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Original article

A clinical study of paraspinal nerve block on treatment of herpes zoster under ultrasonic guidance

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ABSTRACT

Objective. – To study the ultrasound guiding by methylenum coeruleum thoracic paravertebral block analgesia effect and promote healing of herpes zoster.
Methods. – A total of 87 patients with herpes zoster were randomly divided into an observation group and a control group, and the two groups received the same treatment including antiviral drug, nerve nutrition, in order to increase the body's resistance. The observation group were given thoracic paravertebral block with methylenum coeruleum guided by ultrasound, recorded visual analogue scale (VAS) of the two groups of patients for their hypersensitivity to pain 1d, 3d, 1 week, 2 weeks, 1 month after treatment, skin lesion healing time, incidence of postherpetic neuralgia (PHN), patients' satisfaction, etc.
Results. – After administration of thoracic paravertebral block with methylenum coeruleum, VAS of the observation group expectedly decreased. At the same time, the VAS in the observation group was significantly lower than that in the control group, the skin healing time in the observation group was obviously shorter, and the incidence of PHN was lower than that in the control group. The satisfaction of observation group patients was higher than that in the control group ($P < 0.05$).
Conclusion. – To implement thoracic paravertebral block with methylenum coeruleum guided by ultrasound can help reduce the degree of hypersensitivity to pain, promoting the healing of herpes zoster could reduce the incidence of PHN, greatly improving patients' satisfaction.

1. Introduction

Thoracic paravertebral block (TPVB) procedure includes local anesthetics which are injected into the thoracic spinal nerve that passes through intervertebral foramen (lateral thoracic space) [1,2]. The process generates hysteresis in body and sympathetic nerves adjacent to multiple segments in injection site, and then has effect of anesthesia analgesia [1]. Recently, the TPVB technique has been widely popularized in China, and some studies have shown that its effect has not significant difference with analgesic block of the hard abdomen, and complication incidence rate is lower [3], and the hemodynamics are more stable [4]. TPVB can inhibit noxious stimulation to central conduction, reduce adverse pathophysiological reactions stress generated in the perioperative period. In combined total anesthesia, TPVB can largely reduce the degree of anesthetics [5], and then reduce some undesirable effects generated by anesthetics, such as nausea, emesis, delirium, pruritus, etc. The detailed analgesic effect does not influence the conduction of motor nerve, can contribute to coughing, recovering respiratory function, preventing postoperative chronic pain, and then contribute to postoperative recovery and prognosis.

The traditional operative technique of TPVB primarily depends on the intervertebral space determined by spinal and less anatomical landmark. Blind operation determines depth of inserting needle by loss of resistance, and its reliability is not good enough and has technical demands. With the rising of use of support technologies, such as neurostimulator and ultrasound, ultrasound has been widely applied in clinical anesthesia and pain treatment field, and has made great progress in the peripheral nerve block procedure. Paravertebral blocks guided by ultrasound can be safely and effectively applied in clinics [6–8]. Visualized operation is intuitive rather than traditional blind operation, and it can improve the degree of puncture satisfaction, reduce complications, and the blockage effect is more skillful to perform. However, relevant clinical data in China are rare.

Herpes zoster is a type of acute viral infection disease in the aged people, which can lead to dominant pain and skin herpes [9]. In nearly 34% patients with herpes zoster may postherpetic neuralgia (PHN) may occur, and in approximately 70% of patients who are more than 60 years old occur PHN [9,10]. The common method to

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relieve pain mainly includes drug therapy, physical therapy, nerve block etc. If the disease is not treated in time, it can develop into PHN [11]. Oral medication of PHN is the current research hotspot in clinical studies. However, due to the complex pathogenesis of PHN, a reliable clinical treatment method still remains largely controversial. Many common analgesic drugs can be used to treat PHN, but it is not satisfactory in terms of safety and pain relief. Therefore, more exploratory studies need be performed in order to understand drug choice and multiple modes of analgesia [12,13].

Patients with herpes zoster often go to pain clinics due to their severe pain. In this study, based on common antiviral and trophic nerve treatment, increasing the immunity of the body, and employing the necessary analgesic procedure, we also used methylene blue via the lateral nerve block method with ultrasonic guidance to perform a clinical study regarding the treatment of herpes zoster.

