

## EFFICACY OF PERIPHERAL STREPTOMYCIN INJECTION IN THE TREATMENT OF IDIOPATHIC TRIGEMINAL NEURALGIA

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### ABSTRACT

**Objective:** To evaluate the efficacy of peripheral streptomycin injection in relieving the pain of idiopathic trigeminal neuralgia

**Study Design:** Quasi experimental study.

**Place and duration of Study:** Oral and Maxillofacial Surgery Department, Armed Forces Institute of Dentistry Rawalpindi, from 1<sup>st</sup> June 2006 to 31<sup>st</sup> December 2007.

**Patients and Methods:** Thirty patients of idiopathic trigeminal neuralgia were selected. They received five consecutive injections of streptomycin 1g in 3 ml of 2% Lignocaine (Septodont) with 1: 100,000 adrenaline at one week interval. Follow up was carried out at one, two and six months after the last injection.

**Results:** Age ranged from 15-78 years (mean 44.67). Male to female ratio was 1:1.14. Right side of the face was involved in 70% and left side in 30% cases. Mandibular division of trigeminal nerve was involved in 43.3% and maxillary division in 40% of the cases. In the rest both maxillary and mandibular divisions were involved. Pain was significantly decreased from baseline to 1 month ( $p < 0.001$ ). The level of pain was increased a bit but the increase was significant at two months ( $p = 0.006$ ) and at 6 months ( $p = 0.020$ ).

**Conclusion:** Best treatment modality for this devastating disease is yet to evolve. Within the confines of the study it can be stated that efficacy combined with low post treatment morbidity makes streptomycin a useful treatment option.

**Keywords:** Idiopathic, Streptomycin, Trigeminal neuralgia.

### INTRODUCTION

Trigeminal neuralgia (TN) is a well recognized disorder characterized by lancinating attacks of severe, current like, extremely sharp, shooting, paroxysmal facial pain confined to the somatosensory distribution of trigeminal nerve<sup>1</sup>. It is considered to be the worst form of pain experience known to man<sup>2</sup>. The incidence of TN is 3-5 cases per 100,000 per year and it increases with age getting higher above 80 years<sup>3</sup>. TN shows a slight female preponderance with a female to male ratio of 3:24. It is classified as idiopathic and symptomatic according to the presence or absence of structural lesion<sup>5</sup>. Etiology of the disease is controversial but two main theories, central and peripheral try to explain the pathophysiology of the disease<sup>6</sup>.

Diagnosis of TN is at times straight forward owing to its typical symptoms. Identification of the nerve is done by infiltration of 2 ml of 2% lignocaine at three successive intervals of time<sup>7</sup>. Carbamazepine is used as a therapeutic trial to differentiate TN from other oro-facial pains<sup>8</sup>.

Various pharmacological and surgical options are available, all with varying degrees of success. Carbamazepine, phenytoin, clonazepam and baclofen are different medicinal options available<sup>9</sup>. When medicinal treatment is no more effective various surgical modalities can be tried which include peripheral procedures like glycerol and alcohol injections, cryosurgery, peripheral neurectomy and central procedures viz microvascular decompression, radio frequency thermocoagulation, glycerol gangliolysis, balloon compression, percutaneous retrogasserian glycerol rhizotomy and gamma knife radiosurgery<sup>10</sup>.

Streptomycin, an aminoglycoside, is a powerful modulator of excitable tissues and acts as an antagonist to effects of calcium and

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decreases conduction velocity of the nerves<sup>11</sup>. It has been used successfully for various neuropathic pains as well as TN<sup>12</sup>. Pain relief of up to 30 months without loss of sensation has been reported<sup>13</sup>.

The aim of the study was to evaluate the efficacy of peripheral streptomycin injection in the treatment of idiopathic TN.

### PATIENTS AND METHODS

This quasi-experimental study was carried out at oral and maxillofacial surgery department, Armed Forces Institute of Dentistry Rawalpindi from 1<sup>st</sup> Jun 2006- 31<sup>st</sup> Dec 2007. Patients of any age and both gender suffering from idiopathic TN were included in

surgical, were discussed with the patients and only those patients were included who opted to take part in the research. Patients with a history of surgical intervention for TN, patients having renal, hearing or medical problem in which streptomycin may be contraindicated and patients having known allergies to streptomycin were excluded from the study.

