Surgical Management of Complicated Peripheral Neuropathies in Diabetic Patients

AMR M. SAFWAT, M.D.*; AHMED A. TAHER, M.D.*; AHMED E. AHMED, M.D.**; DALIA R.A. ABD EL-RAHMAN, M.D.** and ABD EL-HAMID H. SHADY, M.Sc.*

The Departments of Neurosurgery* and Internal Medicine**, Faculty of Medicine, Cairo University

Abstract

Background: The global prevalence of diabetes mellitus in 2011 was 366 million (8.3%), and this figure is also expected to increase to 552 million (9.9%) by 2030. Diabetic Peripheral Neuropathy (DPN) is a frequent complication of diabetes that affects up to 50% diabetic patients in United States. It is a major cause of morbidity and increased mortality, and is associated with duration of diabetes, hyperlipidemia, and poor glycemic control. The most common form of diabetic neuropathy is the "Distal Sensorimotor Polyneuropathy (DSPN)". DPN is predominantly characterized by sensory symptoms in the "glove-and-stocking" distribution. Diabetic causes DPN by promoting neuronal apoptosis and inhibiting nerve regeneration, which leads to significant deficits in tactile sensitivity, vibration sense, lower-limb proprioception, and kinesthesia. Reduced or absent sensation in the foot can increase the risk of injury and wounds that may develop into serious infections requiring amputations. Diabetes can also affect autonomic nervous system causing autonomic neuropathy affecting the cardiovascular, vasomotor, sudomotor, and gastrointestinal systems. A common phenotype of DPN is Painful Diabetic Neuropathy (P-DPN), as a fairly significant proportion of diabetic population, ranging between 10-26%. Surgical decompression of multiple peripheral nerves is being utilized as an alternative approach to treatment of symptomatic diabetic neuropathy. This is based on the hypothesis that diabetic nerves are more vulnerable to compressive injury at potential sites for entrapment.

Methods: This study was conducted in the Neurosurgery Department, Faculty of Medicine, Cairo University Hospitals in the period from December 2011 to November 2013. The study included fifty patients with complicated diabetic peripheral neuropathy who are surgically managed by peripheral nerve decompression in the region of the carpal and tarsal tunnels. All patients were subjected to: Full history taking, complete general medical examination, fasting blood sugar, postprandial blood sugar and electromyography. Surgical candidates were subjected to division of the flexor retinaculum in the hand or feet.

Results: The patients' age ranged from 35-75 years. The mean age was 58.5 ± 10.3 years. There is a good clinical improvement of 80% of cases by surgical decompression of peripheral nerves. There is an improvement in nerve conduction velocity after decompression of affected peripheral nerves in 84% of patients surgically managed. The improvement was 80%. About 73% of the operated patients showed improvement of ischemia in the periphery as well as about 82% showed improvement of the neurologic condition as regarding neuropathic pain and muscle weakness improvement in the form of improved hand-grip and good walking.

Conclusions: It could be concluded that patients with complicated Diabetic Peripheral Neuropathy (DPN) could be surgically managed successfully by decompression of peripheral nerves at site of compression in carpal and tarsal tunnels with good results in patients resistant to medical treatment.

Key Words: Peripheral neuropathy – Diabetes.

Introduction

THERE are over 250 million people in the world with type 1 and 2 diabetes mellitus [1].

Neuropathy is one of the most common complications of diabetes mellitus and leads to increasingly high morbidity and mortality, resulting in a huge economic burden for diabetic care [2].

Diabetic neuropathy is a heterogeneous condition containing symmetrical neuropathies and focal neuropathies, presenting diverse clinical manifestations. Of all the neuropathies in diabetes, chronic Diabetic Peripheral Neuropathy (DPN) is the commonest [3].

Of all the symptoms in DPN, pain is the most distressing and is the main factor that prompts the patients to seek medical advice [4].

One-third of diabetic patients have symptoms of neuropathic pain according to a recent community-based study and up to 15-20% of patients with DPN may experience painful symptoms. Therefore, a high proportion of patients are suffering from neuropathic pain as well as the relative depression, anxiety and sleep deprivation [5].
Aside from traditional management including glucose control, lifestyle modification and pharmacological treatment, surgical decompression is recommended for pain relief based on the "double crush" hypothesis. Many of the symptoms of diabetic neuropathy, including pain, are similar to those of chronic nerve compression, suggesting that entrapment of nerves may happen in the patients with diabetic neuropathy. Allowing for the currently traditional treatment dilemma on pain relief in patients with diabetic neuropathy, surgical decompression targeting superimposed compression, as an newly emerging promising approach, should be taken into account [6].

