Analgesic choice in patients presenting to emergency department with cancer pain: a prospective study

Abstract. Background. Acute onset pain is one of the common reasons for cancer patients to present to the emergency department. In our study, we compared painkillers used in cancer patients admitted to the emergency department with pain complaints and their effectiveness and the superiorities of these painkillers in pain relief and their superiorities over each other. Materials and methods. The pain scores of the patients were asked at the time of admission by showing a visual analogue scale. Before treatment, pain scores were recorded. The patients were divided into four different groups according to the type of given treatment: non-steroidal anti-inflammatory drugs; opioid painkillers; paracetamol; paracetamol and opioid therapy. After the treatment, we asked which painkiller written in the treatment form was administered to the patient and recorded the pain score. Results. It was observed that the median pain score before and after treatment of the patients in all painkiller groups differed statistically. When the median scores before and after treatment were compared according to drug types, no difference was found between the decrease in pain scores ($p = 0.956$ and $p = 0.705$, respectively). It was concluded that the pre-treatment and post-treatment median pain scores of patients who are using non-steroid anti-inflammatory drugs and opioids at home did not differ statistically ($p = 0.063$). Conclusions. The use of non-steroidal anti-inflammatory drugs, paracetamol or opioids was not found to be superior to each other in patients with acute severe cancer pain.

Keywords: analgesics; cancer pain; emergency care; opioid; paracetamol

Introduction

Cancer patients are referred to the Emergency Department with a range of oncological symptoms such as nausea, vomiting, dehydration, neutropenia, fever and acute pain and treated there. Acute onset pain causes 10 to 41% of all emergency department visits among cancer patients [81]. The rate of referral to emergency services with pain complaints in cancer patients is up to 40%, and this has been associated with the symptoms of the disease and treatment variability [2, 4]. However, cancer pain is affected by many factors such as treatment options and disease progression, as well as by side factors such as environmental change and comorbidity [5].

There are patients who are admitted to the hospital for chronic pain, as well as those who are admitted to the hospital due to newly developed pain. Their pain complaints fail to be noticed by doctors and it affected treatment variability [2]. Although opioid painkillers are used as the preferred pain relievers in this patient group, their use is controversial due to their addictional effects and problems associated with the use of appropriate doses [6].

Purpose. In our study, we compared painkillers’ effectiveness and superiorities of these painkillers in pain relief and their superiorities over each other in cancer patients admitted to the emergency department with pain.
Materials and methods

Study design

This study is a prospective, cross-sectional study. Our study was carried out in 2019 for four months in a tertiary emergency clinic, where 300,000 patients are admitted each year and where the region’s oncology patients are also followed up, situated in the European side of Istanbul. The study was initiated after the approval of the local ethics committee in the hospital and written consent of all patients were obtained (06/11/2019–1342). The study followed the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects.

Patient Selection

Patients older than 18 years of age, who presented to our hospital with pain, but whose source of pain before or after treatment was not attributed to a cause other than cancer pain, who had given written consent, whose general condition did not deteriorate at any stage of the treatment, and who were diagnosed pathologically were included in our study.

Patients under the age of 18 who could not be diagnosed pathologically with biopsy, who left the hospital without permission before or after treatment, whose pain score could not be reached at any time, whose general condition worsened during treatment or whose consciousness was impaired, and whose cause of pain was attributed to an organic reason other than cancer, and who were younger than 18 years, were not included.

Collection of Data

After asking their demographic data (age, gender), localization of pain (where the pain is felt predominantly), additional diseases, medications that the patient routinely used for pain at home, and how many presentations they made to emergency department within a week at the time of admission to the hospital, they were shown a visual analogue scale from 1 to 10 and asked for their current score of his pain. The patient was told that ‘0’ meant that he had no pain and ‘10’ corresponded to the worst pain he had experienced in his/her life so far. 0–3 was accepted as mild, 4–7 as moderate, 8 and above as severe pain. Before treatment, patients’ pain scores were recorded, patients received treatment without interfering with which painkiller the attending physician would administer. After the treatment, we asked which painkiller was administered to the patient and his/her pain score after the treatment. One more question was asked to the patient about whether any painkillers used routinely at home and their types affected the treatment administered in the emergency department or not.