2. Materials and methods

2.1. General information

A total of 87 patients with herpes zoster and PHN from September, 2013 to September, 2015 were treated at the same pain clinic. All of these patients accorded with clinical diagnostic standards, ASA grades were grade I and II, and they were randomly divided into two groups (observation group and control group) according to digital method. The observation group ($n = 43$, aged 46-76, average age: 57.4 ± 8.3 years old) included 23 males and 20 females, their course of diseases were 3-7 days (average course: 4.6 ± 1.8 days), and most of the painful areas were in the back of the chest and waist. The control group ($n = 44$, aged 41-79, average age: 52.8 ± 7.3 years old) included 23 males and 21 females, their course of the diseases were 3-7 days (average course: 4.5 ± 2.1 days), and most of the painful areas were consistent with the observation group (Table 1). All of the relevant indexes did not significantly show any difference in the two groups ($P > 0.05$, Table 1). This study was approved by the hospital ethics committee. Informed consent and written approval were obtained from all the patients and their relations, as well as from volunteers.

Inclusion criteria:

- ASA grades were I and II grade. Patients were diagnosed with herpes zoster, and durative pain exceeded 1 month after wound healing;
- patients were treated with common antiviral and nutritional neurotherapy;
- patients gave their written informed consent and a reception test, and they were volunteers as subjects.

Exclusion criteria:

- patient who suffered from severe high blood pressure and cardiovascular disease;
- patient who suffered from a central nervous system disease and local peripheral neuropathy;
- patient if their coagulant function was unusual;
- patient if their skin was infected on the puncture site, or the spine had a previous history of trauma and surgery, or patients with ridge waste deformity;
- patients who were morbidly obese (BMI > 30 kg/m^2).

2.2. Method of Anaesthesia

Patients underwent normal electrocardiogram and pulse oxygen monitoring. Midazolam (MDZ) was slowly injected via a deep vein with 0.03 mg/kg dose, and thoracic paravertebral blockade was performed after 10 min. For both the two groups, they were treated via the same trophic nerve, antiviral, increasing the immunity of human body treatment, and administered the necessary analgesic. Patients in the observation group were given paravertebral blocks using ultrasonic guidance, and blocking drugs were: 0.2% methylene blue (2 ml: 20 mg, SFDA approval number: H32024827, *Jiangsu Jichuan* Parm. *Co*., Ltd., China) complex solution (1% methylene blue 2 mL, 0.75 ropivacaine (10 ml: 75 mg, Registration number: H20140763, AstraZeneca AB, Sweden) 5 mL, 0.9% Nacl 3 mL).

2.3. Nerve block methods

Patients in the observation group were performed TPVB guided by ultrasound (UMT-500, Mindray, Shenzhen, China) in affected side, and the transducer frequency was 8 Mz. The puncture site was 2-3 cm in the corresponding vertebral spines. By adjusting probe position, a strong echo pleural bright line could be found in ultrasonic windows, and a subulate line on the superior border of the pleura was transverse process of puncture centrum. Paravertebral space was found in the wedge-shaped lower area in the lateral parietal pleura, and position of puncture needle was observed and adjusted under ultrasound via an in-plane injection method. Needle was injected through skin, external intercostal muscles, musculi intercostales interni in turn, and then achieved paravertebral space (Fig. 1). Methylene blue complex solution (0.2%) was injected 10 mL after no blood was detected after needle drawing, and the solution could be observed to spread outside the pleura, and the pleura moved downward toward the abdomen. Patients were required to lie flat within 30 min after finishing blockage, and they were sent to the ward if no adverse reactions were detected.

2.4. Observation indexes

VAS scores were recorded in the two groups, including VAS scores before blockage (T1), 1d after blockage (T2), 3d after blockage (T3), 1 week after blockage (T4), 2 weeks after blockage (T5), 1 month after blockage (T6), time of healing, PHN incidence follow-up at a year, patient's degree of satisfaction (overall satisfaction for the two treatment methods, including excellent, good, general, poor), and untoward effect was simultaneously recorded. Quality of Sleep (QS) was used to assess the sleep quality, 0 means sleep no effect, 4 means completely unable to fall asleep [14].