The results of nerve decompression surgery for cases of DPN in the potential sites of anatomical narrowings is encouraging because it was found that a good percentage of patients showed improvement in pain and sensations, also decompression has been shown to reduce the risk of ulceration, reulceration and amputations [7].

The aim of the work is to evaluate the results of surgical decompression in patients with complicated diabetic peripheral neuropathy.

**Patients and Methods**

This study was conducted in the Neurosurgery Department, Faculty of Medicine, Cairo University Hospitals in the period from December 2011 to November 2013.

The study included fifty patients with complicated diabetic peripheral neuropathy who are surgically managed by peripheral nerve decompression in the region of the carpal and tarsal tunnels.

**Inclusion criteria:**
1. Complicated diabetic patients.
2. EMG-and NCS-proved neuropathy.

**Exclusion criteria:**
1. Entrapment or peripheral neuropathies in non-diabetic patients.
2. Neuropathic patients with other medical diseases.

**Intervention methods:**

All patients were subjected to:
1. Full history taking.
2. Complete general medical examination.
3. Fasting Blood Sugar (FBS) and Postprandial Blood Sugar (PBS).
4. EMG on the affected sites, then follow-up EMG after surgery. The results are analyzed statistically and compared.
5. Patients are surgically managed by division of the flexor retinaculum in the hand or feet.

**Intervention results:**

Results were observed according to primary and secondary outcome parameters.

A- **Primary outcome parameters include:**
1. Improvement of neuropathic pain.
2. Faster healing of diabetic foot ulcers.

B- **Secondary outcome parameters e.g.:**
1. Less medications used in neuropathic pain.
2. Improvement of vacularity of hands and feet after surgery with less incidence of ischaemia or gangrene.
3. Neurologic condition improvement with stronger handgrip or easy walking after surgery.

**Statistical analysis:**

Data were checked, entered and analyzed by using SPSS computer program (Statistical Package for Social Sciences) verison (20.0).

Data were expressed as mean and standard deviation (±SD) for quantitative variables and number and percentage for categorical variables.

Chi-square test is used for association between quilitative data.

$t$-test is used for comparison of mean and standard deviation (±SD) of two groups.

Probability is considered significant when $p$-value equals or is less than 0.05.

$p$-value $>0.05$ = Insignificant difference.

$p$-value $<0.05$ = Significant difference.

$p$-value $<0.001$ = Highly significant.

**Results**

The patients' age ranged from 35-75 years. The mean age was $58.5 \pm 10.3$ years. There is a good clinical improvement of 80% of cases by surgical decompression of peripheral nerves.

There is an improvement in nerve conduction velocity after decompression of affected peripheral nerves in 84% after surgery.
About 73% of the surgically managed patients showed improvement of ischemia in the periphery as well as about 82% showed improvement of the neurologic condition as regarding neuropathic pain and muscle weakness improvement in the form of improved hand-grip and good walking.

Table (1): Demographic data: Frequency of age and sex of the studied patients.

<table>
<thead>
<tr>
<th>Age (years):</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD 58.5±10.3</td>
<td>35-75</td>
</tr>
<tr>
<td>Gender:</td>
<td></td>
</tr>
<tr>
<td>Male:</td>
<td>17 (34%)</td>
</tr>
<tr>
<td>Female:</td>
<td>33 (66%)</td>
</tr>
</tbody>
</table>

Table (2): Fasting and postprandial blood sugar.

<table>
<thead>
<tr>
<th>Patients</th>
<th>FBS:</th>
<th>Mean±SD 188±62.6</th>
<th>Range 90-370</th>
</tr>
</thead>
<tbody>
<tr>
<td>PP:</td>
<td>Mean±SD 289.4±83.6</td>
<td>Range 148-540</td>
<td></td>
</tr>
</tbody>
</table>

Table (3): Persistent complaint by patients.

<table>
<thead>
<tr>
<th>Persistent neuropathic pain</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stock hypothesia:</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Glove hypothesia:</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Stock and glove hypothesia:</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>Diabetic foot ulcer:</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Stock hypothesia and foot ulcer:</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Stock, glove hypothesia and foot ulcer:</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

Table (4): Success rates among patients after surgery.

