

## Case report

## Acupuncture in the Treatment of Erectile Dysfunction among a Diabetic Population of Sildenafil Citrate Non-Responder

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### Abstract

**[Introduction]** This case report concerns the observed effects of manual and electrical acupuncture at Zhongliao (BL-33) and the pudendal nerve point (PN) in a sildenafil non-responder with erectile dysfunction (ED) secondary to diabetes.

**[Case]** This 61-year-old man had suffered from ED in the 2 years since his diagnosis with type II diabetes. Initially, sildenafil citrate, which is a phosphodiesterase type 5 inhibitor, effectively treated his ED. However, the patient's response to this medication deteriorated over time, until he was no longer able to achieve an erection, despite treatment. The patient presented at a university clinic for acupuncture treatment.

**[Results]** Manual acupuncture at BL-33 induced beneficial effects that were sustained throughout the course of acupuncture treatment. Electro-acupuncture to the PN was performed, with the patient subsequently reporting increased erection hardness and sustainability in comparison to the results achieved with the use of BL-33 acupuncture. The patient's answers to a Japanese translation of the 5-item version of the International Index of Erectile Function (IIEF5) questionnaire showed that acupuncture treatment had markedly improved the patient's signs and symptoms since presentation at the first medical examination. In contrast, his glycemic control was unfavourable, because there was no significant change in the patient's HbA1c throughout the acupuncture treatment until the last day from the first medical examination.

**[Conclusion]** Sildenafil non-responder ED patient with DM was dramatically improved by acupuncture, regardless of whether HbA1c was much higher. It seems likely that the reported beneficial effects in this case of ED are due to the acupuncture treatment administered. Additional cases should be studied.

**Key words:** *erectile dysfunction, acupuncture, diabetic mellitus, sildenafil citrate, BL-33*

### I. Introduction

Erectile dysfunction (ED) has been defined as “the persistent inability to obtain or maintain sufficient rigidity of the penis to allow satisfactory sexual performance”. It has been estimated that the worldwide prevalence of ED will be 322 million cases by the year 2025<sup>1)</sup>. Although ED is not a life-threatening disease, it has a dramatic effect on the patient's quality of life. The main risk factors for ED are age, cardiovascular disease, smoking, depression and diabetic mellitus (DM)<sup>2,3)</sup>. Patients with DM are at a greatest risk for developing

ED than patients with other diseases (odds ratio, 3.0)<sup>4)</sup>. It has been reported that approximately 30-70% of DM men experience some form of ED, which represents prevalence much higher than that observed among non-diabetic men<sup>5)</sup>.

There are several treatment options for ED, and a phosphodiesterase type 5 (PDE-5) inhibitors are considered to be the first-line therapy. Sildenafil was the first PDE-5 inhibitor to enter the market and revolutionized ED treatment. The medication significantly improves erectile function, orgasmic function, intercourse satisfaction and overall satisfaction<sup>2)</sup>. Among patients with diabetic ED, 56% reported enhanced erectile function with

sildenafil as compared to 10% with the placebo<sup>6</sup>). However, some ED patients don't have effect by the sildenafil treatment. In fact, substantial proportions of diabetic ED patients and diabetic rats respond poorly to PDE-5 inhibitor therapy<sup>7</sup>. One study found that 44% of DM patients with ED did not respond to sildenafil treatment<sup>6</sup>).

Acupuncture has been performed to treat ED in patients undergoing non-diabetic haemodialysis<sup>8</sup>), as well as those with psychogenic<sup>9</sup>) and/or non-organic ED<sup>10</sup>). However, due to the lack of randomised clinical trials, the effectiveness of acupuncture in treating ED remains uncertain<sup>11</sup>). Although the evidence is insufficient to suggest that acupuncture is an effective intervention for treating ED, select populations of ED patients may benefit<sup>12</sup>).

Acupuncture treatment is known to improve the pathophysiology associated with DM<sup>13</sup>). One aspect of the pathophysiology associated with this condition is ED. Here we present a case of ED in a diabetic patient that ceased to respond to treatment with sildenafil citrate, a PDE-5 inhibitor. This case of ED in a sildenafil non-responder was successfully treated with acupuncture at Zhongliao (BL-33) and at the pudendal nerve point (PN).

## II. Case History

The patient is a 61-year-old man, who was referred to our institution for acupuncture treatment for his ED, 5 years after his diagnosis with type II diabetes and hypertension. The patient's ED had been diagnosed 3 years earlier by a urologist. The patient was treated with sildenafil citrate 25 mg, which initially was successful in treating his ED symptoms. However, this effect decreased gradually over time. Despite an increase in the dosage of sildenafil citrate to 50 mg, the patient could no longer sustain an erection. The patient's haemoglobin A1c (HbA1c) reading remained at approximately 8.1%, and coefficient of variation for the R-R interval (CVR-R) during deep breathing was 1.12%. The patient had an adequate understanding about the purpose of this report by our explanation and was provided with informed consent regarding the publication in this report.

