Spinal Cord (2002) 40, 282–285

www.nature.com/sc

*Original Article*

# Gabapentin for neuropathic pain following spinal cord injury

T-P To*[,1], TC Lim[2,3], ST Hill[2], AG Frauman[4], N Cooper[2], SW Kirsa[1] and DJ Brown[2]

*[1]Pharmacy Department, Austin & Repatriation Medical Centre, Victoria, Australia; [2]Victorian Spinal Cord Service, Austin & Repatriation Medical Centre, Victoria, Australia; [3]Olympia Private Rehabilitation Hospital, Victoria, Australia; [4]Clinical Pharmacology & Therapeutic, Austin & Repatriation Medical Centre, Victoria, Australia*

**Study design:** Retrospective review of patient data.
**Objective:** To present two years of experience in the use of gabapentin for the alleviation of neuropathic pain in spinal cord injury patients.
**Setting:** Supra-regional Spinal Cord Service, Melbourne, Australia.
**Method:** Data were retrieved from the medical records of all spinal cord injury patients prescribed gabapentin for neuropathic pain. Pain was assessed prior to and during treatment at 1, 3 and 6 months with a 10 cm visual analogue scale which ranged from 0 ('no pain') to 10 ('worst pain imaginable'), or by the documentation of a verbal description of pain.
**Results:** Seventy-six per cent of patients receiving gabapentin reported a reduction in neuropathic pain. In those patients with data at all four measurement points, the mean pretreatment score was 8.86. Following treatment with gabapentin the score dropped to 5.23, 4.59 and 4.13 at 1, 3 and 6 months, respectively. Where only a verbal description of pain was documented, the trend was that the pretreatment report of 'unbearable' was replaced by 'liveable' during treatment.
**Conclusion:** Our experience suggests that gabapentin offers an effective therapeutic alternative for the alleviation of neuropathic pain following spinal cord injury. Controlled clinical trials are now required to confirm these observations.
*Spinal Cord* (2002) **40,** 282–285. doi:10.1038/sj.sc.3101300

**Keywords:** gabapentin, neuropathic pain, spinal cord injury

## Introduction

Pain is a frequent and major consequence of spinal cord injury (SCI).[1,2] Recent estimates of occurrence of pain in SCI patients ranged from 30% to in excess of 90%, with approximately 30% of this manifesting as neuropathic pain (NP).[1–3] NP is an intractable form of pain resulting from nerve cell damage or axonal damage caused by a primary lesion (such as SCI) or dysfunction in the nervous system and may not require peripheral nociceptor activation.[2,4] However, it frequently involves both peripheral and central sensitisation. NP is often described as paroxysmal, burning, stabbing, pulsing, electric shock-like or dysaesthesic – a spontaneous or evoked unpleasant abnormal sensation. Hyperalgesia, or heightened response to painful stimuli, may be present in the area of injury or in the surrounding area which is indicative of central sensitisation. Allodynia (pain in response to a non-painful stimulus such as a light touch) also indicates central sensitisation.[4]

While some forms of pain may be managed successfully with simple analgesics and adjunctive therapy (such as physiotherapy, transcutaneous electrical nerve stimulation (TENS)), NP is often more difficult to treat.[1,2,5] Early diagnosis and treatment are preferable, as chronic NP is very difficult to treat. A realistic goal is to reduce the pain to an acceptable level for the patient, as total eradication is rarely possible.[4]

Tricyclic antidepressants, and anticonvulsants such as sodium valproate and carbamazepine, have been widely used in the treatment of NP. While these agents are often effective, adverse effects also frequently occur.[4] Other agents used include membrane stabilisers such as mexiletine, benzodiazepines, and opioids.

Gabapentin is an anticonvulsant structurally related to the neurotransmitter gamma-amino butyric acid (GABA), however, it does not bind significantly to GABA receptors. The mechanisms of gabapentin's

*Correspondence: T-P To, Pharmacy Department, Austin & Repatriation Medical Centre, Locked bag 25, Heidelberg, Vic. 3084, Australia; E-mail: phung@armc.org.au

anticonvulsant and analgesic action remain unclear, but are believed to be different from other anticonvulsants. Gabapentin appears to be quite safe and tolerated with a low incidence of side effects.[6]

Promising results have been reported on use of gabapentin in the treatment of various NP syndromes. Two recent clinical trials have established the effectiveness of this agent for diabetic neuropathy and post-herpetic neuralgia.[7,8]

## Methods

SCI patients prescribed gabapentin were identified from the pharmacy dispensing records and from manual searches through spinal office correspondence. Data were then retrieved from the medical records of those prescribed gabapentin for NP.

Pain was assessed prior to treatment (baseline), and at 1, 3 and 6 months during treatment, with a 10 cm visual analogue scale (Figure 1), which ranged from 0 ('no pain') to 10 ('worst pain imaginable') or by the documentation of a verbal description of pain. The verbal descriptions were based on patients' reports and were not standardised.