2.5. Statistical analysis

Measurement data were described using mean ± standard deviation, and ANOVA analysis was used to estimate the difference among different time points. A student t-test was used to estimate the difference between groups, and enumeration data were compared with χ^2 analysis. A $P < 0.05$ was considered statistical

Table 1
Comparison of general condition between the two groups.

Group	Number	Male/Female	Age	BMI (kg/m^2)	Course of disease (day)
Observation group	43	23/20	57.4 ± 8.3	25.1 ± 3.1	4.6 ± 1.8
Control group	44	23/21	52.8 ± 7.3	24.9 ± 4.1	4.5 ± 2.1

BMI: body mass index.

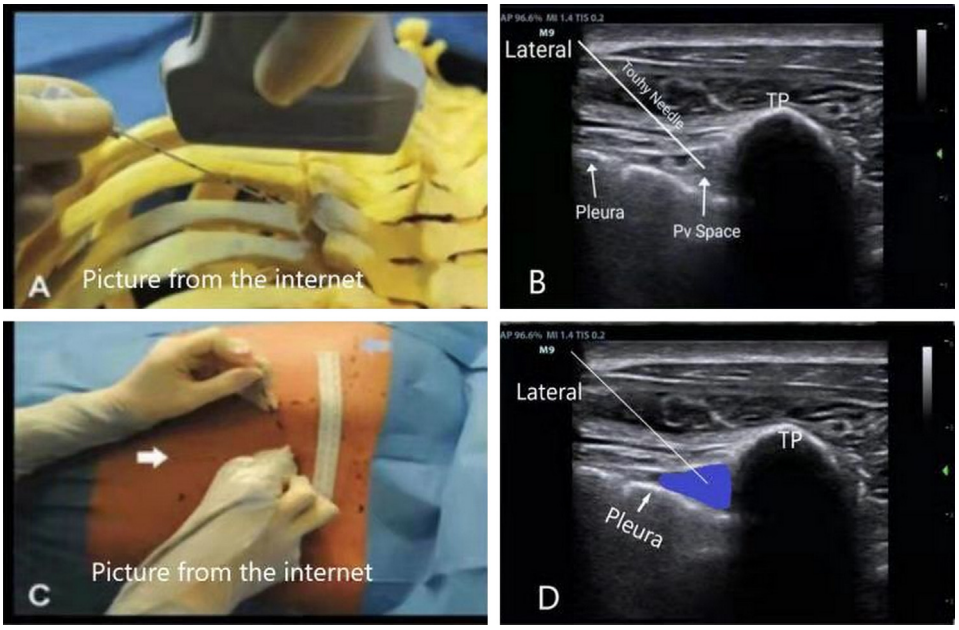

Fig. 1. A view of ultrasonic guidance with needle puncture achieved paravertebral space in the study.

Table 2
Comparison of VAS scores at different time points.

Group	T_1	T_2	T_3	T_4	T_5	T_6
Observation group	7.61 ± 0.53	4.07 ± 1.25	3.51 ± 1.41	2.87 ± 1.59	2.57 ± 1.67	1.34 ± 2.51
Control group	7.59 ± 0.75	7.25 ± 1.51	6.78 ± 1.68	5.91 ± 1.53	4.37 ± 2.14	3.12 ± 2.57
P	0.320	0.041*	0.037*	0.035*	0.180	0.210

Compared with the control group, VAS: visual analog scale.
* $P < 0.05$

different. All the statistical analyses was performed using SPSS 17.0 software.

3. Results

The VAS scores in control group were T1= 7.59 ± 0.75, T2 = 7.25 ± 1.51, T3 = 6.78 ± 1.68, T4 = 5.91 ± 1.53, T5 = 4.37 ± 2.14, T6 = 3.12 ± 2.57, respectively. On the other hand, the VAS scores in observation group were T1= 7.61 ± 0.53, T2 = 4.07 ± 1.25, T3 = 3.51 ± 1.41, T4 = 2.87 ± 1.59, T5 = 2.57 ± 1.67, T6 = 1.34 ± 2.51, respectively. Compared with the control group, VAS scores were significantly reduced in the observation group after surgery, and no significant difference was detected at T1, T5 and T6 time points ($P > 0.05$, Table 2). At T2, T3 and T4 time points, VAS scores were significantly lower than that in the control group ($P < 0.05$).

