J Anesth (2006) 20:240–242
DOI 10.1007/s00540-006-0399-4

Journal of
Anesthesia



*Short communications*

# Comparison between neurotropin and mepivacaine for stellate ganglion injection

Tomoki Nishiyama[1], Takashi Matsukawa[2], and Koichi Yamashita[3]

[1] Department of Anesthesiology, The University of Tokyo, Tokyo, Japan
[2] Department of Anesthesia, Yamanashi University, Medical School, Yamanashi, Japan
[3] Department of Anesthesiology and Critical Care Medicine, Kochi University, Medical School, Kochi, Japan

**Abstract**
Neurotropin, a nonproteinaceous extract from the inflamed skin of rabbits inoculated with vaccinia virus, is reported to decrease pain effectively when used for stellate ganglion (SG) injection. We compared the effects of neurotropin SG injection with those of mepivacaine on pain relief, as well as comparing the side effects. One hundred and eighty-eight SG injections in 15 patients (5 with postherpetic neuralgia and 10 with sudden deafness) were performed either with 1% mepivacaine 6 ml or with neurotropin 3 ml combined with saline 3 ml in turn. Fifteen min before and after the injection, the pain score, according to a visual analog scale (VAS; only in patients with postherpetic neuralgia); blood pressure; and heart rate were checked, and the number of procedures with Horner's sign was determined. VAS scores decreased significantly with both injections. Horner's sign was observed on the block side in all procedures with the mepivacaine injection, but it was seen in only 48 procedures with the neurotropin injection. Blood pressure and heart rate did not change. In conclusion, the SG injection of neurotropin decreased the VAS score in postherpetic neuralgia to the same extent as mepivacaine. The incidence of Horner's sign was significantly lower with neurotropin than with mepivacaine.

**Key words** Stellate ganglion · Neurotropin · Mepivacaine · Horner's sign

Local anesthetic is usually used for stellate ganglion (SG) block, but unpleasant side effects associated with Horner's sign (ptosis, myosis), conjunctival hyperemia, tears, and nasal congestion occur.

Neurotropin, a nonproteinaceous extract from the inflamed skin of rabbits inoculated with vaccinia virus, has been used in Japan to treat chronic pain by oral, intramuscular, or intravenous administration. In this study, we investigated the analgesic effects and side effects of a SG injection of neurotropin in comparison with a SG injection of mepivacaine.

After obtaining approval from the research committee of JR Tokyo General Hospital and informed consent from the patients, 15 patients who were newly scheduled for left SG block twice a week, for sudden deafness ($n = 10$) or postherpetic neuralgia ($n = 5$) were enrolled in this study. The first treatment of each patient was assigned by random numbers to either the SG injection of 1% mepivacaine 6 ml or the SG injection of neurotropin (Neurotropin; Nippon Zoki, Osaka, Japan) 3 ml combined with normal saline 3 ml. The SG injection was performed at C6, with a 25-gauge needle, by a single senior anesthesiologist. Fifteen min before and after the SG injection, the pain score, according to a visual analog scale (VAS; 100-cm scale: 0, no pain; 100, most severe pain, only in patients with postherpetic neuralgia); blood pressure; and heart rate were measured, and the number of procedures with Horner's sign was determined.

Data values are shown as means ± SDs. Statistical analysis was performed with paired and unpaired *t*-tests for the VAS score, blood pressure, and heart rate, and the $\chi^2$ test for the number of procedures with Horner's sign. A $P$ value of less than 0.05 was considered statistically significant.

The age of the patients (seven men and eight women) was 58 ± 19 years (range, 24 – 79 years), and their body weight was 61 ± 14 kg (range, 42 – 79 kg). The duration of the disease before the study was 9 ± 4 days in those with sudden deafness and 14 ± 7 days in those with postherpetic neuralgia. Each patient received 10 to 15 SG injections during the study (6 to 8 weeks). The total number of SG injections studied was 188, 94 for each type of injection. The VAS score, which was measured only in the five patients with post-herpetic neuralgia, decreased significantly after treatment with each agent, without any differences between the agents (Table 1).

*Address correspondence to*: T. Nishiyama, 3-2-6-603, Kawaguchi, Kawaguchi 332-0015, Japan
Received: October 17, 2005 / Accepted: February 24, 2006

**Table 1.** VAS score, blood pressure, and heart rate

| | Mepivacaine injection | | Neurotropin injection | |
|---|---|---|---|---|
| | Before injection | After injection | Before injection | After injection |
| VAS score | 71 ± 21[a] | 24 ± 13*[b] | 75 ± 19[b] | 27 ± 11*[b] |
| Systolic blood pressure (mmHg) | 123 ± 14 | 119 ± 11 | 122 ± 15 | 119 ± 10 |
| Heart rate (beats·min$^{-1}$) | 82 ± 7 | 78 ± 8 | 80 ± 8 | 79 ± 6 |

* $P < 0.05$ vs before injection
The VAS score was measured only in the five patients with postherpetic neuralgia. Data values are means ± SDs
Before injection, 15 min before injection; after injection, 15 min after injection; VAS, visual analog scale
[a] 32 Patients
[b] 26 Patients

Horner's sign was observed on the block side of 94 procedures (all procedures) with the mepivacaine injection, but it was seen in only 48 procedures with the neurotropin injection ($P < 0.001$). No Horner's sign was seen on the non-block side with either agent. Blood pressure and heart rate did not change significantly and were not different between the agents (Table 1).