Statistical Reviews

In summarizing the data obtained from the study, descriptive statistics were tabulated for continuous variables as mean ± standard deviation or median and quartile width, depending on the distribution. Categorical variables were summarized as numbers and percentages. The normality test of numerical variables was checked with the Kolmogorov-Smirnov test. While the Kruskal-Wallis test was used for the comparison of the median pain scores before and after the treatment according to the used drugs. The Wilcoxon test was used to evaluate the effects of each drug separately.

Statistical analysis was performed using Jamovi (Version 1.2.22) and JASP Team (2018). JASP (Version 0.12.2) software, and 0.05 (p-value) was considered statistically significant in statistical analyses; Bonferroni correction was used to evaluate the effectiveness of each drug.

Table 1. Some demographic and clinical characteristics of patients presenting with cancer pain

| Chief Complaint (%) | n (%)/Avg. ± SS |
|---------------------|-----------------|
| Gender (%)          |                 |
| Male                | 44 (53.0)       |
| Female              | 39 (47.0)       |
| Age                 | 61.2 ± 13.3     |
| Comorbidities       |                 |
| HT (%)              | 22 (26.5)       |
| DM (%)              | 15 (18.1)       |
| Coronary Artery Disease (%) | 8 (9.6) |
| Stroke (%)          | 2 (2.4)         |
| COPD (%)            | 2 (2.4)         |
| Asthma (%)          | 1 (1.2)         |
| Chronic Kidney Disease (%) | 1 (1.2) |
| Number of presentations made in a week |             |
| First presentation  | 51 (61.4)       |
| Second              | 20 (24.1)       |
| Third               | 7 (8.4)         |
| Fifth               | 2 (2.4)         |
| Sixth               | 1 (1.2)         |
| Seventh             | 2 (2.4)         |
| Rescue analgesic medication (%) | 32 (38.6) |

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Results

A total of 90 patients were included in our study at the beginning. 4 of these patients were excluded from the study because their post-treatment pain score could not be determined, and 3 of them were excluded because the diagnosis of the disease could not be confirmed by biopsy.

44 males (53 %) and 39 females (47 %) were included in the study. The mean age of the patients was 61.2 ± 13.3 years. When the comorbid diseases of the patients included in the study were examined, it was seen that the highest rates were hypertension (HT) 26.5 % and diabetes mellitus (DM) 18.1 %. It was observed that the patients commonly presented to the emergency service with complaints of body pain (41 %), followed by abdominal pain (31.3 %) and back pain (16.9 %). When the number of presentations patients made to the emergency department in a week was investigated, it was observed that 51 patients (61.4 %) presented for the first time, while 20 patients (24.1 %) presented for the second time. On the other hand, 32 (38.6 %) of the patients were using rescue analgesic medication (Table 1).

The results of the evaluation of pre- and post-treatment pain scores according to drug types were given separately. When the pre and posttreatment scores were evaluated separately to determine the efficacy of each drug, it was observed that the median pain score before and after treatment of the patients given diclofenac differed statistically (*p = 0.017), and that the median pain scores of patients given paracetamol before and after treatment differed statistically (*p < 0.001). It was shown that the median pain scores of the patients treated with tramadol before and after treatment differed statistically (*p < 0.001), and finally the median pain scores of patients using paracetamol + tramadol combination before and after treatment differed statistically (*p < 0.001) (Figure 1). When the median scores before and after treatment were compared according to drug types, the differences between the medians were not statistically significant (p = 0.956 and p = 0.705, respectively). In other words, the efficacy of each drug in reducing pain was similar. It can be said that the pain scores of the patients decreased for each drug after treatment (Table 2).

