35±0.85*□▲

Table 2: QS score evaluation among 3 groups of patients before and after treatment

Group	N	Before treatment	After treatment		
			1 week	3 weeks	6 weeks
A group	30	5.07±0.4	4.14±0.34*	2.89±0.29*	2.7±0.84*
B group	30	5.03±0.44	3.92±0.32*	3.03±4.73*	2.78±0.45*
C group	30	5.08±0.39	2.1±0.2*□▲	0.9±0.17*□▲	0.59±0.13*□▲

Comparison for the number of patients with adverse reaction disease among three groups

Comparison with group A, *P<0.05 As it is shown in table 4 the number of cases with adverse reaction among 3 groups of patients: adverse reaction of dizziness and drowsiness in group B and C is significantly lower than group A (P<0.05). Comparison for adverse reaction of peripheral edema and nausea among group A, B and C has no statistical significance (P>0.05).

Comparison for clinical curative effect under three methods

As it is shown in table 5, it is the clinical curative effect of patients under 3 therapeutic methods. The total effective rate of patients in group C (93.3%) is significantly higher than group B (80%) and A (83.3%). Pain of patients in group B would be eased immediately after accomplishing block, mild pain onset starts on the last half of the week. Six weeks later, its effect is significantly lower than group A (P<0.05). In group A, pain evaluation score of patients could be effectively reduced on the second day, but the final dosage has significantly increased. Oral dosage of pregabalin in group C is significantly lowers than group B.

Table 3: Comparison of dosage in pregabalin treatment group (x ± s)

Group	1 week	3 weeks	6 weeks
Group A (n=30)	425±50	575±75	700±95
Group C (n=30)	210±25*	275±40*	230±35*

DISCUSSION

Intercostal neuralgia is the relatively more common complication, it is maybe because of diseases such as thoracic vertebra degeneration, thoracic tuberculosis, thoracic injury, thoracic spinal pachymeningitis, tumor, ankylosing spondylitis or pathological changes in rib, mediastinal, pleura. The oppression, stimulation generated on intercostal nerve because of above disease is related with inflammatory reaction (Sica *et al.*, 2012; Lamm *et al.*, 2012; Singh *et al.*, 2012; Wilcox *et al.*, 2012).

Pregabalin is a new kind of calcium ion channel regulator, and the structural analogues of inhibitory neurotransmitter. We can inhibit alpha 2-delta protein of voltage dependent calcium channel in central nervous system to reduce internal flow of C a2+ as well as release of noradrenaline in human brain cortex slices, make the excessive excited nerve cell to be normal, and thus to ease neuropathic pain effectively. It is mainly used to cure peripheral neuropathic pain and auxiliary local partial epileptic seizure in clinic (Kavouss, 2006). Union guidelines of European Neurological Society in 2006 recommended that pregabalin, gabapentin to be the medication for PHN treatment on the first line (Dworkin *et al.*, 2007). In 2010, guideline of Britain's national institute of clinical optimization (NICE) recommended that pregabalin was the only drug of curing central and peripheral neuropathy pain. Its pharmacokinetics represents linear correlation and dose dependence, the starting dose is effective, dose adjustment is fast. And it could be accomplished in 1~2 weeks, pain control would be more rapid, it could be taken as one of the choice for curing PHN (Attal *et al.*, 2010). In the process of treatment, adverse reaction of pregabalin is mainly represented as dizziness and drowsiness, with the increase of dosage, occurrence rate would increase.

Vertebral nerve block mechanism mainly uses local anesthetic to block the vicious cycle of pain, expand the blood vessels of nerve distribution area, improve local blood supply, reduce accumulation of local inflammatory substances. Vertebral nerve block is one of the method for curing intercostal neuralgia, the early nerve block could relieve pain outbreak and hyperalgesia. The traditional vertebral nerve block perform piercing on human body surface, adverse reaction always occur and has undesirable effect. Writer's hospital adopts peripheral nerve stimulator to guide vertebral nerve block, it could greatly reduce the occurrence of adverse reaction, the short-term effect is definite, and repeated usage is still effective.

Table 4: Comparison for three groups of patients with adverse reaction

Group	N	Dizzy	Drowsiness	Peripheral edema	Nausea
A group	30	10	4	2	1
B group	30	4*	2*	0	0
C group	30	6*	1*	1	1

Table 5: Comparison for clinical curative effect among three groups

Group	N	Excellence	Effect	Invalid	Total number of effective cases (effective+excellence)
Group A	30	17	8	5	25
Group B	30	14	10	6	24
Group C	30	24	4	2	28

This research found that the single use of pregabalin or paravertebral block had a clear effect on the treatment of intercostal neuralgia. However, the former use gradually larger dosage and had many adverse effects while the latter had quick work but the long-term treatment effect was not ideal. Method for combination of these two, that is, paravertebral block combined with pregabalin achieved good function. The oral pregabalin dosage in group C was obviously less than group A ($P < 0.05$), and the adverse effects were also less than group A ($P < 0.05$). In the perspective of curative effect, the total effective rate of patients in group C (93.3%) was obviously higher than group B (80%) and group A (83.3%). The result was consistent with the previous research result (Oxnard, 2012). We can see that paravertebral block combined with pregabalin can obviously improve the sleep quality and pain degree of patients as well as the prognosis of patients.

CONCLUSION

The three groups of experiments all had the effect of lowering VAS and QS. The curative effect of paravertebral block combined with pregabalin is the most obvious and pregabalin was secondary. The single use of pregabalin had a higher curative effect than paravertebral block; however, its dosage gradually increased and the adverse effect such swirl and sleepiness occurred. Single use of paravertebral block had fewer adverse effect but was not suitable for the long-term treatment. Paracertebral block combined with pregabaline can reduce the dosage of pregabaline under the condition of same curative effect and the adverse effects such as swirl nad sleepiness. Its effective rate was obviously higher than single use of paravertebral block or pregabaline. In conclusion, paravertebral block combined with pregabalin overcame the drawback of single treatment method. It had the characteristics of quick work, small adverse effect, long-term curative effect, etc. and it is worth to promote into clinical application.

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