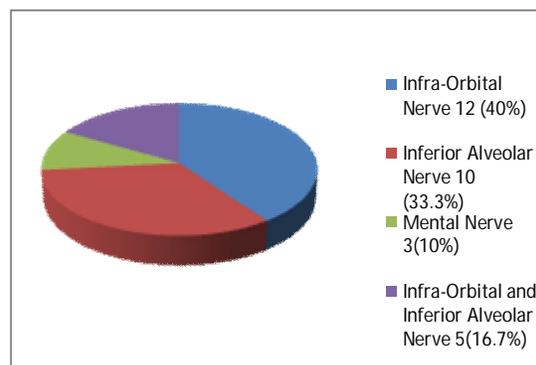
For the included patients, injection was prepared by mixing 1g injection streptomycin sulphate (streptomycin) with 3ml of 2% lignocaine with 1:100,000 adrenaline (septodent). This injection was administered at the site of involved branch using a 5 ml disposable syringe after aspiration. This study

**Table: Follow up of the patients with varying levels of pain relief.**

Pain levels	Baseline	1 Month	2 Months	6 Months
No Pain (Level 1)	0 (0%)	19 (63.3%)	13 (43.3%)	9 (30%)
Occasional Pain (Level 2)	0 (0%)	5 (16.7%)	6 (20%)	9 (30%)
Mild pain controlled by medication (Level 3)	0 (0%)	5 (16.7%)	8 (26.67%)	7 (23.33%)
Moderate pain not controlled by medication (Level 4)	9 (30%)	1 (3.3%)	2 (6.6%)	1 (3.3%)
Severe pain not controlled by medication (Level 5)	21 (70%)	0 (0%)	1 (3.3%)	1 (3.3%)

the study. Permission to conduct the study was obtained from the ethical committee of the hospital and informed written consent was taken from all the patients after explaining possible post operative complications. Total 30 patients were included in the study through non-probability convenience sampling.

For the new patients, initially, a diagnosis of idiopathic TN was made on the basis of history and clinical examination and was confirmed by administering 200 mg carbamazepine tablet every eight hourly for five days. For patients who had already been diagnosed properly, the above mentioned procedure was not carried out. The involved branch was identified by infiltrating 2 ml of 2% lignocaine with 1:100,000 adrenaline. Three successive injections on alternate days were administered to confirm the involved branch. Once diagnosis was confirmed and the correct identification of involved branch was done, various treatment options, both medical and



**Figure: Description of nerves involved in patients with TN.**

injection was administered weekly for five consecutive weeks. After completion, the patient was advised to report back for follow up visits after one month, two months and six months. On these visits, the patients were assessed regarding his/her level of pain and sensory function of the involved branch. The pain was categorized into five levels, no pain

(level 1), occasional pain (level 2), mild pain controlled by medication (level 3), moderate pain not controlled by medication (level 4), severe pain not controlled by medication (level 5).

Data had been analyzed using SPSS version 11. Mean and standard deviation (SD) were calculated for quantitative variables while frequency and percentages for qualitative variables. All cases were analyzed for the level of pain relief and sensory function of the involved branch after one, two and six months.

## RESULTS

A total of 30 patients of idiopathic TN were included in the study. The age ranged from 15-78 years with an average age of 44.67 years (SD = 15.23). Fourteen (46.7%) patients were males and 16 (53.3%) were females with an overall male to female ratio of 1: 1.14. Right side of the face was involved in 21 (70%) patients and only 9 (30%) showed involvement of left side. The distribution of nerves involved is shown in fig.

The results of follow up at 1, 2 and 6 months regarding level of pain are shown in table. Pain was significantly decreased from baseline to 1 month ( $p < 0.001$ ). The level of pain was increased a bit but the increase was significant at two months ( $p = 0.006$ ) and at 6 months ( $p = 0.020$ ). After two months, 3 (10%) and after six months 2 (6.6%) patients showed moderate to severe pain which could not be controlled by medication. For these patients, other treatment options had to be considered.

Eighteen (60%) patients reported with post injection swelling at the site of injection, which persisted for 3-4 days. Six (20%) patients complained of pain at injection site which was subsided within one week with the use of simple analgesics. Two (6.7%) patients complained of trismus which improved by physiotherapy. No other significant side effects were noted.

