Ketorolac Tromethamine in Cancer Pain

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Advances in the diagnosis and treatment of cancer coupled with a better understanding of the pathophysiology, pharmacology and psychology of pain and pain perception have led to improved care of patients suffering from cancer pain (1). Patients with severe cancer pain frequently need repeated doses of potent analgesics. Opioid analgesics are powerful and are widely used in this context, but the associated severe social and medical problems very often prevent them from being satisfactory (2, 3). Ketorolac tromethamine is a non-steroidal anti-inflammatory drug (NSAID) with cyclooxygenase-inhibiting activity (4). It has a potent analgesic, antipyretic and moderate anti-inflammatory activity (4–6). Ketorolac is administered as tromethamine salt orally, intramuscularly, intravenously and as a topical ophthalmic solution (5). The tromethamine salt form enhances its absorption. Clinical studies indicate single dose efficacy greater than that of morphine, pethidine, pentazocine in moderate to severe postoperative pain with evidence of a more favorable adverse effects profile than morphine, pethidine and pentazocine (4). Some studies have also found ketorolac tromethamine to be superior to aspirin, paracetamol and some other non-steroidal anti-inflammatory drugs such as naproxen and indomethacin (4, 7, 8). There are limited data on the use of ketorolac for cancer pain (9, 10). Dipyron, a pyrozolon, is an NSAID with weak anti-inflammatory activity that is widely used in Turkey (11). Dipyron inhibits the prostaglandin biosynthesis, especially in the brain. However, since this inhibition ends when it disappears from the extracellular fluid, antogonism of prostaglandins is also suggested (11). In this study we evaluated the efficacy of oral ketorolac in the relief of severe cancer pain in comparison with dipyron.

Material and Method. A total of 50 patients experiencing severe pain from cancer were enrolled in the study. Twenty-five patients were treated with ketorolac and 25 were treated with dipyron. About half of the patients in both groups had bone metastasis. Mean worst pain scores for the last 24 h were 9.52 in the ketorolac group and 9.76 in the dipyron group. The patients suffered mainly from nociceptive or visceral pain and had not been given regular analgesic treatment. Patients' characteristics are summarized in Table 1. Patients with significant impairment of brain, liver, kidney, lung and heart function and with gastric or duodenal ulcers were not included.

Treatment. Patients were given orally either 10 mg ketorolac tromethamine four times a day or 500 mg dypiron three times a day for two days. Rescue medication was available as paracetamol, if required. No analgesic was allowed within the first two hours of the initial dose. Any patient chronically receiving any kind of analgesics was not included in the study.

Clinical assessment. In the beginning of the study pain was evaluated on a 10-point visual analog scale (VAS). All patients completed the study without any withdrawals because of incompliance, adverse effects, severe pain or because of non-response to the drugs or rescue medicine. At the end of two days the patients were asked to score their pain on the VAS again and were also asked to answer verbally if they had no pain, (complete relief), felt they had benefited from the drug (incomplete relief), or had derived no benefit (no relief).

Statistics. All data analyses were performed using SPSS software. χ^2-tests, student's t-tests and Mann-Whitney U-tests were used, as appropriate. A probability of 0.05 was set as the minimum level of significance.

Results. The patients in the two treatment groups were comparable in terms of age, sex, severity of pain, and their diagnosis. A summary of the results is presented in Table 2. The decrease in VAS score was statistically significant in both treatment groups ($p < 0.05$). However, the intergroup difference was not significant ($p > 0.05$). Nevertheless, ketorolac was more successful in promoting complete relief of pain. With ketorolac pain was relieved completely in 13 patients, whereas dypiron

Table 1

Patient characteristics

	Ketorolac	Dipyron
No. of patients	25	25
Sex		
Male	15	16
Female	10	9
Age (years)		
Median	54	52
Range	25–70	22–68
Bone metastases	48%	46%
Initial VAS* score	9.52	9.76
Reduction in VAS score	6.36	6.07
Remaining pain	3.16	3.69

VAS: Visual Analog Scale

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Table 2

Responses to ketorolac and dipyron

	Ketorolac n:25		Dipyron n:25		p-value
	No. of pts*	%	No. of pts	%	
Complete relief	13	52	4	16	<0.05
Incomplete relief	7	28	17	68	<0.05
No relief	5	20	4	16	>0.05

* Patients

relieved the pain completely in only 4 patients ($p < 0.05$). Most of the patients in the dipyron group achieved only partial relief. Although the number of patients stating no relief was higher in the ketorolac group, this was not statistically significant ($p > 0.05$). No significant adverse effect was observed in either group.

Discussion. Although no difference was found in terms of decrease in the VAS score in both groups, ketorolac seems to be superior to dipyron in achieving complete relief of pain. These results may indicate that ketorolac can be successfully used in the treatment of severe cancer pain. Seventy-two percent of the patients in the the ketorolac group and 84% in the dipyron group confirmed having derived benefit. The reason for this relatively higher response to NSAID might be that the patients were not chronic analgesic users. Therefore we believe that NSAIDs can be an alternative to opiates in the first-step treatment of severe cancer pain.

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