

A new method to evaluate the part of stress in pain: injection of dextrose 5% (neural prolotherapy) on acupuncture points corresponding to the stellate, coeliac and mesenteric ganglions. A pilot study

JACQUES BECO¹, JACK MOUCHEL², LAURENCE SEIDEL³, ADELIN ALBERT^{3,4}

¹ Department of Gynecology and Obstetrics, University Hospital of Liège, Liège, Belgium

² Avenue d'Haouza, Le Mans, France

³ Biostatistics, University Hospital of Liège, Liège, Belgium

⁴ Department of Public Health Sciences, University of Liège, Liège, Belgium

Abstract: In neuralgia (neuropathic pain), the skin rolling test is painful (allodynia to pinch) but when painful everywhere on the body (polyneuralgia) it often indicates that the patient lives stressed out, in a fight of flight situation. Thus, when starting a treatment, it is important to differentiate between these patients and those who have perineal pain only.

The aim of this study was to evaluate the effect on pain and stress of a neural prolotherapy treatment (dextrose 5% injections) at seven acupuncture points linked with orthosympathetic ganglia. The studied population comprised 55 patients treated in two private clinical settings (authors 1 and 2). The short-term effect on pain was studied by comparing the pain induced by the arm skin rolling test before and 15 minutes after injections. To evaluate the long term effect on pain, the average level of body pain during the two weeks preceding the treatment was compared with that following treatment. The WHO (Five) Well-Being Index was used to evaluate the patient's level of stress before and two weeks after injections. Fifteen minutes after dextrose injections, pain induced by the skin rolling test at the arm level was decreased (-3.0 ± 1.6 ; $p < 0.0001$). Two weeks after treatment, the global pain score was significantly reduced (-2.0 ± 0.7 ; $p < 0.0001$) and the total WHO score increased ($+21.0 \pm 20.5$; $p < 0.0001$). Treatment of polyneuralgic patients with neural prolotherapy of seven acupuncture points significantly improves well-being sensation and reduces pain.

Keywords: Fibromyalgia; Acupuncture; Neural prolotherapy; Post-traumatic stress disorders; Chronic pain

INTRODUCTION

When pain occurs in a specific area, a diagnosis of neuralgia (neuropathic pain) can easily be done by the skin rolling test (pinch test, Kibler's fold test)¹⁻⁴. This test is painful (or positive) in case of allodynia to pinch, one of the classical signs of neuralgia. A painful skin rolling test at perineum level is one of the three clinical signs of the pudendal syndrome⁵. When initiating care management in a patient with perineodynia (perineal pain), it is of utmost importance to differentiate patients with perineal pain only from patients who have pain everywhere on the body (polyneuralgia). In the latter, the skin rolling test is painful everywhere on the body surface and perineodynia is just part of a general "illness" which could be called fibromyalgia or central sensitization. This indicates that the patient lives stressed out, under pressure, in a fight of flight situation (with possible heightened sensitivities across all senses: touch, light, sound, odor). All senses become hypersensitive probably due to a mammal adaptation aiming to better detect the approach of a potential predator.

Quite often, this state is part of a post-traumatic stress disorders (PTSD)⁶. Severe chronic pain or stressful experiences in the patient's history (rape, aggression, surgery, death of a close relative, etc.) are the main causes of this psychological state. Pain intensity during the arm skin rolling test tends to be correlated with the patient's stress level (personal unpublished data).

Strong emotional events can stimulate the sympathetic nervous system for a long time⁷. According to recent studies, the stellate ganglion is connected with the emotion centers such as the amygdala known to be involved in the development of PTSD based on functional MRI studies (Figure 1)^{6,8}. There is substantial evidence that stellate ganglion blocks have a significant effect on PTSD^{8,9}. Sadly, inadvertent intra-arterial injection of a local anesthetic during stellate ganglion blockade may cause life-threatening complications¹⁰.

According to Wancura-Kampik¹¹, each sympathetic ganglion can be treated indirectly by acting on some acupuncture points. Neural prolotherapy (perineural injection therapy with dextrose 5%) as described by John Lyftogt may be considered as an effective method to treat neuralgias^{12,13}.

The aim of this pilot study was to evaluate the effect of neural prolotherapy on seven acupuncture spots linked to three sympathetic ganglions in the management of stress and polyneuralgia.