## DISCUSSION

TN is a chronic facial pain syndrome characterized by paroxysms of excruciating pain that adversely affects patient's quality of life<sup>14</sup>. Millions of patients are affected across the globe. Pharmacotherapy allows most patients at least some degree of relief but a substantial

number 30-70% remain either refractory to treatment or side effects of drugs prevent their use<sup>15</sup>. When medicinal treatment fails, only surgical modalities are left which vary in their level of invasiveness and effects.

Peripheral injections of streptomycin sulphate have been tried in various neuropathic pains. Different proposed mechanisms of action include, membrane stabilization effects, decreased release of acetylcholine at the ganglion level, reduction in conduction velocity of nerves and antagonization of physiological effects of calcium in neural tissues<sup>11,13,16</sup>. It affects protein synthesis, cellular respiration in mitochondria and phosphoinositide system<sup>11</sup>. Streptomycin is available in Pakistan as a sulphate and is soluble in water. It is stable at pH 2-11 with optimum pH in the alkaline range. It is slowly released with a tissue half life varying between 40-700 hours<sup>12</sup>.

When we analyzed age in our study, it was ranged from 15-78 years with a mean age of  $44.46 \pm 15.23$  years and a reasonable number of patients falling in fourth and fifth decades of life. Various studies have shown the peak age of onset between fifth to eighth decade<sup>17</sup>. Study by Kanpolat<sup>17</sup> showed a mean age of 54.9 years while Sohail et al<sup>18</sup> reported mean age to be 52 years. On the other hand, study by Khitab<sup>19</sup> showed mean age of 43.3 years.

Regarding gender, various authors have observed a female preponderance. In our study male to female ratio of 1:1.14 was observed. Katusic et al<sup>20</sup> reported female predilection with a ratio of 5.9:3.4. Zakrazewska<sup>21</sup> on the contrary, observed equal involvement of both genders.

For involvement of side, results of our study coincide with other studies<sup>18,19,20,22</sup> in which frequent involvement of the right side is observed. No case of bilateral TN was seen in our study although authors have reported bilateral involvement in a very small number<sup>23</sup>.

Mandibular division was more affected than the maxillary as in our study<sup>20</sup>. Ophthalmic division was not affected in any case and 16.7% showed involvement of both maxillary and mandibular nerves.

Stajcic et al<sup>24</sup> studied the effects of streptomycin in patients with idiopathic TN and concluded that it was initially effective.

This finding coincides with our study as well in which initially 80% responded very affectively to the treatment. Skolovic et al<sup>13</sup> found that almost 80% remained pain free for up to 30 months. In our group, approximately 60% remained pain free for up to six months. A point worth mentioning here is that these studies talked about duration of pain relief but did not highlight degree of pain relief. We monitored and recorded the level of pain in our patients during the follow up period. Patients who remained pain free and those who experienced mild pain made almost 83.33% of the total patients.

Peripheral streptomycin injection did not cause any statistical change in the appreciation of light touch and pin prick in our study. This fact has also been reported by McLeod and Patton<sup>25</sup>, Sokolovic et al<sup>13</sup> and Stajcic et al<sup>24</sup>. Post injection swelling at the site of injection was also reported by other authors<sup>13,25</sup>.

A number (16.67%) of patients had recurrence of pain which is almost same as reported by Sokolovic et al<sup>13</sup> while Stajcic et al<sup>24</sup> reported a slightly higher rate of recurrence.

One patient did not benefit from our study injection and quit after the second month of follow up, while three others had an early recurrence of symptoms after two months. These patients were then shifted to other treatment modalities.

All other treatment modalities are associated with some degree of complications. Peripheral injections of alcohol and glycerol do produce some degrees of trismus and transient to permanent paresthesia in the nerve distribution. Streptomycin did not show such post injection complications.

It is our suggestion that further studies should be carried out on the subject with a longer follow up period and larger sample size and so the benefits can be documented in our population and the reliability of streptomycin sulphate in the treatment of idiopathic TN can be enhanced.

## CONCLUSION

Streptomycin injections can be used effectively for the management of intolerable pain of TN especially when other modalities fail to provide satisfactory pain relief or are

associated with side effects. Streptomycin is associated with minimal side effects and is easily available and quite economical.

## CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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