The sleep quality was access by QS in the study. The QS values in control group wereT1 = 3.4 ± 0.8, T2 = 3.3 ± 0.7, T3 = 3.0 ± 0.8, T4 = 2.7 ± 0.6, T5 = 2.5 ± 1.1, T6 = 2.6 ±2.57, respectively. The QS values in observation group were T1= 3.5 ± 0.7, T2 = 2.1 ± 1.0, T3 = 1.8 ± 0.8, T4 = 1.5 ± 0.9, T5 = 1.3 ± 1.0, T6 = 1.1 ± 0.8, respectively. There was no statistically significant difference in sleep between the two groups before treatment (T1) ($P > 0.05$). The sleep quality score in the two groups were reduced after treatment. Interestingly, compared with the control group, the sleep quality score in observation group was lower. There was significant difference in the treatment point ($P < 0.05$) (T2, T3, T4, T5, T6) (Table 3).

Time of healing in the observation group was shorter than that in the control group, PHN incidence rate was significantly lower, and patient's degree of satisfaction was significantly higher than that in the control group ($P < 0.05$, Table 4). In the observation group, one patient, who was 75 years old, suffered PHN one month after treatment, which might have be related to reduced ability of resistance of viral.

In the observation group, no obvious complication of vertebral nerve puncture, ropivacaine and methylene blue poisoning, or other untoward effects were found, and some patients felt slight skin numbness in relevant region in consciously block. The phenomenon of slight skin numbness was recovered after follow-up 1 month.

4. Discussion

Recently, visualization technology has been greatly improved, and regional nerve block technology guided by ultrasound has achieved better clinical effect [15,16]. With the development of ultrasound-guided technique, thoracic paravertebral block (TPVB) has more accurate positioning under the visual of ultrasound, and previous authors have reported its feasibility has been reported. [17,18]. Anatomical structure of the lateral thoracic vertebra is quite crucial in this operation, and thoracic paravertebral space block is a wedge lacuna near centrum (left side is larger than right side). The backbone of the intercostal nerves is located between the innermost and intercostal muscles, and further extended to cutaneous branches of the side. Diffusion of an injected contrast agent in thoracic paravertebral space block can be tracked by imaging methods:

- confined to the primary location;
- spread to the upper and lower interval via caput costae and collum costaeta;
- spread to offside through the intervertebral foramen;
- spread to intercostal levels.

Table 3
Comparison of QS scores at different time points.

Group	T_1	T_2	T_3	T_4	T_5	T_6
Observation group	3.5 ± 0.7	2.1 ± 1.0	1.8 ± 0.8	1.5 ± 0.9	1.3 ± 1.0	1.1 ± 0.8
Control group	3.4 ± 0.8	3.3 ± 0.7	3.0 ± 0.8	2.7 ± 0.6	2.5 ± 1.1	2.6 ±2.57
P	0.450	0.031*	0.029*	0.028*	0.027*	0.025*

Compared with the control group, QS: Quality of Sleep.
* $P < 0.05$.

Table 4
Comparison time of healing, PHN incidence and patient's degree of satisfaction.

Group	Time of healing (d)	PHN (*n*)	Degree of satisfaction			
			Excellent (*n*)	Good (*n*)	General (*n*)	Poor (*n*)
Observation group	7 ± 1.57	1	27	13	3	0
Control group	15 ± 5.68	6	10	15	11	8
P	0.022*	0.031*	0.017*	0.095	0.029*	0.026*

Compared with the control group, PHN: post-herpetic neuralgia.
* $P < 0.05$.

Traditional TPVB mainly uses a classical blind method to locate the thoracic interstitial space through loss of resistance. However, it is difficult to accurately locate, prone to damage pleura and lead to damage of blood vessel and nerve, and failure rate may be up to 10%. Moreover, traditional TPVB may lead to pain and increase potential risk of pneumothorax (0.5%), because it is necessary to adjust inserting needle with multiple times due to unidentified processus transversus. Application of ultrasonic technique in TPVB has effectively improved degree of satisfaction following the operation. Subsequently, we found that all patients completed the thoracic lateral blockade successfully by ultrasonic guidance, and the degree of satisfaction is 100%. In ultrasound images, thoracic paravertebral space block, parietal pleura and thoracic vertebra transverse process can be easily found, which will contribute to an accurate location in thoracic paravertebral space block. More importantly, the state of the entire inserting needle can be visualized and clearly presented, which can avoid pleura trauma and further lead to pneumothorax due to the excessive depth of needle the needle. Simultaneously, it can be further determined whether the puncture is successful through the lower pressure of the pleural, and vascular damage can be effectively prevented because blood vessel can be avoided under the Doppler model.

