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RESEARCH ARTICLE

COMPARATIVE EVALUATION OF EFFICACY OF STANDARD ANALGESICS IN PALLIATION OF CANCER PAIN

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ABSTRACT: Background: Pain is a prevalent symptom experienced by cancer patients and its management in most set up has been weak. In the present study, we assessed the efficacy of the analgesics in cancer patients with pain. **Methods**: This was a prospective study and was done with cancer patients with severe pain. The patients were asked to rate the severity of the pain on the Numeric Rating Scale (NRS) score and prescribed with the standard analgesic drug. They were then again asked to rate the decrease in the pain at various post drug administration time (15 min to 3 hr) using the NRS. **Results**: It was found that the out of 150 patients, 73 received tab morphine (10 mg orally every 4 hrs), 42 patients received a combination of tramadol and paracetamol (32.5mg+325mg) 8th hr, 15 patients received tab tramadol (50mg) 8th hr, 12 patients received tab paracetamol (500mg) 8th hr, 8 patients who were in very severe pain received morphine 10 mg iv diluted in 100ml normal saline and given every 4th hourly. Morphine was the analgesic of choice for mitigating severe cancer pain. The non-steroidal anti-inflammatory agents (NSAID) either alone or in combination with a weak opioid was also found to be effective in reducing medium pain. **Conclusion:** Analgesic therapy alleviates cancer pain in its multitude form. Morphine was the most common analgesic used with the NRS ranging from severe to very severe and found to be very useful.

KEYWORDS: Pain; analgesics; Numeric Rating Scale; morphine; tramadol; paracetamol

INTRODUCTION:

In people with cancer, pain is widespread morbidity, and estimates are that 25% for those newly diagnosed, 33% for those undergoing active treatment, and approximately 75% for those with the advanced disease suffer from it[1,2].

Additionally, pain continues to be a prevalent symptom experienced by approximately 33% of cancer survivors, and this affects their daily activities and quality of life[2]. Although vital, management of pain has not been emphasized and remains prevalent, neglected and undertreated in

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most healthcare setups[3]. Decades after the publication of the World Health Organization's analgesic ladder, cancer pain is still a significant cause of suffering for patients with cancer and the morbidity affects millions of people worldwide. Reports indicate that despite the availability of useful treatment options, successful treatment of cancer pain is underutilized and many patients suffer from insufficiently controlled pain and that there is a need to increase awareness among healthcare providers for the management of cancer pain[2].

The pain associated with cancer is because of several reasons, the tumor per se giving rise to pain is the most common cause of pain, and it can also be due to metastasis of the tumor to other organs, especially when the tumor pressing on to a nerve[3]. Involvement of the bone by the tumor can lead to very severe pain. Poorly managed pain can have radical catastrophic effects on the patients. Thus proper management of pain is the foremost priority in the management of patients with cancer pain. The critical components in the management of pain are the assessment of pain, adopting a standard analgesic regime and integration with other therapies. Our study attempts at assessing the intensity of cancer pain and its management. Treatment of cancer pain has many options. We have compared the efficacy of various analgesic formulations in the treatment of cancer pain.

MATERIALS AND METHODS:

The study was conducted at the oncology ward of Father Muller Medical College, Mangalore, Karnataka and the study period was from January 2012 to December 2013. With the approval of the institutional ethics committee, 150 patients were enrolled in the study. All patients were evaluated and written informed consent was obtained. The numeric rating scale (NRS) scale was used to assess the intensity of pain. The inclusion criteria included Cancer patients above the age of 12 years admitted to the oncology wards. The exclusion criteria included patients with comorbidities like severe diabetes, AIDS and those with diminished mental competence, deafness, visual disturbances which would prevent them from comprehending the numeric rating scale (NRS).

This was a cross-sectional prospective descriptive study. The patients coming to the pain and palliative care OPD and the patients admitted in the cancer wards and who have pain due to cancer were recruited in the study, all patients were given a general physical examination, and the clinical parameters like pulse rate BP were recorded, a brief history about the case is noted. The patients were first ascertained to have pain due to cancer. All patients were asked to describe the pain, and a detailed history of the symptom was obtained. The patients were informed about the study, and a signed informed consent was obtained from each of the patients.

