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# Octreotide, a small peptide, alleviates burning pain and hyperaesthesia: a preliminary study*

WLADISLAW V. ELLIS MD

*Department of Orthopedics, University of California, San Francisco Medical Center, 2445 Carleton Street, Berkeley, CA 94704, USA*

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**summary** Octreotide, an octopeptide analogue of Somatostatin, relieves specifically burning pain and cutaneous hyperaesthesia. Topical application with a penetrant (dimethylsulphoxide; DMSO) controls these symptoms in the majority of patients tested at a dosage of 0.5–2.0 μg/day.

*Key words:* octreotide; Somatostatin; burning pain; hyperaesthesia.

**introduction**

Small peptides affect neuronal transmission and are thought to be involved in nociception.[1–4] Substance P, vaso-active intestinal peptide, cholecystokinin, and neuropeptide Y, among others, have been implicated in the pathogenesis of neurogenic oedema and in the perpetuation of chronic pain states.[5–7]

Somatostatin exerts modulatory effects, usually inhibitory, on peptides, hormones and cyclic adenosine monophosphate (cAMP) mediated transmission.[8–11] The major drawback in the clinical use of Somatostatin has been its very short half-life. Thus, the availability of a long-acting analogue, octreotide, prompted a trial of this peptide as an analgesic. Octreotide showed no effect on acute incisional pain, but eliminated the local hyperaesthesia as demonstrated by a similar control incision.

**methods**

Octreotide (Sandostatin, Sandoz) was administered topically as a 1 μg/ml solution in a dimethyl sulphoxide (DMSO) 60 per cent solution.[12,13] Twenty per cent by weight of urea was added to decrease the annoying short-term burning and pruritis produced by the DMSO;[14] the resulting solution was termed Octosol. Octreotide (5 μg), in physiological saline, was also injected subcutaneously as a 1 ml bolus in three of the subjects.

Eight females and 15 males ranging in age from 24 to 76 years, afflicted with neuroskeletal diseases (group 1), and four men and three women with post-herpetic neuralgia, aged 46–86 years (group 2), participated in this study. All had burning pain and/or hyperaesthesia of 2 months–12 years duration. Informed consent was obtained from all individuals tested.

Since DMSO has therapeutic effects of its own, a double-blind study was carried out on eight of the participants in order to determine what effect, if any, the DMSO had on burning pain and hyperaesthesia.

In all patients the topical solution was applied with a glass eyedropper to the skin surface in the area of the burning pain and/or hyperaesthesia. Results were apparent within 40 min of the topical application. Results from the subcutaneous injection of a 5 μg bolus took less than 5 min to appear.

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## results

Because of the therapeutic actions of DMSO in its own right, a double-blind experiment was done on eight patients who had previously used DMSO and had experienced the subjectively beneficial action of Octosol. Vials, identical except for their numbering, contained either Octosol or a DMSO 60 per cent and urea 20 per cent solution. Subjects were asked to determine whether or not they experienced pain relief. The observer (W.V.E.) did not know which vials contained octreotide when issuing them. All subjects correctly identified the presence or absence of octreotide on the basis of their pain relief.

Twenty of the 23 group 1 subjects (87 per cent) experienced complete relief from burning and hyperaesthesia. This relief lasted from 8 to 24 h and showed no decrease with subsequent reapplication of Octosol to the symptomatic skin surface. Continued use resulted in the eventual disappearance of all symptoms (see Table I). There were three exceptions to the above progression. These were subjects who had significant pain relief initially, but required up to two subcutaneous injections of octreotide per day for continued relief. No other subjects received injections.

**Table I.**
Effects of topical octreotide (Octosol) on burning pain and hyperaesthesia

| | Reflex sympathetic dystrophy | Degenerative diseases of the spine | Fibromyositis | Post-herpetic neuralgia |
|---|---|---|---|---|
| Absence of burning and hyperaesthesia | 8 | 8 | 4 | 2 |
| Partial relief | 0 | 0 | 0 | 4 |
| No response | 3 | 0 | 0 | 1 |
| Daily dosage topical octreotide | 0.3–3 μg | 0.5–5 μg | 0.5–2 μg | 0.5–20 μg |
| Time until complete symptom resolution | 7 weeks | 4 weeks | 2 weeks | No resolution |
| Continued use | 3 | 0 | 0 | 4 |

Relief from the symptoms of burning pain and hyperaesthesia was complete in two of the seven group 2 subjects (28 per cent), whereas relief was complete in all responding group 1 subjects. Various degrees of partial relief occurred in four of the group 2 subjects and no response in one subject. Four subjects have used Octosol daily for 3–7 months.

Pain other than of a burning character (grabbing, stabbing, swelling, etc.) was not consistently affected. Of interest, anecdotally, is the observation that subjects who responded well to Octosol reported improvement of a variety of other symptoms (mood, lowered blood pressure, diabetic control, lessened peripheral oedema, etc.).

## discussion

The topical application of 150–500 ng of octreotide, a cyclic, long-lasting, octopeptide analogue of Somatostatin, to a skin surface of 100–500 $cm^2$, results in the specific disappearance of burning pain and hyperaesthesia. The addition of a skin penetrant (DMSO) was necessary, but not sufficient to achieve this effect alone, as demonstrated by a double-blind study.

An effect was seen in 88 per cent of subjects with pain of neuromuscular aetiology and the specific symptoms resolved with continued application of the experimental solution. Results were less dramatic with a small population of subjects suffering from post-herpetic neuralgia. Two of seven (29 per cent) experienced disappearance of burning pain and hyperaesthesia. Four subjects experienced enough relief to continue daily administration of Octosol. Continued application of Octosol in group 2 subjects did not result in a lessening of their burning pain and hyperaesthesia as did occur with group 1 subjects.

In group 1, the three subjects who reported no benefit were all stage III reflex sympathetic dystrophy. In group 2, the one subject who reported no benefit complained of increased burning, due, presumably, to the DMSO. No

other side effects or complaints were noted.

The mechanism of action explaining these results remains unknown. Observations that Somatostatin inhibits and/or modulates the actions of many peripherally active neuromodulators suggest that octreotide might function in the same manner by, possibly, desensitizing C-receptors.[15]

The specificity of octreotide in its effect on subsets of pain (burning and hyperaesthesia) raises numerous questions. Are other kinds of pain affected by other peptides? Is "pain", in some significant sense, an epiphenomenon, the result of a change in the state of a sensory network, rather than the activation of specific fibres?

Furthermore, evidence that Somatostatin as well as other neuropeptides affect neutrophil and eicosanoid function evokes the possibility of involvement of the immune system in certain pain states.[16,17]

Given the unusual nature of these results, confirmation is of primary importance and can then be followed by exploration of the above issues.

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