<table>
<thead>
<tr>
<th>Improved</th>
<th>Not improved</th>
<th>χ²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Persistent neuropathic pain (n=16)</td>
<td>13</td>
<td>81.25</td>
<td>3</td>
</tr>
<tr>
<td>- Stock hypothesia (n=10)</td>
<td>8</td>
<td>80</td>
<td>2</td>
</tr>
<tr>
<td>- Glove hypothesia (n=4)</td>
<td>4</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>- Stock and glove hypothesia (n=9)</td>
<td>7</td>
<td>77.8</td>
<td>2</td>
</tr>
<tr>
<td>- Diabetic foot ulcer (n=8)</td>
<td>6</td>
<td>75</td>
<td>2</td>
</tr>
<tr>
<td>- Stock hypothesia and foot ulcer (n=2)</td>
<td>1</td>
<td>50</td>
<td>1</td>
</tr>
<tr>
<td>- Stock, glove hypothesia and foot ulcer (n=1)</td>
<td>1</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>- Total (n=50)</td>
<td>40</td>
<td>80</td>
<td>16</td>
</tr>
</tbody>
</table>

Table (5): Results of Electromyography (EMG) and Nerve Conduction Studies (NCS).

<table>
<thead>
<tr>
<th>Improved</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not improved</td>
<td>8</td>
<td>16</td>
</tr>
</tbody>
</table>

Table (6): Surgical procedures.

<table>
<thead>
<tr>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carpal tunnel division</td>
<td>35</td>
</tr>
<tr>
<td>Tarsal tunnel division</td>
<td>34</td>
</tr>
<tr>
<td>Both carpal and tarsal tunnel divisions</td>
<td>1</td>
</tr>
</tbody>
</table>

Table (7): Postoperative complications.

<table>
<thead>
<tr>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non</td>
<td>45</td>
</tr>
<tr>
<td>Wound infection</td>
<td>2</td>
</tr>
<tr>
<td>Delayed wound healing</td>
<td>3</td>
</tr>
</tbody>
</table>

Table (8): Secondary outcome parameter comparison between the two groups.

<table>
<thead>
<tr>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascularity improvement (ischemia or gangrene)</td>
<td>8/11</td>
</tr>
<tr>
<td>Neurologic improvement (neuropathic pain and muscle weakness)</td>
<td>32/39</td>
</tr>
</tbody>
</table>

Discussion

Diabetic neuropathy has traditionally been considered as an irreversible condition and the treatments are mostly symptomatic aiming to prevent the development of complications rather than to target the underlying pathologic mechanisms [8].

However, the proposal of "double crush" hypothesis contributed by the combination of increase endoneurial water content and consequent slow axoplasmic flow offers hope to people with diabetic neuropathy and superimposed nerve compression since neurolysis of these entrapped nerves may give symptomatic relief and possess potential for reversibility. So such, over the past two decades, surgical decompression of peripheral nerves has become an increasingly popular method for treating patients suffering from painful diabetic neuropathy [9].

Although the exact pathophysiological mechanisms of neuropathic pain in diabetes remain enigmatic, several mechanisms including peripheral and central mechanisms have been postulated based on the result of experiments in animal model of neuropathic pain [10].

It is suggested that all levels of the nervous system, from peripheral nerve to the brain, were affected by the diabetic neuropathy. Both metabolic and mechanical (compressive) mechanism may be the source of the painful symptom [11].
Diabetes causes deposition of collagen in the small arteries that supply the peripheral nerves, hypothetically resulting in a length-dependent sensorimotor neuropathy. Increased aldose reductase activity in diabetes converts glucose to sorbitol, which is hydrophilic and draws water into the nerve, rendering the peripheral nerve susceptible to mechanical compression and decreasing the slow axoplasmic transport in the diabetic nerve. As a consequence, proteins for structural repairs could not be transported to the impaired site within the diabetic nerve [12].

Injured peripheral nerve fibers give rise to the intense and prolonged input of ectopic activity to the central nervous system. After that, neurons in the spinal and the brain may change their response characteristics and exhibit signs of hyperexcitability in a fashion, mimicking that presented after peripheral nerve injury [13].

The management is rather complicated. Aside from the current medical therapies including tricyclic antidepressants, the serotonin and noradrenaline re-uptake inhibitor and anti-convulsants, and so forth, an unmet need still exists for pharmacological agents targeting the underlying mechanisms due to the ineffectiveness and the side effects of the available drugs [14].

Therefore, surgical decompression is also encouraged among the patients with diffuse painful DPN when the Tinel sign is positive, which indicates the existence of entrapment and regeneration of axons [15].

The most important implication of this review is that diabetic nerve decompression is not for every patient with PDPN. The clinical features such as: Positive Tinel’s sign, negative neuropathic signs (sensory, motor and/or reflex deficits), and other compression signs (palpation/digital pressure, positive special tests) should be present in order to derive maximum benefits of surgery [16].

The presence or absence of a positive Tinel’s sign is a prognostic indicator for determining outcome for surgical decompression procedures in PDPN with a sensitivity of 88%, a specificity of 50%, and a positive predictive value of 88% [17].

