Medication and Pain Control: Experience of a Brazilian Palliative Care Referral Center

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Medicamentos e Controle de dor: Experiência de um Centro de Referência em Cuidados Paliativos no Brasil

Medicamentos y Control del Dolor: Experiencia de un Centro de Referencia en Cuidados Paliativos en Brasil

Simone Garruth dos Santos Machado Sampaio[1]; Luciana Branco da Motta[2]; Celia Pereira Caldas[3]

Abstract

Introduction: Pain is one of the most prevalent symptoms in cancer patients, especially in the last year of life, and its inadequate control is frequent. **Objective**: Outline the profile of drugs used for pain control in an exclusive oncology palliative care hospital unit. **Method:** A cross-sectional study with longitudinal follow-up of all hospitalized patients between September and November 2016. Numeric Rating Scale (NRS), functionality and drugs with analgesic potential used were collected through medical chart review. **Results:** The 399 hospitalized patients presented 461 hospitalization episodes, of which 429 (93%) were patients with pain symptom (controlled or not). The mean age was 62 years, with an average of 8 days of hospitalization motivated by pain in 18% of the cases and in 35%, the pain symptom was not controlled. Of these, NRS was quantified as zero after 2 days in average. According to the Analgesic Ladder, 29% were in the 1st step, 11% in the second and 82% in the third. The use of common analgesic and of adjuvant was verified in more than 80% of the episodes. The mean equivalent dose of oral morphine was 117 mg/day. **Discussion:** Pain control observed was higher and earlier when compared to other similar works. The mean opioid dose (analgesic equipotent) was analogous to the observed in other studies. However, the use of strong opioids and adjuvants was more frequent than what was noticed in other services. This difference may justify the better pain control. **Conclusion:** The action of skilled team grants better symptom control.

Key words: Drug Therapy; Palliative Care; Pain Management; Cancer Pain.

Resumo

Introdução: A dor é um dos sintomas mais prevalentes em pacientes com câncer, especialmente no último ano de vida, sendo frequente o controle inadequado. **Objetivo:** Delinear o perfil de medicamentos utilizados para controle de dor em uma unidade hospitalar de cuidados paliativos oncológicos. **Método:** Estudo transversal com acompanhamento longitudinal de todos os pacientes internados entre setembro e novembro de 2016. Escala Verbal Numérica (EVN), funcionalidade e medicamentos com potencial analgésico utilizados foram coletados por revisão de prontuário. **Resultados:** Os 399 pacientes internados compuseram 461 episódios de internação, sendo 429 (93%) com o sintoma dor (controlada ou não). A idade média foi 62 anos, oito dias em média de internação, motivada por dor em 18% dos casos; e, em 35%, o sintoma dor não estava controlado. Destes, a EVN foi quantificada como zero após dois dias em média. Segundo a escada analgésica, 29% estavam no primeiro degrau, 11% no segundo e 82% no terceiro. O uso do analgésico comum e de adjuvante foi verificado em mais de 80% dos episódios. A dose média equivalente de morfina oral foi 117 mg/dia. **Discussão:** O controle de dor observado foi superior e mais precoce se comparado com outros trabalhos semelhantes. A dose média de opioide (equipotência analgésica) foi semelhante à observada em outros estudos. Entretanto, o uso de opioide forte e de adjuvantes foi mais frequente do que o notado em outros serviços. Essa diferença pode justificar o melhor controle álgico. **Conclusão:** A ação da equipe especializada proporciona melhor controle de sintomas.

Palavras-chave: Tratamento Farmacológico; Cuidados Paliativos; Manejo da dor; Dor do Câncer.