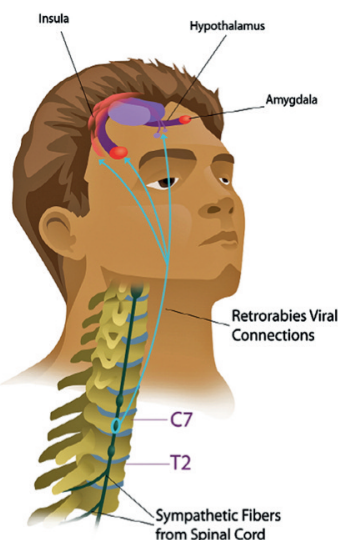


Figure 1. – Sympathetic fibers originate from the spinal cord at the thoracic level and enter the sympathetic chain leading to the brain. Reprinted from “Sympathetic system modulation to treat post-traumatic stress disorder (PTSD): a review of clinical evidence and neurobiology” from Lipov E, Kelzenberg B., *J Affect Disord* 2012;142:1-5, Copyright by Elsevier⁸ (reprinted with permission).

MATERIAL AND METHODS

The study material consisted of 55 patients (54 women and 1 man), aged 45.2 ± 10.3 years, from two private clinical practices (Author 1, N=41 and Author 2, N=14); all patients had a positive skin rolling test at the level of the arm (pain level 4 or more).

The patients had to fill in the WHO (Five) Well-Being Index questionnaire (OMS 1998)^{14, 15}, which is a simple method to measure emotional well-being during the two weeks preceding the visit. It consists of five items related to positive mood, vitality and general interests. Each value must be an average for the last fifteen days. It has been shown as a reliable measure of emotional functioning and a good screener for depression¹⁴. Each of the five items is rated from 0 (absent) to 5 (constantly present). Scores are added and multiplied by four giving values between 0 and 100. A score below 50 is indicative of low mood. A score of 28 or below indicates likely depression. After having filled in the questionnaire, patients had also to give an average level of body pain on a 10 cm visual analog scale (VAS) for the last 2 weeks before the visit (all pain inclusive).

Treatment consisted of injecting seven acupuncture points with a dextrose 5% solution buffered with bicarbonate to have a neutral pH (needle 27G)¹³. These spots were selected according to Wancura-Kampik¹¹. Most of them were clearly painful on palpation or by using the skin rolling test (allowing for a more precise location). They were marked precisely with a cross on the skin using a ball-point pen. The two Spleen 6 points (SP 6 - Sanyinjiao in Chinese) are located on the medial aspect of the lower leg 4 fingers breadth (or 3 cun; one cun = one Chinese anatomical inch¹⁶) above the medial malleolus on the posterior border of the tibial bone. They are painful on palpation. The two Pericardium 6 points (PC6 - Neiguan) are located on the palmar aspect of the forearm, 3 fingers breadth (2 cun) above the transverse crease of the wrist between the tendons of m. palmaris longus and m. flexor carpi radialis. They are rarely painful. The three remaining spots are located on the Conception Vessel (CV) meridian (or Ren Mai). This meridian is situated in the anterior midline. CV 6 – Ren 6 (Qihai) is also known as “Sea of energy”. It is located two finger widths (1.5 cun) below the center of the belly button. It is easily identified by using the pinch test perpendicularly to the meridian. CV 12 – Ren 12 (Zhongwan) is situated half way between umbilicus and sternocostal notch. This point is also painful by using the pinch test. CV17-Ren 17 (Tanzhong) is known as “Sea of tranquility” because it can be used in acupressure to reduce stress. It is located at the level of the 4th intercostal space, at the midpoint between the two nipples. It is usually painful at palpation and/or with skin rolling. According to Wancura-Kampik¹¹, CV17 and PC6 are connected with the stellate ganglion while CV6 and SP6 are linked with the mesenteric ganglions and CV12 with the celiac ganglion. Four of these points were injected subcutaneously with 1-2 ml of dextrose 5% (two SP6 and two PC6) while the others were treated intra-cutaneously forming 1.5 cm “quaddles” according to the German neural therapy approach² (Figure 2). The points were injected in the following order: two SP6, CV6, CV12, two PC6 and at the end CV17.



Figure 2. "Quaddle" after intracutaneous injection.

The skin rolling test was performed at the right arm level (all around) before and 15 min after the injections. Pain levels were evaluated using the 0-10 cm VAS.

Two weeks after the treatment patients had to complete again the WHO (Five) Well-Being Index questionnaire and to evaluate pain on the VAS. Moreover they had to inform the investigator on the questionnaire about any other change (e.g. sleep, bowel, urinary).

Statistical analysis: Results were expressed as mean ± standard deviation (SD). Frequency tables were used for categorical data. Group mean values were compared by the Student t test while within patient mean differences were compared by the paired t test. The comparison of proportions was done the classical chi-squared test. The correlation coefficient was calculated to assess the association between two variables. Results were considered significant at the 5% critical level (p<0.05). All calculations were performed with the SAS version 9.4 and R version 3.3.3 statistical packages.

