

These have also been looked at in a previous article on Opioid medication for neuropathic pain.

It has been found that elevation of the anti-opioid peptide cholecystokinin (CCK) is one of the likely causes of incomplete analgesia with opioid medication. This has been demonstrated in animal studies ( [\[i\]](#) ).

Nerve injury results in a rise in plasma CCK ( [\[ii\]](#) ) so that administration of an antagonist such as proglumide (originally developed as an anti-ulcer drug) may affect a return to the pain being opiate-responsive.

McCleane ( [\[iii\]](#) ) has found that proglumide can augment the analgesia from sustained-release morphine for neuropathic pain.

CCK is also raised by chronic opioid use and may contribute to development of tolerance. ( [\[iv\]](#) )  
) Watkins et al ( [\[v\]](#) )  
) have shown that proglumide can potentiate opiate analgesia and reverse morphine tolerance.

More studies need to be done to determine the best clinical use of these findings.

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[\[i\]](#) Xu X-J hao J-X, Seiger A, Hughes J, Hokfelt T, Weisenfeld-Hallin Z *Pain* 1994;56:271-7  
Chronic pain-related behaviours in spinally-injured rats; evidence for functional alterations of the endogenous cholecystokinin and opioid systems.

[\[ii\]](#) Xu X-J, Puke MJC, Verge VMK, Weisenfeld-Hallin Z, Hughes J, Hokfelt T. *Neuroscience Letter* 1993;152: 129-132. Up-regulation of cholecystokinin in primary sensory neurones is associated with morphine sensitivity in experimental neuropathic pain in the rat.

[iii] McCleane GJ *The Pain Clinic* 1998;11;103-107 The cholecystokinin antagonist proglumide enhances the analgesic effect of morphine in chronic benign nociceptive and neuropathic pain.

[iv] Hoffmann O, Weisenfeld-Hallin Z *NeuroReport* 1994;5:2565-2568 The CCK-B receptor antagonist CI 988 reverses tolerance to morphine in rats.

[v] Watkins LR, Kinscheck IB, Mayer DJ *Science* 1984; 224: 395-6 Potentiation of opiate analgesia and apparent reversal of morphine tolerance by proglumide.