

A STUDY ON CANCER PAIN AND SLEEP PARAMETERS OF CANCER PATIENTS: HYDROMORPHONE HYDROCHLORIDE

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INTRODUCTION

Sleep is necessary for the continuance of psychophysiological health. Sleep deprivation is reported to reduce immune condition by decreasing secretion of cytokine. Antitumoral cell levels are affected by sleep. Abnormal sleep pattern affects cortisol levels, which affects number of function of natural killer cells. This much effect on the immune system can cause cancer progression in the organism, which already struggles with cancer cells.[1]

While health providers around the world have more than eighty opioid options, unfortunately there is only a limited number of opioids that can be used in pain treatment in Turkey. Hydromorphone is an opioid analgesic, which is 5 times stronger than morphine. It has oral, subcutaneous, rectal, iv and spinal preparations in other countries. However, only push-pull form osmotic-controlled release oral delivery system (Oros) was introduced in Turkey. It began to be used in moderate-severe cancer pain treatment

In this study, we evaluated hydromorphone hydrochloride, which is a recent opioid option in Turkey. We studied the effectiveness, tolerability and side effects of the medication on patients' cancer pain. We aimed to analyze the effect of hydromorphone hydrochloride on sleep quality and contribution to emotional well-being in addition to elimination of pain in cancer patients; and to present its effects on feelings of depression, worthlessness, indifference. Thus, we analyzed ratios of improvement of family relationships and performing daily life without help.

METHOD

Study design

This is a descriptive study carried out between the years of 2010-2012.

Location of the study

The study was carried out in Konya province, in department of Algology.

Population and sampling

Patients with chronic cancer pain for at least 6 months and those using hydromorphone hydrochloride due to malign cancer pain ² were included in the study. Charts of 50 patients who were diagnosed with various cancers constituted the sampling.

LIMITATIONS OF THE STUDY

Patients with intolerable nausea, vomiting, pregnant women, patients with dysphagia, those who were diagnosed with colon cancer, patients who cannot use drugs due to allergy, patients with severe liver-kidney failure, severe neurologic disorder, with opioid-related hypotension, severe respiratory dysfunction, severe ventricular dysfunction, hypothyroidism, ureteral stricture and prostate hypertrophy were excluded from the study.

Demographic characteristics, duration of hydromorphone hydrochloride use and dose pain types, episodic pain, adjuvant treatments of the patients were recorded by screening patient charts in 2010-2012 period. Whether the patients needed different medications despite the treatment was noted. Location of pain (back, chest, neck, leg) was noted and neurologic component was analyzed.

Reliability, side effects and severity of side effects of the medication were noted. The dose starting side effects and the response of side effect to medical treatment were noted. Patients who withdrew from medication and number of patients who could not tolerate side effects were recorded. The patients who were excluded from the study for any reason were recorded.

After the analysis of the charts, control visits were performed by the author for patients with ongoing hydromorphone hydrochloride treatment and telephone visits for the patients with no control visits and no chart register.

Evaluation of Data

Statistical Package for Social Sciences (SPSS) Windows 16 software was used for statistical analysis of data. Data was used as average, standard deviation and number. VAS (Kruskal Wallis analysis of variance), Brief Pain Inventory and MOS sleep scale of patients were evaluated. Chi-square test was used for body pain localization, medication doses, medication use period, adjuvant use, side effects, reasons for withdrawal from medication and additional medications. ¹ $p < 0.05$ level was considered as statistically significant.

Ethics

⁴ Approval of Necmettin Erbakan University Meram Faculty of Medicine Ethics Committee (2012-73) was taken for the study.

Results

¹ Of a total of 50 patients who were included in the study, 33 were male, 17 were female. Mean age of the patients was 60.82 ± 11.401 . Of the patients, 15 (30.0%) had back pain, 12 (24%) had low back pain, 8 (16%) had leg pain, 7 (14%) had chest pain and 8 (16%) had head-neck, shoulder, heel and extensive body pain complaints. ² No statistically

significant difference was observed between the genders in terms of location of pain ($p>0.05$) [Table . 1]

Analysis of duration of medication use of the patients after inclusion in the study revealed that 26 (52%) patients used hydromorphone hydrochloride for one month; 9 (18%) used for two months; 3 (6%) used for three months, 5(10%) used for four months, 1 (2%) used for five months and 2 (4%) patients used hydromorphone hydrochloride for six months. 4 (8%) patients used the medication for a period shorter than one month. There was a statistically significant difference between duration of medication use and gender of the patients ($p<0.05$).[table 3] This difference was believed to result from higher number of male participants.

Analysis of the treatments of the patients revealed that 22 (44%) of the patients did not take adjuvant; 28 (56%) used adjuvant together with opioid treatment. As for the adjuvants, 14 (28%) patients used gabapentin; 7 (14%) patients used pregabalin and 2 (4%) patients used amitriptyline. Some patients were observed to use two adjuvants in combination. Weak opioid (tramadol) was added to the treatment of 5 (10%) patients.

VAS values (VAS I) before hydromorphone hydrochloride use of patients with nociceptive, neuropathic and mixed pains were found to be 7.5 ± 1.05 , 7.5 ± 0.70 and 7.5 ± 0.96 respectively; while VAS values (VAS 2) after hydromorphone hydrochloride use were 2.7 ± 1.80 , 1.5 ± 0.70 and 2.6 ± 1.56 respectively. Although patients with neuropathic pain had lower VAS II mean scores, intergroup comparisons found no statistically significant difference due to non-homogenous distribution of number of patients (VAS I= $p>0.992$, VAS II= $p>0.613$).[Table 2]

31 (62%) patients who did not have episodic pain did not need additional treatment to opioid treatment, while 13 (26%) of 19 patients used tramadol, 6 (12%) used transmucosal fentanyl.