Herpes zoster has some symptoms, mainly including paroxysmal cutting pains, burning pain, prickling-like pain and skin herpes, and the main reason is that herpes virus invades nerve when the body's immune function decreased, and further expands skin along corresponding sensory nerve fiber generating nerve and skin damage [19,20]. Current main treatment methods, mainly including antiviral treatment, trophic nerve, increasing body immunity, analgesia, physical therapy, light therapy and treatment by Chinese herbs, but these treatments have a shortcoming that is they need a long courses to perform. In this study, methylene blue was used to treat using TPVB guided by ultrasound, visualization technology contributes to accurate locate and track drug expansion. Compared with the traditional method, this method is more secure and reliable, and it has satisfied retardant effect. Furthermore, occurrence rate of complications can be largely reduced, such as nerve injury, hematoncus, pneumothorax (occurrence rate of pneumothorax in the traditional method may up to 0.07%-19.0%), local anesthetic toxicity and administration of anesthetics into the spinal canal. In our study, when local anesthetics were injected, we found that drug fluid increased on the outside of the pleural membrane forming weak echo group through location under ultrasound. This drug fluid further depresses the pleura and the lung tissue, which is a mark of successfully blocking the thoracic lateral nerve. Our method greatly reduces the adverse events of puncture, and no patient was detected pneumothorax.

Methylene blue is a kind of long acting analgesic, and it has been widely applied in clinics. Its traditional analgesia mechanism is due to destroy the myelin sheath of nerve fibers to achieve the long-term effect of pain relief [21,22]. Other theories also exist, for example:

- receptor theory;
- oxide nerve film theory;
- Sodium channel block;
- hydrogen theory;
- methylene blue can interdict pain conduction through influencing NO-cGMP in spinal cord based on rat experiments [23,24].

Some studies have shown that a low concentration of methylene blue has no nerve damage [25], and low concentration of methylene blue has not any effect on conduction function and structure of lumbar spinal cord and nerve root [26]. Methylene blue may activate pain in block area after 3-4 h in treatment of malignant tumor ostealgia, and therefore we used compound of methylene blue and ropivacaine to perform our study. Ropivacaine is a new type of amide local anesthetic with lower toxicity (low concentration of ropivacaine can avoid motor block), and its action time can reach 240-400 min. The two kinds of drug recombination can eliminate the irritation of methylene blue, no analgesic window period, and the analgesic effect can last 1-3 weeks. The better analgesic effect can inhibit transmit of nociceptive information from peripheral nerve to nervous centralis, improve blood circulation in the pain area, accelerate the retreat of herpes, increase endogenous antibiotics and therefore play an anti-infection role [27]. The course of treatment can be shortened, early treatment is especially effective.

Globally, compared with the traditional methods, our method has many advantages: visualization of topography contributes to observe puncture needle and needle point, spread and distribution of local anesthetics, and even shorten onset time of local anesthetics, shorten blockage time of the paravertebral, prolong the block time, reduce dosage of an anesthetic agent, reduce mortality and incidence of complication, and relieve an uncomfortable feeling. However, the relevant studies are fewer, and further studies should be performed based on a large amount of clinical randomized trial data.

5. Conclusion

In this study, we performed methylene blue paravertebral block under ultrasonic guidance to treat patients, and this method can help an accurate positioning to ensure the drug reaches lesions

in the nervous system. No corresponding complication of insertion occurs. Methylene blue is long-acting analgesics, no analgesic window period, and it then significantly reduces pain, shortens course of disease, reduces PHN incidence rate, untoward effect is not detected, and most patients are satisfied. Patient with PHN was further treated with methylene blue paravertebral block, the symptom decreases and improved the disease. The mechanism of treatment of methylene blue paravertebral block on PHN needs further study.

Disclosure of interest

The authors declare that they have no competing interest.

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