Resumen

Introducción: El dolor es uno de los síntomas más frecuentes en pacientes con cáncer, especialmente en el último año de vida, y el control inadecuado es frecuente. **Objetivo:** Delinear el perfil de los medicamentos utilizados para el control del dolor en una unidad hospitalaria de cuidados paliativos para el cáncer. **Método:** Estudio transversal con seguimiento longitudinal de todos los pacientes hospitalizados entre septiembre y noviembre de 2016. La Escala Numérica Verbal (EVN), la funcionalidad y los medicamentos con potencial analgésico utilizados se recogieron mediante revisión de registros médicos. **Resultados:** Los 399 pacientes hospitalizados constituyeron 461 episodios de hospitalización, de los cuales 429 (93%) tuvieron dolor de síntomas (controlado o no). La edad promedio fue de 62 años, 8 días en promedio. La hospitalización fue motivada por dolor en el 18% de los casos y en 35% el síntoma de dolor no fue controlado. De estos, EVN se cuantificó como cero después de 2 días en promedio. Según la Escalera Analgésica, el 29% estaba en el primer paso, el 11% en el segundo y el 82% en el tercero. El uso de analgésicos y adyuvantes comunes se observó en más del 80% de los episodios. La dosis equivalente promedio de morfina oral fue de 117 mg/día. **Discusión:** El control del dolor observado fue superior y anterior en comparación con otros trabajos similares. La dosis promedio de opioide (equipamiento analgésico) fue similar a la observada en otros estudios. Sin embargo, el uso de opioides y adyuvantes fuertes fue más frecuente que en otros servicios. Esta diferencia puede justificar el mejor control del dolor observado. **Conclusión:** La acción del equipo de expertos proporciona un mejor control de los síntomas.

Palavras clave: Tratamiento Farmacológico; Cuidados Paliativos; Manejo del Dolor; Dolor em Câncer.

[1] Palliative Caret Unit of Hospital do Câncer IV (HC IV) do Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0001-5537-7399

[2] Senior Care Center (NAI) of "Universidade do Estado do Rio de Janeiro" (UERJ). Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0001-9959-9719

[3] NAI/Uerj. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0001-6903-1778

Address for correspondence: Simone Garruth dos Santos Machado Sampaio. Rua Visconde de Santa Isabel, 274 – Vila Izabel. Rio de Janeiro (RJ), Brazil. CEP 20560-120
E-mail: simonegarruth@gmail.com

INTRODUCTION

Pain is a symptom present in 80% of the patients with cancer in the last year of life and classified as severe in one fourth of these patients [1].

In 1986, the World Health Organization (WHO) issued its first protocol about management of oncologic pain based in the "analgesic ladder". The strategy was to evaluate and adapt the drugs utilized according to the necessity of the patient at each moment, sequentially and progressively. It is estimated that the relief of the symptom may be reached in 70% to 90% of the cases with the method proposed [2-5].

Despite WHO efforts, there was no reduction of the prevalence of pain if compared to the periods of 1965-2004 to 2005-2014[6].

Though the analgesic treatment is available for 70% to 90% of the patients with cancer, in 40% to 50% of the cases it is inappropriate[7,8]. There are several literature narratives about inappropriate pain control in oncologic patients [9].

The importance and the positive results because of actions of a skilled team specialized in symptoms control, among them, pain, are well documented. It is important that each service is aware of its indicators and pursues strategies to improve the service [10,11].

The present manuscript is one of the stages of a study to evaluate the treatment of the pain in patients in oncologic palliative care attended in a reference center. The aim of this study was to design a drugs profile utilized to control pain in a hospital facility of oncologic palliative care.

METHOD

Cross-sectional, prospective study where all the patients admitted in the unit between September 1, 2016 and November 30, 2016 were followed up longitudinally during the hospitalization through chart review.

The work was developed in a public oncologic palliative care hospital considered a national reference center in the city of Rio de Janeiro, Brazil. At the facility, only patients with cancer without possibility of specific oncologic treatment are attended.

For the objective quantification of the pain and the functionality, it were used widely utilized scales in the world literature and in the study setting.

The pain was quantified through the Numeric Visual Scale (NVS), obtained after asking the patient to assign a score from 0 to 10 to its pain, being "0" the absence of pain and "10" the most acute imaginable possible pain[12-15].

The functionality of the patients was documented with the *Karnofsky Performance Status* (KPS), which is a numerical scale with 11 options of classification varying from 100% (no complaints, absence of evidence of disease) to 0% (death)[16].

Sociodemographic data were obtained about the oncologic disease, motive of the hospitalization, KPS and NVS at admission and daily at routine evolution and drugs administered with analgesic potential (hourly and rescue).

It were considered "with pain" all the patients who used some common analgesic (dipyrone, paracetamol) or opioid even with NVS zero. The pain was considered controlled when NVS was zero. Report of "no pain" was considered as NVS zero. Use of opioid or antithermic exclusively for dyspnea or fever were disconsidered. Drugs with standard analgesic potential [5,17-19] in the unit in the moment it were collected: dipyrone, paracetamol (common analgesic); diclofenac and tenoxicam (non-hormone anti-inflammatory); codeine and tramadol (weak opioid); morphine, methadone, oxycodone and transdermal fentanyl (strong opioid); amitriptyline, sertraline, citalopram and venlafaxine (antidepressant); gabapentin and pregabalin (anticonvulsant); dexamethasone and prednisone (corticosteroid); baclofen (GABA agonist); haloperidol and risperidone (neuroleptic); pamidronate and zoledronate (bisphosphonate); cetamin and venous lidocaine.