## Results

Forty-four patients were identified as being prescribed gabapentin for NP. Six of these patients had little or no further information other than the fact that therapy for two patients was subsidised by Veteran Affairs and another two by accident compensation.

Of the 38 patients with information, the mean age was about 47 years, with a range of 15–75 years. There were more males ($n=28$) than females ($n=10$). There were slightly more paraplegic ($n=19$) than tetraplegic patients ($n=16$) and almost three times more chronic ($n=24$), compared to acute ($n=9$), patients. ('Acute' in this situation is defined as less than 6 months from time of injury). Table 1 shows the breakdown in patient deomgraphics.

There were various documentations of verbal reports of pain described by the patients. These reports ranged from constant, severe, shooting, burning pain, to constant tingling pain on movement and touching of 'normal' areas. Some examples of the verbal reports of pain documented prior to treatment with gabapentin are found in Table 2.

Information on previous medications used for NP was found for 32 of the 38 patients. On average, each patient took around four medications, and this ranged from one to eight. Table 3 contains a list of the types of medications taken by the patients.

The initial dose of gabapentin was 900 mg per day, usually as 300 mg three times a day. The median maintenance dose was 2400 mg daily, usually as 800 mg three times a day or 600 mg four times a day. The range was 900 mg to 4800 mg daily.

Based on visual analogue scores (VAS) and patients' verbal descriptions, 29 of the 38 patients (76%) had some improvement from gabapentin therapy. In total, there were eight reports of adverse effects. The majority of complaints were drowsiness, especially initially, dizziness, and somnolence. Nine patients ceased therapy – four of these because of adverse effects, in particular dizziness and somnolence. In the other five patients, gabapentin was deemed ineffective. In all nine cases, therapy was ceased within the first month (Table 4).


**Figure 1** Visual analogue scale

**Table 1** Patient demographics

| | |
|---|---|
| Number of patients identified | 44 |
| *Patients with information* | 38 |
| Age: Mean | 46.8 (SD 13.7) |
| Range | 15–75 |
| Males | 28/38 (74%) |
| Females | 10/38 (24%) |
| Paraplegia | 19/38 (50%) |
| Tetraplegia | 16/38 (42%) |
| No information | 3/38 (8%) |
| Acute | 9/38 (24%) |
| Chronic | 24/38 (63%) |
| No information | 5/38 (13%) |

**Table 2** Verbal reports of pain prior to treatment

- sharp, burning pain increasing in intensity over the years
- severe neuropathic discomfort
- burning pain legs and buttocks
- severe NP left foot
- constant burning pain (legs and buttocks)
- pain and dysaethesia left arm
- severe NP both legs
- tingling, pain on movement and touching normal areas
- perineal pain, numbness
- severe pain left thigh and groin
- right sided neuropathic discomfort
- 'shooting' left sided leg and testicular pain
- bilateral paraesthesia
- sharp NP exacerbated by sitting

Twenty-eight of the 38 patients originally identified had baseline VAS. Nineteen of these had scores at 1 month, 14 had scores at 3 months, and 16 had scores at 6 months of therapy. Of the 28 patients, 22 had more than one VAS (Table 5).

Prior to treatment, the mean baseline VAS for the 28 patients was 8.88. At 1 month of therapy, the mean score for 19 of these 28 patients was 5.47. From a sample of 14 and 16 patients, respectively, the mean score continued to drop at 3 and 6 months, although not as dramatically (Table 6). Eleven patients had data at all four measurement times and this data was analyzed using a one-way repeated measure analysis of variance (ANOVA). The mean pretreatment VAS was 8.86. At 1, 3 and 6 months of therapy, the score dropped to 5.23, 4.59 and 4.13, respectively. A statistically significant difference was found between times ($F_{3,30}=24.92$, $P<0.001$) with a significant curvilinear trend ($F_{1,10}=23.63$, $P=0.001$). Contrast testing indicated that the major difference lay between baseline and follow-up times with no significant differences apparent between 1, 3 and 6 months (Figure 2).

Apparent improvements were also noted with the verbal reports of pain following therapy with gabapentin. Comments such as 'life/pain is liveable' and 'increase in quality of life' were described by a number of patients. Table 7 lists some of the documented verbal reports relating to NP following treatment with gabapentin.

**Table 3** Previous medications used for NP

| | |
|---|---|
| Anticonvulsants | carbamazepine, sodium valproate |
| Tricyclic antidepressants | clomipramine, amitriptyline, imipramine, dothiepin |
| Other antidepressants | sertraline, paroxetine, fluoxetine |
| Membrane stabilisers | lignocaine infusion, mexiletine |
| Benzodiazepines | diazepam, clonazepam |
| Compound analgesics | Panadeine®, Panadeine Forte®, Digesic® |
| Opioid analgesics | intrathecal and oral morphine, methadone, oxycodone |
| NSAIDs | indomethacin, naproxen |
| Others | phentolamine, thiamine, prazosin, dantrolene, TENS |

