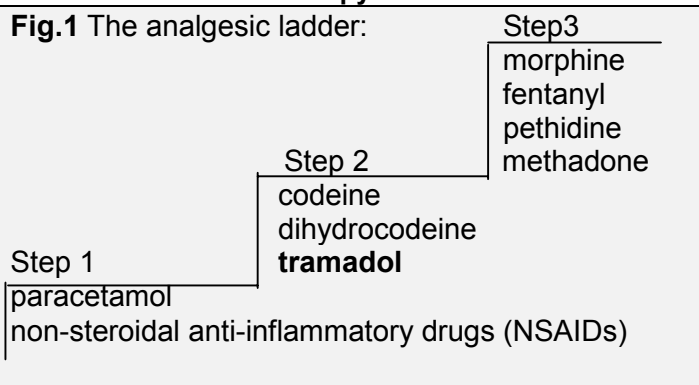


Tramadol - its place in pain therapy - another update

In the first half of this financial year (July to December 2002) the cost of tramadol use at Christchurch Hospital was \$8,290. This represents an increase from the same period in 2001 of \$1,123 (16%).

Tramadol's Place in Therapy

Fig.1 The analgesic ladder:



Patients take a step up the analgesic ladder once the maximum dose on each step no longer controls the pain (Fig 1). It is **not logical** to co-administer a Step 2 drug with a Step 3 as these agents are all opioids. Step 1 drugs are often used in combination with Step 2 or Step 3 drugs as they are not opioids and act synergistically. In most post-operative patients progress is down the ladder as the pain reduces.

Mechanism of Action

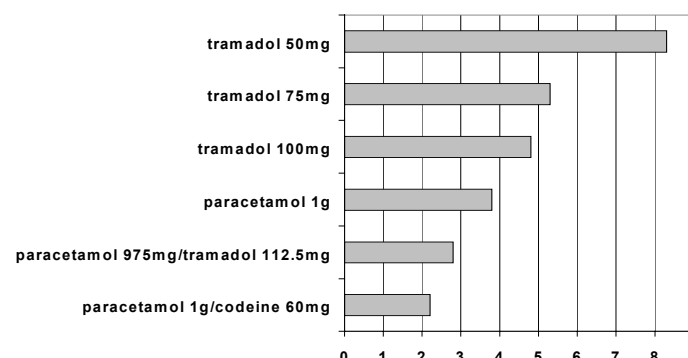
Tramadol has two mechanisms of action. As an opioid analgesic it stimulates opioid receptors. It also has an effect on noradrenaline and serotonin in the descending inhibitory pain pathways of the spinal cord. This second mechanism of action is thought to be similar to that of tricyclic antidepressants in neuropathic pain and may account for the increased incidence of nausea/vomiting compared with codeine.

Efficacy

Tramadol is on the same step of the analgesic ladder as codeine and dihydrocodeine. In a meta-analysis of analgesics comparing number needed to treat to get a reduction in pain of at least 50% in one patient compared with placebo (NNT), it was found that the number needed to treat with tramadol was 4.8 (100mg), 5.3 (75mg) and 8.3 (50mg). This improved to 2.8 when 112.5mg tramadol was combined with 975mg paracetamol. In comparison the NNT was 2.2 with paracetamol 1g/codeine 60mg (Fig 2). Paracetamol/codeine appears to be more effective than tramadol either on its own or combined with paracetamol.

The second mechanism of action of tramadol (the effect on noradrenaline and serotonin in the descending inhibitory pain pathways of the spinal cord) suggests it may have a place in the treatment of neuropathic pain. There is literature to support the use of tramadol in the treatment of diabetic neuropathy pain although there is little evidence for its use in general neuropathic pain.

Fig. 2 Number of patients needed to treat to achieve at least a 50% reduction in pain score in one patient (NNT)



Adverse drug reactions

	codeine	tramadol
nausea/vomiting	+	+++*
dizziness	+	+
sedation	++	+
respiratory depression	++	+
constipation	++	+

*worse with iv administration

There have also been several reports of confusion, hallucinations, convulsions and serotonin syndrome with tramadol. Reports of abuse of tramadol can be found in the literature and tramadol should not be given to past abusers of drugs.

Interactions

Carbamazepine may increase the metabolism of tramadol - an increase in tramadol dose may be required. N.B. Avoid tramadol in patients at risk of seizures. There is also a risk of serotonin syndrome with this combination. *Tricyclic antidepressants*, *SSRIs* and *neuroleptics* increase the risk of seizures and serotonin syndrome with tramadol. SSRIs may also inhibit the metabolism of tramadol via CYP2D6 inhibition.

MAOIs - risk of serotonin syndrome - contraindicated.

Ondansetron - may impair the analgesic efficacy of tramadol and may not be effective in tramadol induced nausea and vomiting.

Warfarin - tramadol may decrease the prothrombin activity - monitor INR.

Cost

Cost per day	oral	i.v.
400mg tramadol (not slow release)	\$3.12	\$9.04
240mg codeine+4g paracetamol	\$0.96	
20mg morphine		\$1.40

Summary

Codeine with paracetamol should be used as first line Step 2 analgesic therapy. The more expensive tramadol should only be used in patients for whom the first line choice is inappropriate.

Tramadol is not funded by Pharmac and is expensive for patients on discharge.