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Perispinal TNF-alpha inhibition for discogenic pain

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Summary

Objective: To examine the potential of etanercept, a biological inhibitor of tumour necrosis factor-alpha (TNF), delivered by perispinal administration, for the treatment of pain associated with intervertebral disc disease.

Methods: Charts from 20 selected patients treated at our private clinic by perispinal delivery of etanercept 25 mg for severe, chronic, treatment-resistant discogenic pain were reviewed. Therapeutic benefit was assessed clinically and was documented by changes in a validated pain instrument, the Oswestry Disability Index. The patients were treated off-label with etanercept as part of our usual practice of medicine. Five detailed case reports are presented, including three additional patients.

Results: Rapid, substantial and sustained clinical pain reduction was documented in this selected group of patients. The cohort of 20 patients had a mean age of 56.5 and mean duration of pain of 116 months. Nine of the patients had undergone previous spinal surgery; 17 had received an epidural steroid injection or injections (mean 3.2). This group of patients received a mean of 1.8 doses (range 1–5, median 1.0) of etanercept during the observation period. The mean length of follow-up was 230 days. Clinical improvement was confirmed by a decrease in the calculated Oswestry Disability Index from a mean of 54.85 ± 12.5 at baseline, improving to 17.2 ± 15.3 ($p < 0.003$) at 24 days and ending at 9.8 ± 13 ($p < 0.003$) at 230 days.

Conclusions: TNF inhibition by etanercept delivered by perispinal administration may offer clinical benefit for patients with chronic, treatment-resistant discogenic pain. Further study of this new treatment modality is warranted.

Key words: tumuor necrosis factor; TNF; etanercept; discogenic pain; cervical radiculopathy; lumbar radiculopathy; failed back syndrome

Introduction

The biological TNF inhibitors, consisting of etanercept, infliximab, adalimumab, CDP 870, onercept and other molecules in clinical development, constitute a new class of therapeutic agents which have proved remarkably effective for a variety of treatment-refractory chronic inflammatory disorders [1–6]. Etanercept, an anti-TNF fusion protein, was the first recombinant TNF inhibitor to be available for subcutaneous use. It functions as a selective and potent inhibitor of the biological action of TNF. Etanercept is currently approved for the treatment of rheumatoid arthritis in children [7] and adults [8] and psoriatic arthritis [9]. It has also been shown to be effective in relieving refractory back and neck pain associated with ankylosing spondylitis [10]. Because of the fundamental involvement of TNF in generating the inflammatory response, etanercept has potential for treating a diverse group of systemic and localised clinical disorders. It is currently being studied with a view to treating Wegener's granulomatosis, dermatomyositis, histiocytosis, psoriasis, cancer cachexia, temporomandibular disorders, pain and swelling after molar extraction, and a number of other inflammatory disorders with documented involvement of TNF.

A central role of TNF in one localised inflammatory disorder, pain associated with intervertebral disc disease, has been suggested by an elegant series of experiments conducted over two decades. It is known that disc herniation can lead to pain by mechanical compression of adjacent nerve roots. However, a subset of patients have pain without demonstrable compression, or continue to have pain despite seemingly successful surgical removal of the offending protruding disc [11]. A chemical component of the pain, independent of structural deformation, was suspected [12, 13]. Subsequent research showed that a component of the intervertebral disc, the nucleus pulposus, was inherently inflammatory and could cause nerve damage without compression [14, 15]. Investigation has confirmed that TNF duplicates nucleus pulposus-induced inflammation and neuropathy [16]. TNF

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