**Table 4** Cessation of therapy

| | n = *38* |
|---|---|
| Effective | 29 (76%) |
| Ceased | 9 (24%) |
| ineffective | 5 (13%) |
| adverse effects (AEs) | 4 (10.5%) |
| Total AEs | 8 (21%) |

**Table 5** Number of patients with VAS

| | |
|---|---|
| Baseline VAS | 28/38 (74%) |
| 1 month VAS | 19/28 (68%) |
| 3 months VAS | 14/28 (50%) |
| 6 months VAS | 16/28 (57%) |
| Number with greater than one VAS | 22/28 (76%) |

**Table 6** Mean VAS over the four times of measurement

| | *Mean VAS* | *95% Confidence interval* | *Mean VAS* (n = *11*) |
|---|---|---|---|
| Baseline ($n=28$) | 8.88 | 8.49–9.27 | 8.86 |
| 1 month ($n=19$) | 5.47 | 4.58–6.36 | 5.23 |
| 3 months ($n=14$) | 4.36 | 3.11–5.61 | 4.59 |
| 6 months ($n=16$) | 4.03 | 3.24–4.82 | 4.13 |

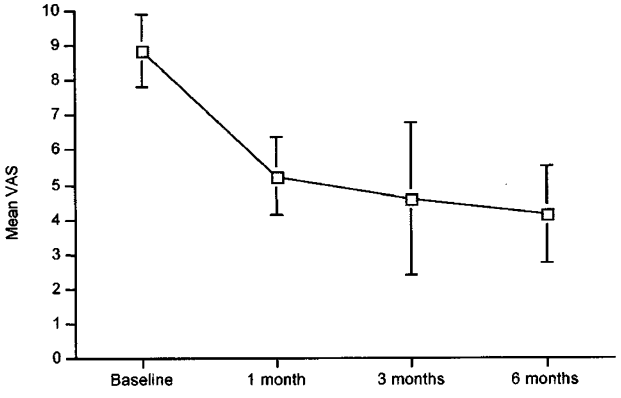


**Figure 2** Visual analogue scores

**Table 7** Verbal reports following treatment with gabapentin

- increase in quality of life
- pain reduced by 70%
- 95% better
- liveable
- managing with comfort
- able to sleep
- life unbearable without it
- neuropathic discomfort resolved with gabapentin
- no reduction in intensity but reduction in episode
- good reduction in shoulder and back pain
- pain increased to 9/10 when gabapentin stopped
- more functional/participate in domestic duties
- increase in functional capacity
- pain better than previous 14 years

## Discussion

These results support the effectiveness of gabapentin for NP following SCI, especially when taking into consideration that many of these patients had trialled a number of other medications with limited success. The results also indicate that effectiveness was evident within the first month of therapy. In the nine patients where therapy was deemed ineffective, gabapentin was ceased within the first month. Most improvement occurred in the first month of treatment and there was a marginal continued improvement at 3 and 6 months of therapy.

Limitations of the results stem from the uncontrolled and non-standardised manner in which VAS and pain observations were made and obtained. In addition, not every patient had a complete set (four) of VAS. This was difficult to achieve given that it was not a formal clinical trial. Considerations that may confound results include whether NP is chronic or acute (as chronic NP may be even more difficult to treat). The type and location of NP may be an important factor, as may the level of SCI, and also whether the lesion is a complete or incomplete injury. Co-medications in particular can confound results, however, it was very difficult to retrospectively extract this information primarily due to the majority of these patients being out-patients and had their other medications attended to elsewhere.

In conclusion, although clinical controlled trials are required to confirm these results, our experience suggests that gabapentin offers an effective therapeutic alternative for the alleviation of NP following SCI.

## References

1 Kristjan T, Ragnarsson MD. Management of pain in persons with spinal cord injury. *J Spinal Cord Med* 1997; **20:** 186 – 199.
2 Eide PK. Pathophysiological mechanisms of central neuropathic pain after spinal cord injury. *Spinal Cord* 1998; **36:** 601 – 612.
3 Siddall PJ, Taylor DA, Cousins MJ. Classification of pain following spinal cord injury. *Spinal Cord* 1997; **35:** 69 – 75.
4 National Health and Medical Research Council (NHMRC). Acute pain management: information for general practitioners. Commonwealth of Australia 1999. Ampersand editorial & design, Canberra.
5 New PJ, Lim TC, Hill ST, Brown DJ. A survey of pain during rehabilitation after acute spinal cord injury. *Spinal Cord* 1997; **35:** 658 – 663.
6 Neurontin (gabapentin) approved product information. Park Davis Pty Ltd. Date of TGA approval or last amendment: 18 April 2000.
7 Backonja M *et al*. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus: a randomized controlled trial. *JAMA* 1998; **280:** 1831 – 1836.
8 Rowbotham M, Harden N, Stacey B, Bernstein P, Magnus-Miller L. Gabapentin for the treatment of postherpetic neuralgia: a randomized controlled trial. *JAMA* 1998; **280:** 1837 – 1842.