The results of nerve decompression surgery for cases of DPN in the potential sites of anatomical narrowings is encouraging because it was found that a good percentage of patients showed improvement in pain and sensations, also decompression has been shown to reduce the risk of ulceration, reulceration and amputations, as observed by Nickerson et al., [7] and Dellon et al., [18].

In our study, we compare results of surgical decompression of peripheral nerves in cases of complicated diabetic peripheral neuropathy with the results of conservative medical treatment.

Our study included 100 cases of complicated diabetic peripheral neuropathy patients proved clinically and by Electromyography (EMG) and Nerve Conduction Studies (NCS). Fifty cases are treated by nerve decompression surgically in the region of carpal or tarsal tunnel and EMG and NCS are done postoperatively for follow-up.

In our study, the patients of diabetic peripheral neuropathy were complicated with persistent neuropathic pain, decreased sensations in the form of stock or glove hypothesia or both and food ulcers.

Our results showed that in the surgically managed group (50 patients), 40 patients were improved as regarding these complications in a success rate of 80%.

Also, there was improvement in peripheral nerve functions by Electromyography (EMG) and Nerve Conduction Studies (NCS) by 84% in the surgical group.

In comparison with our study, we found that decompression surgery for cases of persistent neuropathic pain showed improvement of 81.25% of cases (13 of 16 cases in the surgical group), and we found in agreement with these results that Dellon [19] in 31 patients with diabetic neuropathic pain the improvement after nerve decompression surgery was 85%.

Also, Chaffe [20] operated upon 58 cases of diabetic persistent neuropathic pain and 86% of cases showed improvement of pain. Also, Yao [21] showed improvement of 94% of 90 cases operated for persistent painful diabetic neuropathy.

In the study of Perierra [22] also in 120 patients exposed to peripheral nerve decompression surgery for painful diabetic peripheral neuropathy, 80% of patients showed improvement of pain.

In our study as regarding cases with impaired sensations or hypothesia in the form of stock or glove hypothesia or both, we operated upon 23 of 50 patients in the surgical group. We observed improvement of touch and sensibility in 19 patients in a success rate of 82.6%.

In comparison with these results, Aszmann [23] did peripheral nerve decompression surgery for 16
diabetic cases with impaired foot sensations and showed that 69% of cases improved for touch sensations. In comparison with these results. This difference is attributed to advanced state of DPN in his study than that in our study.

Also, Valdivia et al., [24] did surgery for diabetic peripheral neuropathy and hypothesia in 60 cases and showed improvement of 87% of cases for neuropathic pain and improvement of 85% of cases for touch sensation.

Shaffiroff [25] studied 300 patients with DPN with impaired sensations, he observed improvement of 80% of patients for touch and 85% of patients for pain after decompression surgery of peripheral nerves for these patients.

As regarding cases with diabetic foot ulcers, in our study in the surgical group, 11 patients out of 50 (22%) diagnosed with diabetic foot ulcers and treated by peripheral nerve decompression by division of the tarsal tunnel. We found that 8 patients out of 11 (72%) improved in the form of faster rate of ulcer healing.

Nickerson et al., [7] reported 80% reduction in risk of foot ulceration recurrence. Also, they found in a 3-year prospective study of unilateral nerve decompression surgery after diabetic foot ulcer that in the non-operated intact legs have 5.5 times the risk of ulceration than operated legs.

Also, Zhang et al., [26] study included 208 patients with distal symmetrical polyneuropathy who underwent bilateral decompression. They reported that no patient had new ulcers, reulceration, wound infections or amputation in an 18-month follow-up.

Some studies found the role of surgery for patients with DPN is still controversial. As in study of Biddinger and Amend [27], they noted that the performance of decompressive surgery to alleviate chronic neuropathic pain in patients with DPN remains controversial and has yielded equivocal results.

Also, Chaudhry et al., [28] recommended performing more randomized controlled trials for approval of the utility of surgical decompression for treatment of diabetic peripheral neuropathy.

Finally, according to our study results and according to all supporting results mentioned and opposing opinions, we found that surgical decompression of peripheral nerves is considered a new and growing modality for treatment of complications of diabetic peripheral neuropathy patients to limit progression of the disease and improve patients’ quality of life. But, more studies with large sample size are still needed to prove the effectiveness and utility of this modality.

**Conclusion:**

It could be concluded that patients with complicated Diabetic Peripheral Neuropathy (DPN) could be surgically managed successfully by decompression of peripheral nerves at site of compression in carpal and tarsal tunnels with good results in patients resistant to medical treatment.

**References**