Figure 1. Pain scores of 4 different painkiller groups before and after administration as measured by visual analogue scale.
When median scores before and after treatment were compared according to using routine painkiller types, the differences between medians were not statistically significant ($p = 0.289$ and $p = 0.536$, respectively). On the other hand, when the pre- and post-treatment scores are evaluated separately to determine the efficacy of each drug:

It was observed that the median pain scores of patients using NSAIDs routinely before and after treatment differed statistically ($p < 0.001$), and that the pain scores of the patients using NSAIDs at treatment decreased. When the median pain scores of patients using opioid routinely before and after treatment were compared, the differences between scores were statistically significant ($p < 0.001$). It was found that the pain scores of the patients using opioids at treatment decreased. When the pre-treatment and post-treatment pain scores of patients not using routine painkillers were compared, the differences between the median scores were statistically significant ($p < 0.001$).

However, it was concluded that the pre-treatment and post-treatment median pain scores of patients using NSAIDs and opioids at home did not differ statistically ($p = 0.063$) (Table 3).

### Discussion

In our study, the mean age of the patients who presented to the emergency department with cancer pain was $61.2 \pm 13.3$ years. In a study on cancer pain, mean ages were similar with our results [7]. Studies have shown that cancer patients most frequently present to the emergency room with abdominal pain [2, 3, 7]. In our study, the most common complaints were found to be widespread body pain and abdominal pain.

According to the World Health Organization’s cancer pain management guideline, paracetamol and NSAIDs are not recommended as initial treatment for moderate and severe cancer pain. Strong opioids are recommended for the treatment of moderate and severe oncological pain. Other drugs can be combined with opioid analgesics depending on the severity of pain [8, 9]. In our study, no significant difference was observed between four treatment groups: paracetamol, diclofenac, tramadol, and paracetamol plus tramadol therapy. Decrease in median pain scores in these four groups was detected statistically significant and similar (Figure 1). In one study, despite the guideline recommendations, there was no consensus on initial pain treatment, and it was stated that the use of NSAIDs alone or in combination with opioids was beneficial [10].

In the pathogenesis of cancer pain, apart from the organic causes of the disease, environmental factors such as comorbidities, complications of treatment, emotional stress, depression or anxiety caused by the intensity of the emergency department are involved [5, 11]. Therefore, it may be useful to evaluate different analgesic strategies in the initial treatment in the emergency department, instead of the stepped care recommended by the World Health Organization.

In our study, while 47 patients were using routine pain medication (20 patients used only NSAIDs, 18 patients only opioids, 9 patients used NSAIDs and opioids together), and 36 patients did not use any painkillers routinely. In a study, similar to our study, 47.4 % of patients with acute cancer pain were found to have opioid prescriptions at home [7]. In a study conducted in Europe, while the rate of patients who did not use any analgesic drugs at home was 21 %, the rate of those using non-opioid analgesic drugs was 56 %; in our

### Table 2. Evaluation of the pain scores before and after treatment according to the drugs used and the effects of each drug

| Used Medication | All Patients | Diclofenac (n = 8) | Paracetamol (n = 28) | Tramadol (n = 36) | Paracetamol + Tramadol (n = 13) | $p^*$ |
|-----------------|--------------|--------------------|----------------------|------------------|-------------------------------|------|
| Initial score (median [IQR]) | 9.0 [8.0–10.0] | 9.5 [7.0–10.0] | 9.5 [8.0–10.0] | 9.0 [8.0–10.0] | 9.0 [8.0–10.0] | 0.956 |
| Final score (median [IQR]) | 5.0 [3.0–7.0] | 4.5 [2.8–6.2] | 6.0 [3.0–7.8] | 5.0 [3.0–8.0] | 4.0 [4.0–6.0] | 0.705 |
| $p^{**}$ | 0.017 | < 0.001 | < 0.001 | 0.002 |

* — Kruskal-Wallis test was used; ** — The Wilcoxon test was used. Descriptive statistics were summarized as median [Q1-Q3]. $p$ values indicated in bold were considered statistically significant ($p < 0.05$). Q1 — First quartile, Q3 — Third quartile.