The patients were explained in their own words about the numeric rating scale and were shown how to use it. After this, the patients were asked to rate the severity of the pain on the numeric rating scale provided to them. The NRS score was noted (baseline). The patients were then given their prescribed analgesic formulation and were asked to rate the pain on the NRS at 15 min, 30 min, 1 hr, 2 hr, 3 hr the ratings were noted. The measure of the efficacy of the analgesic formulations used is the relief of pain the patient feels and is denoted by the drop in the ratings of the NRS.

Statistical analysis:

The collected data were analyzed by mean, standard deviation, frequency percentage, demographic evaluation, sex distribution, chi-square test. Multiple comparisons were analyzed by ANOVA, and the level of significance is measured. SPSS version 17 will be used for analysis.

RESULTS:

In the study, most of the patients were afflicted by cancers of H&N and lung (23%) (Figure 1).

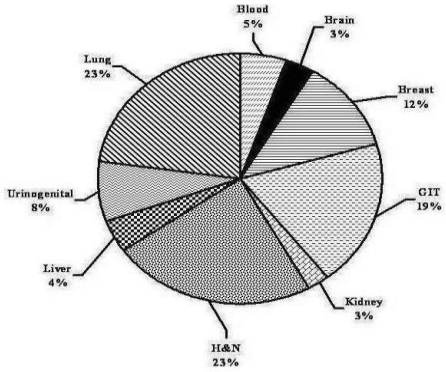

Figure 1: The distribution of cancer patients based on the site

The age of the patients enrolled for the study varied from 25 to 79 years with a maximum number of patients in the age group of 50-60 years (Figure 2).

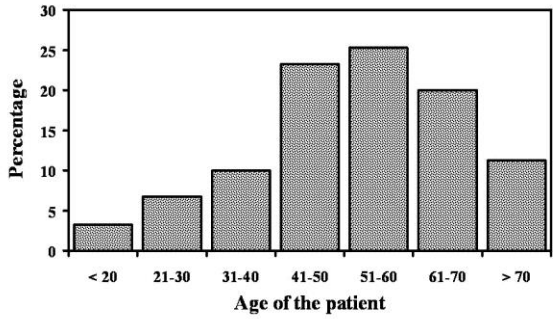

Figure 2: The distribution of cancer patients based on age

The sex distribution graph showed 47% were males and 53% were females (Table 1). It was found that the out of 150 patients, 73 received tablet morphine 10 mg orally every 4 hrs, 42 patients received a combination of tramadol and paracetamol (32.5mg+325mg) 8th hr, 15 patients received tab tramadol (50mg) 8th hr, 12 patients received tab paracetamol (500mg) 8th hr, 8 patients who were in very severe pain received morphine 10 mg iv diluted in 100ml normal saline and given every 4th hourly.

Table 1: Gender distribution in the various analgesic treatments

Gender	Group					Total
	Morphine	Tramadol+ Paracetamol	Tramadol	Paracetamol	Morphine IV	
Females (%)	35 (47.9%)	21 (50.0%)	10 (66.7%)	9 (75.0%)	5(62.5%)	80 (53.3%)
Males (%)	38 (52.1%)	21 (50.0%)	5 (33.3%)	3 (25.0%)	3 (37.5%)	70 (46.7%)
Total	73 (100%)	42 (100%)	15 (100%)	12 (100%)	8 (100%)	150 (100%)

On comparing the mean pain score according to the NRS of the patients in different groups it was found that, in oral morphine group the NRS score was 6.27, 3.25, 1.74, 1.37, 1.22 at 15 min, 30 min,1 hr, 2 hr, 3 hr after taking medication from the baseline mean score of 8.8 (Table 2; Figure 3).