Of those who were hospitalized with uncontrolled pain, it was calculated the necessary time (in days) to control the symptom (NVS zero). The hospitalizations were classified according to the WHO analgesic ladder and the use of common or opioid analgesic. The dose of the opioids was converted to oral morphine[20].

For analysis purposes, the basic unit considered was hospitalization – called episode – and not the patient. It was conducted a descriptive analysis of the variables collected with determination of frequencies, measures of central tendency and dispersion. The measures of association were calculated with the chi-square tests for categorical variables, Mann-Whitney for numerical variables and pairwise Wilcoxon for pairwise numerical variables. All these variables collected present non-normal distribution according to the Shapiro-Wilk test. It was utilized the statistical software R.

The Institutional Review Board of "Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA)" and of Hospital Universitário Pedro Ernesto of the "Universidade do Estado do Rio de Janeiro (UERJ)", approved the study, report number 1.630.518, dated June 11, 2016 (CAAE 54919016.4.0000.5274).

RESULTS

From September 1, 2016 and November 11, 2016, 399 patients were hospitalized at the unit, a total of 461 episodes of hospitalizations, being 348 patients with one

episode, 41 patients with two episodes, nine patients with three episodes and one patient with four episodes.

The majority of the population were females (63.4%) between 17 and 94 years old, mean of 62 years (+/- 4.5, median 62). The most frequent sites of primary tumor were: breast (15%), cervix (13.3%) and lungs (13.3%). In Table 1, the study population is described.

The mean global time of hospitalization was 8.2 days (+/-7.1). In 429 episodes of hospitalization (370 patients), it were used analgesic drugs and, because of this, the episodes classified "with pain" (Table 2). In 32 episodes (29 patients), the patients did not receive analgesic drugs during the entire hospitalization or used morphine exclusively for dyspnea and, consequently, were classified as "no pain" and excluded of the later analyzes.

Considering the evaluation of the pain at the moment of admission, in 144 episodes (33.6%), pain was uncontrolled (NVS>0). Of these, in 90 episodes (62.5%) pain was documented as controlled in until 24 hours after admission. The mean time to control the pain was 2.1 days (+/-1.9; CI 95% 1.7-2.4), varying from zero to ten days. Only one patient failed to control the pain during hospitalization.

Of the 429 episodes using analgesics, in 29 (6.8%) the medication utilized corresponded to the first step of the analgesic ladder; in 46 (10.7%) to the second step and in 354 (82.5%) to the third step. There was a report of use of opioid before the hospitalization in 356 (83%) episodes.

The association with common and adjuvant analgesics in the patients classified as second and third steps is described in Table 3. In 351 episodes, (87.8%) using opioids, common analgesic was maintained.

The most utilized opioid was morphine. It was administered through intravenous route continuously in 41 episodes during 2.6 days in average (+/- 1.7, variation from 1 to 8 days). The morphine rescue medicines (SOS) were utilized in 165 episodes, mean of 1.4 rescues per day (+/-0.7), varying from one to 15 rescues a day. The utilization of opioids with its regular dose and as rescue is described in Table 4.

The mean dose of opioid converted in oral morphine was 117.1 mg (CI 95% 10.,2-129.0). The mean dose of morphine raised during hospitalization. In the first day of hospitalization, the mean was 94.1 mg (+/-105.3, CI 95% 83.2-104.9) and in the last day, 139.2 mg (+/-158.2 CI 95% 12.2-155.3), with statistical significance (p-value <0.00).