Analysis of quality of life of the patients after inclusion in the study revealed that emotional well-being of 26 (52%) patients improved; family relationships of 7 (14%) improved and 6 (12%) patients were observed to walk comfortably without pain, while 7 (14%) patients reported depression-indifference and 4 (8%) patients reported no change in their lives after taking the medication.

Some of the patients in patient group had certain diagnosis-related side effects prior to using the medication since our patient group consisted of cancer patients. Of the patients, 26 (52%) had no side effects, while 10 (20%) had nausea, 6 (12%) had constipation and 8 (16%) had other side effects. The most common side effects were nausea, constipation, dizziness, vomiting, respiratory failure and diarrhea respectively [Table 4]. Some patients were found to have more than one side effect. It was found that primary diagnosis for the patient with respiratory failure was lung cancer and that he/she was given iv morphine in addition to the recommended treatment.

35 (70%) of the patients continued the treatment without withdrawing from medication.

Sleep levels of the patients showed that 40 (80%) of the patients reported that they could sleep painlessly; 10 (20%) reported that they could not sleep. As for sleep levels of patients after hydromorphone hydrochloride treatment, 45 (90%) patients reported that they fell asleep in 1-5 minutes, while 3 male patients described falling asleep as poor and 2 male patients described going to sleep as uneasy. When the patients were questioned about adequacy of sleep after starting the medication, 41 (82%) reported that they were not getting enough sleep, 9 patients reported that they were getting enough

sleep and that they could sleep for 7-8 hours a day. While 39 (78%) patients did not have daytime dizziness, 43 (86%) patients reported snoring during sleep and 9 (18%) reported shortness of breath.

30 (60%) of the patients who were included in the study were satisfied with reduced pain. [table 6] When the patients were requested to evaluate decrease of pain in % when compared to initial pain, 18 (36.9%) patients reported that their pain decreased by 30%; 18 (36%) reported that their pain decreased by 50% and 14 (28%) patients reported that their pain decreased by 70%.

Decrease of pain in patients was evaluated by Brief Pain Inventory (BPI). 32 (64%) patients reported that pain elimination was good and that pain after the treatment was at minimum level.

Evaluation of effectiveness of treatment after the treatment was described as very good by 18 patients

DISCUSSION

Hydromorphone hydrochloride was observed to be effective in treatment of chronic cancer pain. It was found to decrease cancer pain especially in breast cancer patients. Pain-related sleep disorders significantly improved. Emotional well-being increased, while depression, worthlessness and indifference decreased. The treatment was observed to contribute to quality of life like improved family relationships, ability to walk and perform daily tasks without help.

Hydromorphone 3-glucuronoid metabolite of hydromorphone hydrochloride formed by hepatic glucuronidation is inactive. The fact that the metabolite does not interact with other medications in patients group who receive multiple medications can make it preferable in patients with potential organ dysfunction.[2]

In this study, decrease of pain after the treatment was 64% according to brief pain inventory. In 36% of patients, 50% of initial pain was eliminated. Side effects were not serious and response was taken to medication ($p > 0.100$). Our findings are consistent with those of Carla I et al.[6]

Episodic pain is temporary exacerbation periods of stable pain treatment and can be triggered by movement and physical activity. It is treated by oral, nasal, transmucosal opioids. Portenoy et al., defined prevalence of episodic pain between 19-95%. [2]

Prevalence of episodic pain was found to be 38% in our study and transmucosal fentanyl and tramadol were used for treatment. Low frequency of episodic pain was lower when compared to some literature can be explained by the fact that it causes less fluctuation in valley-peak levels of the used hydromorphone hydrochloride. [3]

In our study, number of nausea, which was 4 before medication use, increased to 6; number of dizziness, increased from 2 to 3; number of constipation remained the same; 1 diarrhea, 1 vomiting and 1 respiratory depression was observed. [table 4]

Warning the patients about potential nausea, vomiting and constipation prior to the treatment and providing early medication can be effective. We believe that cancer stages of patients affect incidence of side effects.

Analysis of quality of patients in 50 patients we screened in this study showed that the patients who previously could not use their arms, couldn't even hold a glass, dress and walk without help and who couldn't perform daily tasks due to pain were able to perform those tasks after the provision of effective analgesia and that they felt happier. The ratio of painless sleep was 80% in our study.

26 (52%) of the patients showed no side effects, while 10 (20%) had nausea and 6 (12%) had constipation. 8 (16%) of the patients were found to have other side effects.

The frequency of those side effects was nausea, constipation, dizziness, vomiting, respiratory failure and diarrhea respectively. [table 4]

Constipation, nausea and vomiting, which are the most common side effects reported in clinical studies (n=647) can be managed by dose reduction, laxatives and effective use of antiemetics.

A large number of studies which evaluated health-related quality of life with special scales have shown that effective pain control is concerned with increased quality of life. [4,5,6,7],

Hydromorphone hydrochloride helped to eliminate sleep disorder, shortness of breath and snoring and relatively improved amount of sleep and adequacy of sleep. It was found that 90% of our patients were able to fall asleep in 1-5 minutes; however 82% did not have enough amount of sleep. 78% of patients had no feeling of dizziness during the day; 82% did not have shortness of breath; 80% reported that they slept without pain, while 41% reported that they did not sleep at all.

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| 4 | Li, Feng, Hong-Ming Yang, and Hong-Wei Wang. "Disseminated Cryptococcosis with Widespread Necrotizing Fasciitis and Cryptococchemia Occurring in an Immunosuppressed Patient", Annals of Dermatology, 2014.
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