Table 2: Decrease in the pain as evaluated by the NRS after the administration of analgesics

Analgesic treatment	Pain evaluation at various time points					
	Baseline	15 min	30 min	1 h	2 h	3h
Morphine	8.67±0.85	6.32±1.44	2.44±0.93	1.74±0.73	1.37±0.92	1.22±0.88
Tramadol + Paracetamol	6.05±1.08	5.5±1.15	3.14±1.07	2.90±0.91	2.17±1.27	2.05±1.12
Tramadol	6.87±1.35	6.27±0.96	4.53±0.99	3.67±0.98	2.80±1.08	2.27±1.10
Paracetamol	4.00±0.74	3.92±0.51	3.25±0.62	2.92±0.67	2.50±0.67	1.92±0.67
Morphine IV	8.88±0.64	1.00±0.00	1.00±0.00	1.00±0.00	1.00±0.00	0.75±0.46

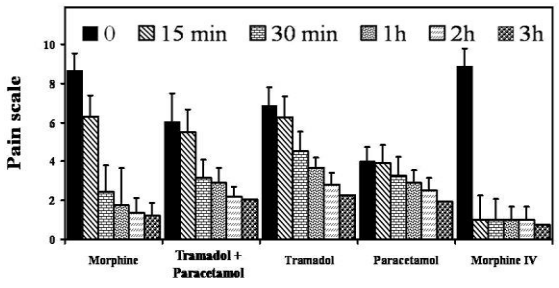

Figure 3: The data indicating reduction in pain as evaluated by thr Numeric rating Scale (NRS) after the administration of analgesics

In oral tramadol + paracetamol group the NRS score was 6.50, 3.14, 2.90, 2.50, 2.05 at 15 min, 30 min, 1hr, 2hr, 3hr after taking medication from the baseline mean score of 6.05 (Table 2; Figure 3). In oral tramadol group, the NRS score was 6.27, 4.53, 3.67, 2.80, 2.27 at 15 min, 30 min, 1 hr, 2 hr, 3 hr, after taking medication from the baseline mean score of 6.87 (Table 2; Figure 3).
In oral paracetamol group, the NRS score was 3.92, 3.25, 2.90, 2.17, 1.92 at 15 min, 30 min, 1 hr, 2 hr, 3 hr, after taking medication from the baseline mean score of 4.00 (Table 2; Figure 3). In IV morphine group the NRS score was 1.00, 1.00, 1.00, 1.00, 0.75 at 15 min, 30 min, 1 hr,2 hr, 3 hr, after taking medication from the baseline mean score of 8.88.the respective percentage change from the baseline for oral morphine was 88.68% at the end of 15 min, 30 min,1hr,2hr, respectively (Figure 4).

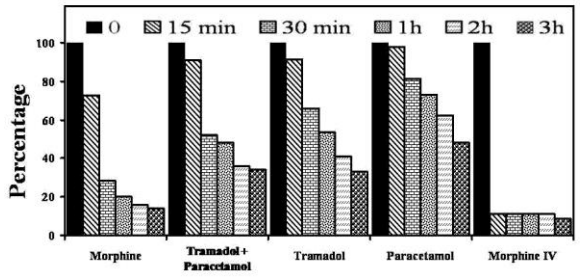

Figure 4: Percentage decrease in the pain after the administration of analgesics at various time points

DISCUSSION:

The experience of pain in cancer is widely accepted as a significant affecter of quality of life. Accordingly, the relief of pain has emerged as a priority in oncology care. Pain is associated with both the disease as well as treatment, and management is essential from the onset of early disease through long-term survival. Through this study, we have attempted understanding cancer pain in its different forms, compared the efficacy of the various analgesics used in the treatment of cancer pain and shed light on the safety profile of the medications[1-3].

Our study aims at improving the knowledge levels of the healthcare professionals in effectively managing the symptom of pain. This study investigated the pattern of use of the analgesics in the palliation of cancer pain. The age distribution of the study showed that the majority of the patients (25.3%) in the study population were 50-60 years which is due to the well-established fact that cancer affects the elderly more than any other age group4. Head and Neck cancer patients were more than any other cancers, and these observations are consistent with that reported from other parts of the country[4].

The analgesics given to the inpatients in the study varied from oral morphine 48%, tramadol + paracetamol 28%, tramadol 10%, paracetamol 8%, i.v morphine 5.3%. Thus we note that the most popular analgesic formulation preferred for use in cancer pain palliation was morphine and is in agreement to earlier reports[5,6]. Patients who scored a lower than 5 on NRS received paracetamol only, while in some cases NSAID was combined with tramadol when the pain was more. In very severe pain conditions the patients received oral or intravenous morphine and following the tenets of the analgesic ladder[1-3].