The association of adjuvant medications was effective for the early pain control. With its use, pain was controlled in 0.8 days (+/-0.4; CI 95%, 6-1.1) *versus* 2.2 days average (+/-2.0; CI 95% 1.8-2.5) without the use of these. Even excluding the use of corticoids and anti-psychotic, there

Table 1. Characterization of the patients hospitalized in the oncologic palliative care unit between September 1, 2016 and November 30, 2016: sociodemographic aspects, site of the tumor and oncologic treatment received

	Absolute Figure	%
Gender		
Male	146	36.6
Female	253	63.4
Primary tumor		
Gynecologic	90	22.6
Digestion	88	22.1
Breast	60	15.0
Lung	45	11.3
Head and neck	43	10.8
Skin	19	4.8
Urinary	19	4.8
Sarcoma	13	3.3
Others	22	5.5
Sites of disease progression		
Local	293	73.4
Lymph node	188	47.1
Lung	128	32.1
Bone	94	23.6
Liver	84	21.1
Peritoneum	68	17.0
Central nervous system	60	15.0
Pleura	49	12.3
Skin	7	1.8
Adrenal	6	1.5
Ovary	5	1.3
Bone marrow	3	0.8
Pancreas	1	0.3
Intravascular	1	0.3
Other	1	0.3
Oncologic Treatment Applied		
RT* and CT**	65	16.3
Surgery. RT e CT	54	13.5
CT exclusively	49	12.3
Surgery and CT	45	11.3
RT exclusively	37	9.3
Surgery exclusively	34	8.5
Surgery and RT	32	8.0
CT. RT and BCT***	21	5.3
Surgery. RT. BCT and CT	4	1.0
RT and BCT	2	0.5
Without specific treatment	56	14.0

Captions: * RT = radiotherapy; **CT = chemotherapy; ***BQT = brachytherapy.

Table 2. Description of the episodes of hospitalization where it were used drugs with analgesic potential at the unit of oncologic palliative care between September 1, 2016 and November 11, 2016

	Episodes with pain	
	n	%
Number of hospitalizations (episodes)	429	93.1
Time of hospitalization		
Mean	8.4	
Standard deviation	7.3	
Minimum	1	
1st quartile	4	
Median	6	
3rd quartile	11	
Maximum	56	
Origin of the patient		
Ward	72	16.8
Emergency	260	60.6
In-house transference	95	22.1
Off-house transference	2	0.5
Motive of hospitalization		
Transference	87	20.3
Pain	78	18.2
Dyspnea	59	13.8
Vomits	31	7.2
Dehydration	26	6.1
Somnolence	23	5.4
Delirium	19	4.4
Infection	16	3.7
Bleeding	15	3.5
Social issues	11	2.6
Others	54	12.6
KPS at admission		
10%	6	1.4
20%	43	10
30%	187	43.6
40%	121	28.2
50%	50	11.7
60%	11	2.6
70%	4	0.9
80%	1	0.2
Not informed	6	1.4
KPS at release		
20%	4	2.7
30%	30	20.5
40%	57	39
50%	34	23.3
60%	9	6.2
70%	2	1.4
80%	0	0
Not informed	10	6.8
Outcome of the episode		
Release	146	34
Death	283	66

Caption: KPS = *Karnofsky Performance Status* Scale.

was faster control of the pain: 1.7 days (+/-1.4; CI 95% 1.3-2.0) *versus* 2.4 days (+/-2.2; CI 95% 0.9-2.9) in average, respectively. These associations were statistically significant (p-value<0.00).

The adjuvants utilized are described in Table 5. The calculations were made considering only the days when they were prescribed for.

In only 16 of the 323 episodes using dexamethasone it was mentioned the indication for pain. In Table 5, it was included the global dose of the drug.

The use of haloperidol for pain was mentioned in three of the 148 episodes, in eight of the 71 for midazolam and in one of the 87 for diazepam. Similarly as dexamethasone, frequently, pain was one of the reasons for its prescription.

Prednisone and risperidone were not prescribed for pain control in any case. In five episodes, midazolam was prescribed orally and parenterally amounting to 71 episodes with the substance.

Pamidronate 90 mg was prescribed in 20 episodes, four of them for pain control. Zoledronate 15 mg was utilized in 24 episodes and in 17 of them, the indication was pain. Both bisphosphonates were prescribed in one cycle per episode.

Dexmedetomidine was utilized in three episodes in continuous infusion with mean dose of 0.6 mcg/kg/h (+/-0.18), varying from 0.5 to 0.9 mcg/kg/h.

There was no use of cetamin and lidocaine in the period studied.

One patient utilized non-standard medication in the hospital: duloxetine 60 mg/day and alprazolam 4 mg/day

DISCUSSION

The population is similar to the described by Lima et al.[21] in an oncology ward of a hospital university in Brazil Northeast: predominance of women (65%) and most common primary sites (breast 10% and cervix, 15.2%). Though in the referenced paper the scenario investigated was an oncology ward, (patients in specific and palliative oncologic treatment), 95% were in staging III or IV.