## III. Interventions

The physician prescribed omeprazole sodium, lisinopril hydrate, triazolam, glybenclamide, voglibose, epalrestat and cimetidine. The patient was not taking any medication other than the above-mentioned medications at the start or at any point during the course of acupuncture treatment.

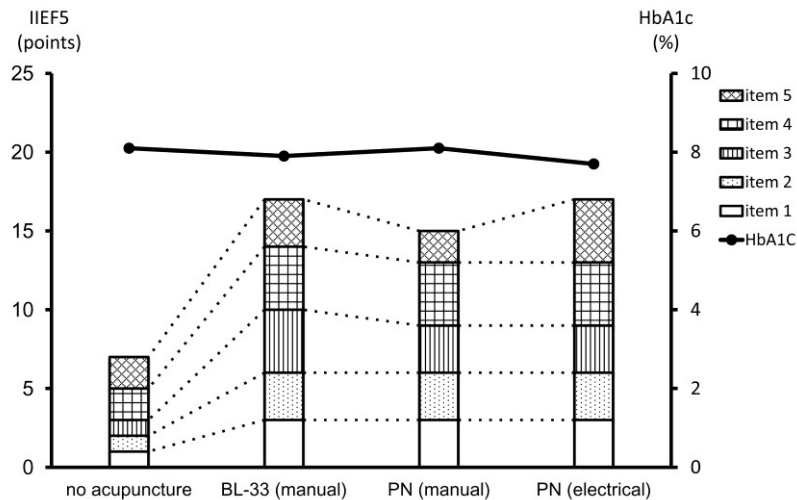
The first medical examination was regarded as no treatment session. The patient was treated with 3 sessions: 1) manual acupuncture at BL-33 (BL-33 session), 2) manual acupuncture to PN (M-PN session), 3) electrical acupuncture to PN (E-PN session). A

disposable needle (diameter 0.3 mm, length 60 mm) was inserted at BL-33 bilaterally, at a depth of 50–60 mm, and twirling manually for 15 minutes<sup>14</sup>). The point for acupuncture stimulation of the PN is located in the gluteal region (at a point 50-60% of the distance along a straight line from the posterior superior iliac spine to the lower inner edge of the ischial tuberosity). An acupuncture needle (diameter 0.3 mm, length 90 mm) was inserted into the PN bilaterally until the patient felt stimulation arising in the pudendal area. The needles were then twirling manually for 15 minutes or stimulated using electrodes for low-frequency electro-acupuncture treatment (stimulation frequency: 10 Hz, stimulation time: 15 minutes, stimulation strength: sufficient for sensation in the pudendal area)<sup>15</sup>). The treatment of each session was performed once a week for 5 weeks. The outcome of DM and of ED was assessed as HbA1c and the 5-item version of the International Index of Erectile Function (IIEF5) questionnaire, respectively. The IIEF5 questionnaire, has been translated to Japanese, is a validated instrument for diagnosing and assessing ED<sup>16</sup>). The questionnaire is administered to measure changes in erectile function and investigates 5 items: confidence in the erection (item 1), hardness of the erection (item 2), maintenance of the erection during sexual intercourse (item 3), maintenance of the erection to intercourse completion (item 4) and satisfaction with the quality of sexual intercourse (item 5). The evaluation of outcomes had been obtained from compare of no treatment session and end of each treatment sessions.

## IV. Results

Observation showed a significant improvement in the patient's morning erection after the first treatment. After the fourth treatment, the patient was able to participate in sexual intercourse. Manual acupuncture at BL-33 induced beneficial effects that were sustained throughout the course of acupuncture treatment. Electro-acupuncture to the PN achieved a further increase in erection hardness and sustainability.

The patient's HbA1c and IIEF5 responses were shown in Figure 1. There was no significant change in HbA1c reading throughout the course of acupuncture treatment. At no treatment session, total IIEF5 score of patient was 7. After the BL-33 session, the patient scored 17. After each treatment, marked improvement in comparison to the answers obtained at no treatment session was achieved for total IIEF5 score investigated, especially, manual acupuncture at BL-33 and electro-acupuncture to the PN. All item of IIEF5 were also higher by each treatment than no treatment session, although slightly decreased in manual acupuncture to the PN. Manual acupuncture at BL-33 was significant for item 3 of IIEF5, and electro-acupuncture to the PN was significantly improvement for item 5.