On comparing the mean pain score according to the NRS of the patients in different groups it was found that, in oral morphine group the NRS score was 6.27, 3.25, 1.74, 1.37, 1.22 at 15 min, 30 min, 1 hr, 2 hr, 3 hr after taking medication from the baseline mean score of 8.8.the respective percentage change from the baseline for oral morphine was 27.10%, 71.66%, 79.74%, 84.14% and 85.82% at the end of 15 min, 30min, 1 hr, 2hr,3 hr respectively ($p < 0.001$). These observations are in agreement to earlier observations[6] and validate the use of morphine in severe pain.

In oral tramadol + paracetamol group, the NRS score was 6.50, 3.14, 2.90, 2.50, 2.05 at 15 min, 30 min, 1 hr, 2 hr, 3 hr after taking medication from the baseline mean score of 6.05, the respective percentage change from the baseline for oral morphine was 8.85%, 47.32%, 51.60%, 64.86% and 66.70% at the end of 15 min, 30 min, 1 hr, 2 hr, 3 hr respectively (p-value <0.001). Previous studies have shown that combining tramadol with paracetamol was effective in reducing the intensity of pain and improved the quality of life at nontoxic concentrations[7-10]. In this regard, the observations of Mullican and co workers[9] that the combination of tramadol-acetaminophen (37.5 mg/ 325 mg) was as effective as codeine/ paracetamol capsules (30 mg/ 300 mg) is noteworthy and indicates its usefulness as an alternative to the low dose of oral morphine.

In oral tramadol group the NRS score was 6.27, 4.53, 3.67, 2.80, 2.27 at 15 min, 30 min, 1 hr, 2 hr, 3 hr, after taking medication from the baseline mean score of 6.87.the respective percentage change from the baseline for oral morphine was 7.35%, 31.87%, 44.54%, 58.56% and 66.60% at the end of 15 min, 30 min, 1 hr, 2 hr, 3 hr respectively (p-value <0.001). Previous studies have shown that the analgesic effects of 50 mg of tramadol were equal to that of 5 mg oral morphine but less effective than 10 mg morphine[11], indicating the usefulness of tramadol as an alternative to low doses of morphine. Additionally, studies have also shown that high dose tramadol (300 mg) could be an alternative for low dose morphine (60 mg) when nonopioids alone are not effective[11].

In oral paracetamol group, the NRS score was 3.92, 3.25, 2.90, 2.17, 1.92 at 15 min, 30 min, 1 hr, 2 hr, 3 hr, after taking medication from the baseline mean score of 4. The corresponding percentage change from the baseline for oral morphine was 1.39%, 17.36%, 25.69%, 35.42% and 50.69% at the end of 15 min, 30 min, 1 hr, 2 hr, 3 hr respectively. Previous studies by Stockler and co workers[12] have shown that acetaminophen (paracetamol) improves pain and well-being in people with advanced cancer already receiving a stable opioid regimen indicating its usefulness.

In IV morphine group the NRS score was 1.00, 1.00, 1.00, 1.00, 0.75 at 15 min, 30 min, 1 hr, 2 hr, 3 hr, after taking medication from the baseline mean score of 8.88.the respective percentage change from the baseline for oral morphine was 88.68% at the end of 15 min,30 min,1 hr, 2 hr, respectively. The response to iv morphine was immediate and useful in a prospective, within-patient, crossover study of continuous intravenous and subcutaneous morphine for chronic cancer pain study done by Nelson and associates [13] it was found that IV and SC routes are equianalgesic for most patients when administered as a continuous infusion. Pain control and side-effect profiles are quite similar and acceptable. SC morphine is an excellent alternative to IV morphine in both inpatients and outpatients requiring parenteral morphine for pain.

CONCLUSIONS:

This cross-sectional prospective observational study revealed that cancer of the oral cavity was the most prevalent cancer in males and cervical cancer the most prevalent in the females. Oral morphine was the most widely used analgesic used, among the others used the most common one is a combination of weak opioid tramadol and paracetamol, morphine had an excellent efficacy reducing the severity of the pain to half in 30 min.

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