The SG injection of neurotropin decreased the pain score in postherpetic neuralgia to the same extent as the SG injection of mepivacaine, but with a decreased incidence of Horner's sign.

We did not compare the effects of each agent on the outcome of the patients because more SG injections than those performed during the study were necessary in most patients.

We administered neurotropin with saline. Saline itself is reported to have no block action on SG in dogs [1]; therefore, the effects seen with the neurotropin injection in the present study would appear to be due to neurotropin, not saline. It was reported that the SG injection of neurotropin 3 ml with saline 5 ml induced analgesia in 14.6 min, while intravenous neurotropin did not induce analgesia in 15 min in various human head, neck, and/or shoulder pain [2]. In our study also, neurotropin worked in 15 min. These findings suggest that neurotropin acted directly on the SG, and not through the systemic circulation.

When systemically administered, neurotropin 100 and 200 units·kg$^{-1}$ has analgesic effects on mechanical hyperalgesia in a rat model [3] and on the pain caused by reflex sympathetic dystrophy in a child [4]. The mechanism of the antinociceptive effect of systemically administered neurotropin is through the descending pain inhibitory pathways of the serotonergic and noradrenergic $\alpha_2$ systems in the spinal dorsal horn [5] or the $\gamma$-aminobutyric acid $(GABA)_A$ system [6]. Neurotropin, when administered intracisternally, intrathecally, or intraperitoneally at up to 200 mg·kg$^{-1}$ was reported to produce therapeutic effects by normalizing the autonomic nervous system and the immune system under stress, without discernibly affecting normal functions in mice [7]. There are no reports to suggest the mechanism of the effects of the SG injection of neurotropin. However, it is possible that the SG injection of neurotropin has effects on the sympathetic nervous system that are similar to those seen when it is systemically administered [5], because, in some patients, Horner's sign was observed.

Horner's sign was observed in about half the procedures with the SG injection of neurotropin, while it was shown in all the procedures with the SG injection of mepivacaine. Horner's sign may be induced by either a pharmacological or a mechanical block of the sympathetic nerves. The reason that it occurred with only half of the SG injections of neurotropin is not known; it may have been due to different sensitivities of the patients (pharmacological block) and/or different locations of the injected drugs, i.e., different techniques (mechanical block). However, as all the procedures in our study were performed by the same anesthesiologist, it seems that technical differences would not be the reason. In any case, a drug with which there is a lower incidence of Horner's sign may be more beneficial for patients if the analgesic effects are the same as those of a drug with a high incidence of the sign.

In conclusion, the SG injection of neurotropin decreased the VAS score in patients with postherpetic neuralgia to the same extent as mepivacaine. The incidence of Horner's sign was significantly lower with neurotropin than with mepivacaine.

## References

1. Okuda Y, Kitajima T (1994) Experimental stellate ganglion block using physiologic saline solution (in Japanese with English abstract). Masui to Sosei (Anesthesia and Resuscitation) 30:7–9
2. Ochiai Y, Tsuchida S, Matsuda T, Kajiki H, Kitagawa R (1993) Clinical investigation of stellate ganglion injection with neurotropin on its analgesic effect (in Japanese). Pain Clinic 14:621–623
3. Toda K, Muneshige H, Ikuta Y (1998) Antinociceptive effects of neurotropin in a rat model of painful peripheral mononeuropathy. Life Sci 62:913–921

4. Okada T, Maeda M, Takeuchi T, Tomoda T, Wakiguchi H, Kurashige T (1997) Reflex sympathetic dystrophy in childhood: a case report. Acta Paediatr Jpn 39:690–693
5. Kawamura M, Ohara H, Go K, Koga K, Ienaga K (1998) Neurotropin induces antinociceptive effect by enhancing descending pain inhibitory systems involving 5-$HT_3$ and noradrenergic alpha$_2$ receptors in spinal dorsal horn. Life Sci 62:2181–2190
6. Hata T, Kita T, Itoh E, Oyama R, Kawabata A (1988) Mechanism of the analgesic effect of neurotropin. Jpn J Pharmacol 48:165–173
7. Hata T, Kita T, Yoneda R (1976) Central activity, antihypertensive action and antiulcerogenic effects of Neurotropin. Folia Pharmacol Jpn 72:879–890