**Figure 1. The clinical course of IIEF5 and HbA1c**

This figure showed the IIEF5 (left vertical axis) and the HbA1c (right vertical axis). Item 1, confidence in the erection; item 2, hardness of the erection; item 3, maintenance of the erection during sexual intercourse; item 4, maintenance of the erection to intercourse completion; item 5, satisfaction with the quality of sexual intercourse. The IIEF5 of this patient increased significantly in that it intervene acupuncture, although there was no significant change in the patient's HbA1c.

## V. Discussion

In this case report, erectile dysfunction of this patient improved significantly in that it intervene acupuncture. Manual acupuncture at BL-33, which was performed in the first treatment session, was increased in total IIEF5 score and its all items score. Improved erectile function of this patient was maintainable in spite of the changed treatment to manual or electrical acupuncture to the PN. These results suggested that all methods of acupuncture were useful for treating ED. When acupuncture stimulation was applied to segment of afferent input is close to the segment of visceral autonomic nerves, that induced the reflex effects of acupuncture occur via spinal segmental reflex pathways<sup>17)</sup>. Somatic afferent of both BL-33 and the PN is conveyed to same spinal segment, which is region of sacral 2<sup>nd</sup> and/or 3<sup>rd</sup> and both acupuncture can stimulate somatic nerve of sacral 2<sup>nd</sup> and/or 3<sup>rd</sup>. It is suggested that improvement of ED by acupuncture is an important for exciting somatic afferent nerve of same segmental levels. In contrast, manual acupuncture at BL-33 and electro-acupuncture to the PN was significantly improve for maintenance of the erection during sexual intercourse (item 3) and satisfaction with the quality of sexual intercourse (item 5), respectively. It was unclear whether these improvements were particular response by stimulation methods and points. Moreover, it was a possibility that manual acupuncture at BL-33, but not other treatment, was only affected and maintained. Further case series and basic research would clarify it.

This patient had been suffering from diabetes mellitus (DM) for 5 years prior to the development of ED, with persistently high HbA1c readings. Bodie et al<sup>18)</sup> assessed laboratory abnormalities among 3547 men with ED and found that a large number of men presenting with a primary complaint of ED had elevated HbA1c levels. These results suggest that ED in diabetic patients is a manifestation of DM induced-autonomic neuropathy. In the case presented here, manual and electro-acupuncture at BL-33 and PN significantly improved erectile function, despite continuously high HbA1c levels. The mechanism by which acupuncture treatment improved symptoms associated with neuropathy appears to be independent of blood glucose control.

Acupuncture affects various visceral organs via the somato-autonomic reflex<sup>17)</sup>. We reported that the same pathway was involved in erectile function of rats<sup>19)</sup>. Namely, to effect of acupuncture on erectile function, the consequence is activity of autonomic nerve, that is almost pudendal nerve. On the other hand, it is well known that normal erectile function is a hemodynamic neurovascular process involving relaxation of the cavernous. The principal neurotransmitter in penile erection is nitric oxide (NO), which is produced by the nitregic neurons with the help of neuronal NO synthase (NOS) in response to sexual stimulation. Within the smooth muscle, NO activates soluble guanylyl cyclase, which raises the intracellular concentration of cyclic guanosine monophosphate (cGMP). cGMP induced relaxation of the smooth muscle by a drop in cytosolic calcium concentrations, resulting in the evoked erection. During return to

the flaccid state, cGMP is hydrolyzed to GMP by PDE-5<sup>20</sup>). Sildenafil is a selective inhibitor of PDE-5. When sexual stimulation releases NO into penile smooth muscle, the inhibition of PDE-5 by sildenafil causes a marked elevation of cGMP concentrations, resulting in improved erection. Sildenafil has no effect on the penis in the absence of parasympathetic nerve and sexual stimulation<sup>20</sup>). Hence the effects of both acupuncture and sildenafil require the excitation of parasympathetic neurons and sexual desire. In this case, although a patient had been treated by sildenafil citrate 50 mg without any effect, his ED was improved by acupuncture. Since acupuncture could not work under conditions of absence of somatic and autonomic neuron, the possibility remains that this case of ED was psychogenic in nature. Engelhardt et al<sup>9</sup>) reported that acupuncture could be an effective treatment option in more than two-thirds of patients with psychogenic ED. However, the effects of acupuncture on various types of ED remain to be elucidated. Therefore, these results suggest that there were significantly effects on his ED, which caused diabetic autonomic neuropathy and/or the absence of sexual desire.

In summary, manual or electrical acupuncture treatment at BL-33 or PN improved ED in a DM patient who did not respond to sildenafil treatment. Sildenafil has become the drug of choice for most men with ED. However, there are complications associated with sildenafil use, and the drug loses efficacy in some patients over time. These findings suggest that manual acupuncture to BL-33 and/or EA to PN represents a valid alternative for the treatment of ED in DM patients.

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