RESULTS

Fifteen minutes after dextrose injections, pain induced by the skin rolling test at the arm level was significantly reduced from 7.1 ± 1.5 to 4.2 ± 1.9 (p<0.0001). There was also a clear improvement of the global WHO score which increased from 36.8 ± 18.1 to 57.8 ± 22.2 (p<0.0001) 14 days after treatment. As seen in Table I, the mean value of all items of the WHO index increased markedly after injection, although improvement was less significant for the fifth item: “My daily life has been filled with things that interest me”. The global pain value was also significantly reduced two weeks after treatment (6.0 ± 2.1 before vs. 4.1 ± 2.5 after; p<0.0001).

TABLE 1. WHO score before and 14 days after treatment (N=55).

WHO index	Before injection Mean ± SD	After injection Mean ± SD	P-value
Item 1 (/5)	2.1 ± 1.1	3.0 ± 1.2	<0.0001
Item 2 (/5)	1.7 ± 1.2	3.0 ± 1.2	<0.0001
Item 3 (/5)	1.6 ± 1.3	2.8 ± 1.3	<0.0001
Item 4 (/5)	1.3 ± 1.2	2.6 ± 1.4	<0.0001
Item 5 (/5)	2.5 ± 1.5	3.0 ± 1.3	0.0036
Total score (/100)	36.8 ± 18.1	57.8 ± 22.2	<0.0001

WHO-1: I have felt cheerful and in good spirits; WHO-2: I have felt calm and relaxed; WHO-3: I have felt active and vigorous; WHO-4: I woke up feeling fresh and rested; WHO-5: My daily life has been filled with things that interest me.

Results from authors 1 and 2 were comparable except for pain induced by the skin rolling test at the arm level before and after treatment. Pain induced by Author 1 before treatment was significantly stronger than that induced by Author 2 (7.5 ± 1.4 vs. 6.1 ± 1.2; p=0.0028) and likewise after treatment (4.7 ± 1.9 vs. 2.8 ± 1.3; p=0.0012) but pain reduction was similar for both authors (-2.80 ± 1.7 vs. -3.4 ± 1.3; p=0.26).

No correlation was found between pain intensity reduction during arm skin rolling test after treatment and WHO score improvement after two weeks (r=-0.17, p=0.21) but this correlation was almost significant for global pain reduction (r=0.26, p= 0.058).

Soon after the treatment, patients felt in general completely “Zen” and their muscles relaxed. Some patients described warming of the arms and face. Pain in different body areas often had disappeared before the patient left the office. A number of patients slept in their car before driving. Several stress related symptoms disappeared (e.g. restless legs, urinary frequency, urge incontinence, heartburn, or diarrhea).

DISCUSSION

In this pilot study, dextrose injections on seven acupuncture spots linked with the sympathetic ganglions had a marked immediate effect on stress. Most often patients left the office free of stress and this state persisted for some days. Moreover, after 2 weeks, results were seen as highly positive because a 10% improvement of the WHO score is already considered as clinically significant¹⁴.

The novel treatment approach described herein may be used to evaluate the part of pain due to stress in the patient's condition. It opens doors for communication about past psychological trauma and adapted care (EMDR, hypnosis). It could also help many patients who suffer awful stress to feel better immediately. Hyperactivity of the sympathetic system may partly explain fibromyalgia (or polyneuralgia) because short-term improvement of pain was obtained with low-dose of propranolol or by Xenon irradiation of the stellate ganglion^{17, 18}. Failure in case of strong chronic pain suggests that the trigger pain must be treated before using psychological treatments.

Polyneuralgic patients are at risk of inappropriate and useless surgeries (for pain or psychosomatic induced illnesses) and should be diagnosed as soon as possible. The skin rolling test at the arm level is in our experience the best screening test but it could be also painful in case of brachial neuralgias independently of stress (radial, medial antebrachial, intercosto-brachial, medial brachial cutaneous). In case of doubt, the skin rolling test must be done at many different places of the body to confirm the diagnosis (painful everywhere). According to the German neural therapy approach, quaddle injections are far more effective than subcutaneous injections². This can be explained by the fact that 90 % of all autonomic nerve substances are in the skin and that the nerve endings and bulbs have no more connective tissue sheath at this level, letting dextrose 5% solution having a direct interaction with the neural tissue². However, because the skin is so thin on SP6 and PC6, injections were done subcutaneously at these points.