### Table 3. Evaluation of pre-treatment and post-treatment pain scores according to routine pain medication types and the effects of each drug

| Routine Pain Relief | NSAID (n = 20) | Opioid (n = 18) | NSAID + Opioid (n = 9) | None (n = 36) | $p^*$ |
|---------------------|----------------|----------------|-----------------------|---------------|------|
| Initial score (median [IQR]) | 10.0 [7.8–10.0] | 9.0 [8.0–9.0] | 9.0 [7.0–9.0] | 10.0 [8.0–10.0] | 0.289 |
| Final score (median [IQR]) | 4.0 [3.0–6.0] | 6.0 [3.0–8.0] | 6.0 [4.0–6.0] | 6.0 [3.8–7.2] | 0.536 |
| $p^{**}$ | < 0.001 | 0.001 | 0.063 | 0.001 |

* — Kruskal-Wallis test was used; ** — The Wilcoxon test was used. Descriptive statistics were summarized as median [Q1-Q3]. $p$ values indicated in bold were considered statistically significant ($p < 0.05$). Q1 — First quartile, Q3 — Third quartile.
study these rates were 43.3 and 24 %, respectively [12]. In our study, the decrease in pain scores was statistically significant and similar in patients who used only NSAIDs, only opioids or who did not use drugs in their daily life, regardless of the drugs we gave in our emergency department. However, no statistically significant decrease was observed in the median pain scores of the patients who used NSAIDs and opioids together in their daily life after the treatment. In some studies, the causes of failure in the treatment of acute cancer pain in patients using opioids include advanced disease, development of intolerance to opioid drugs, or patient’s non-compliance with treatment [1, 11]. In addition, opioid abuse and the use of drugs for psychological and physiological pleasure are among the reasons affecting the treatment [6, 13].

Conclusions

NSAID, paracetamol or opioid use was not found to be superior to each other in patients admitted to the emergency department with acute severe cancer pain. The efficacy of paracetamol, NSAID, or opioid drug treatments given in emergency treatment decreases in patients who use opioids and NSAIDs in their daily life. Further research is needed to determine whether the decrease between pre- and post-treatment median pain scores in patients, who routinely use opioids and those who do not, is significant or not.

Limitations

Being a single-center study is the biggest limitation of our study. Future studies with many centers and larger patient groups may yield better results. Another limitation is that the cancer types of the patients included in the study and the current mental state of the patients were not differentiated. In future studies, it may be shown that the pain threshold between cancer types and psychological variables in patients will be effective in feeling pain and reducing it after treatment.

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Вибір знеболювання в пацієнтів, які надходять до відділення невідкладної допомоги з раковими болями: проспективне дослідження

Резюме. Актуальність. Гострий біль є однією з найпоширенішіших причин, через які пацієнти з раком можуть потрапляти до відділення невідкладної допомоги. У нашому дослідженні ми порівняли ефективність знеболювальних препаратів, що застосовуються в онкозахворюваннях, які надійшли до відділення невідкладної допомоги зі скаргами на біль, а також переваги цих засобів одного над одним. Матеріали та методи. Біль у пацієнтів оцінювали під час надходження за допомогою візуально-анalogової аналогової шкали. Перед лікуванням реєстрували оцінку білю в балах. Хворих розподілили на чотири різні групи за типом проведеної лікування: нестероїдні протизапальні препарати; опіоїдні знеболювальні; парацетамол; парацетамол з опіоїдною терапією. Після лікування ми запитували, яке знеболювальне отримував пацієнт, і реєстрували оцінку болю.

Результати. Було відзначено, що середній показник болю до і після лікування хворих у всіх групах знеболювальних препаратів статистично відрізнявся. Коли середні показники до і після лікування порівнювали за типами препаратів, не було виявлено різниці в зменшенні показників болю (р = 0,956 і р = 0,705, відповідно). Зроблено висновок, що середній показник болю до і після лікування пацієнтів, які вдома використовують нестероїдні протизапальні препарати й опіоїди, статистично не відрізнявся (р = 0,063).

Висновки. При використанні нестероїдних протизапальних препаратів, парацетамолу або опіоїдів не встановлено переваги жодного засобу над іншими в онкозахворюваннях із сильними гострими болями. Ключові слова: анальгетики; біль при раку; невідкладна допомога; опіоїд; парацетамол.