This is a pilot study. The skin rolling test and the injections were done by the two same physicians who were not blinded. It is likely that the pressure induced by the fingers was not exactly similar before and after the injections or between physicians (a statistically significant difference was observed between Author 1 and Author 2). Since there was no sham treatment and the patients were completely informed of the study objective, a significant placebo effect may partly explain the results. Long term efficacy of the method has to be evaluated. Probably, a single treatment will not suffice, knowing that an isolated neuralgia requires on average 3 neural prolotherapy sessions (at two weeks interval) to heal. The choice of the acupuncture points to be injected can also be discussed. It could be that treating only CV17 with the two PC6 (which are connected with the stellate ganglion) will be sufficient to obtain relaxation but we preferred to relieve a great part of the sympathetic system by adding the four other points. The efficacy of this approach in reduction of stress and pain suggests that treatment of other acupuncture points with dextrose 5% injections should help healing other illnesses.

CONCLUSION

Treatment of polyneuralgic patients with dextrose 5% injections at seven acupuncture points connected with three sympathetic ganglions significantly improves their well-be-

ing sensation and reduces their pain. If the present findings are confirmed by well-controlled studies, this treatment could become quite helpful in the management of stressful and painful patients and probably in many psychosomatic disorders. It could also be attempted in cases of acute stress.

DISCLOSURES

This study has been approved by the Ethic Committee of Liège University. Jacques Beco, Jack Mouchel, Laurence Seidel and Adelin Albert have no conflicts of interest or financial ties to disclose.

REFERENCES

1. Carnett JB. Intercostal neuralgia as a cause of abdominal pain and tenderness. *Surg Gynecol Obstet*, 1926, 42, 625-632.
2. Dosch P. Manual of neural therapy according to Huneke. Heidelberg: Haug Publishers, 1984.
3. Maigne R. Low back pain of thoracolumbar origin. *Arch Phys Med Rehabil* 1980, 61, 389-95.
4. Carnett JB, Bates W. The Treatment of Intercostal Neuralgia of the Abdominal Wall. *Ann Surg* 1933, 98, 820-9.
5. Beco J, Klimov D, Bex M. Pudendal nerve decompression in perineology : a case series. *BMC Surg* 2004, 4, 15.
6. Liberzon I, Martis B. Neuroimaging studies of emotional responses in PTSD. *Ann N Y Acad Sci* 2006, 1071, 87-109.
7. Westerhaus MJ, Loewy AD. Central representation of the sympathetic nervous system in the cerebral cortex. *Brain Res* 2001, 903, 117-27.
8. Lipov E, Kelzenberg B. Sympathetic system modulation to treat post-traumatic stress disorder (PTSD): a review of clinical evidence and neurobiology. *J Affect Disord* 2012, 142, 1-5.
9. Mulvaney SW, Lynch JH, Hickey MJ et al. Stellate ganglion block used to treat symptoms associated with combat-related post-traumatic stress disorder: a case series of 166 patients. *Mil Med* 2014, 179, 1133-40.
10. Chaturvedi A, Dash H. Locked-in syndrome during stellate ganglion block. *Indian J Anaesth* 2010, 54, 324-6.
11. Wancura-Kampik I. Segmental anatomy. The key for mastering acupuncture, neural therapy and manual therapy. Munich: Elsevier GmbH, 2012.
12. Lyftogt JA. Pain Conundrums: Which Hypothesis? Central Nervous System Sensitization versus Peripheral Nervous System Autonomy. *Australasian Musculoskeletal Medicine* 2008, 72-74.
13. Lyftogt J. Subcutaneous prolotherapy treatment of refractory knee, shoulder, and lateral elbow pain. *Australasian Musculoskeletal Medicine* 2007, 12, 110-112.
14. Topp CW, Ostergaard SD, Sondergaard S et al. The WHO-5 Well-Being Index: a systematic review of the literature. *Psychother Psychosom* 2015, 84, 167-76.
15. Henkel V, Mergl R, Kohnen R, et al. Identifying depression in primary care: a comparison of different methods in a prospective cohort study. *BMJ* 2003, 326, 200-1.
16. Coyle M, Aird M, Cobbin D et al. The Cun Measurement System: an Investigation into its Suitability in Current Practice. *Acupunct Med* 2000, 18, 10-14.
17. Nakajima F, Komoda A, Aratani S et al. Effects of xenon irradiation of the stellate ganglion region on fibromyalgia. *J Phys Ther Sci* 2015, 27, 209-12.
18. Light KC, Bragdon EE, Grewen KM, et al. Adrenergic dysregulation and pain with and without acute beta-blockade in women with fibromyalgia and temporomandibular disorder. *J Pain* 2009, 10, 542-52.

Correspondence to:

Dr Jacques Beco
Avenue Hanlet 9a, B-4802 Heusy, Belgium
jacques.beco@skynet.be