According to the criteria established in the present study, the great majority of the population (370 patients, 92.7%) presented the symptom "pain" corresponding to 429 episodes of hospitalization (93.1%) in the period studied. In only 35.2% of the episodes, pain was not controlled in the moment of the hospitalization. Disregarding the hospital transference (where the symptom that motivated the hospitalization was not identified), pain was the main cause of hospitalization (78 cases, 22.8%). Similar was the rate of hospitalization per pain encountered in a study in Denmark (20%), though it has been mentioned as present in 70% of the hospitalization cases [22].

Table 3. Distribution of the episodes of hospitalization at the unit of oncologic palliative care according to the classification of the analgesic ladder and use of adjuvant drugs, between September 1, 2016 and November 30, 2016

	Step 1 (n 29)		Step 2 (n 46)		Step 3 (n 354)	
	n	%	n	%	n	%
Use of common analgesic (dipyrone or paracetamol)	29	100	41	89.1	310	87.6
Use of adjuvant (any class)	25	86.2	39	84.8	323	91.2
Antidepressant	0	0	7	15.2	59	16.7
Gabapentin or pregabalin	1	3.4	7	15.2	114	32.2
Baclofen	0	0	0	0	9	2.5
Neuroleptic	11	37.9	13	28.2	132	37.3
Corticosteroid	18	62.1	28	60.9	280	79.1
Use of adjuvant (excluded neuroleptic and corticosteroid)	1	3.4	12	26.1	133	37.6

Table 4. Daily dose of opioid analgesic prescribed at the unit of oncologic palliative care between September 1, 2016 and November 30, 2016

Opioid analgesic	Frequency of use *	Mean (+/-standard deviation)	Min.	Max.
Oral regular morphine (mg)**	225	119.9 (+/-111.7)	18	800
Oral rescue morphine (mg)**	137	38.4 (+/-47.0)	3	231
Tramadol (mg)	85	251.9 (+/-103.4)	50	400
Codeine (mg)	12	135 (+/-41.5)	90	240
Oxycodone (mg)	18	129.4 (+/-97.0)	20	320
Transdermal Fentanyl (mcg/h)	21	68.5 (+/-79.9)	12	253
Oral methadone (mg)**	51	34.5 (+/-32.6)	4	144

Captions: *Number of episodes where the drug was prescribed; **The prescriptions or parenteral route were converted to oral route.

Table 5. Description of the daily doses of analgesic and adjuvant drugs at the unit of oncologic palliative care between September 1, 2016 and November 30, 2016

Medication	Mean	Median	Min.	Max.	Frequency of use*	
					n	%
Dipyrone (g)	6.2	6.0	1.0	12.0	364	84.8%
Paracetamol (g)	3.0	3.0	3.0	3.0	2	0.5%
Tenoxicam (mg)	34.3	40.0	20.0	40.0	7	1.6%
Amitriptyline (mg)	35.3	25.0	25.0	75.0	26	6.1%
Sertraline (mg)	48.4	50.0	25.0	77.0	9	2.1%
Citalopram (mg)	19.8	20.0	15.7	20.0	24	5.6%
Venlafaxine (mg)	47.4	37.5	37.5	75.0	16	3.7%
Baclofen (mg)	17.7	12.7	8.0	30.0	9	2.1%
Gabapentin (mg)	1.478.3	1.200.0	300.0	3.600.0	105	24.5%
Pregabalin (mg)	124.8	150.0	75.0	212.5	18	4.2%
Clonidine (mg)	0.2	0.2	0.2	0.3	3	0.7%
Dexamethasone (mg)	11.8	12.0	2.0	18.5	323	75.5%
Prednisone (mg)	25.0	25.0	10.0	40.0	4	0.9%
Haloperidol (mg)	5.9	5.0	0.5	16.3	148	34.5%
Risperidone (mg)	1.3	1.0	0.5	2.0	17	4.0%
Midazolam parenteral (mg)	12.4	5.0	2.0	103.5	55	12.8%
Midazolam oral (mg)	11.1	11.3	7.5	15.0	21	4.9%
Diazepam (mg)	7.8	6.0	2.5	20.0	87	20.3%

Caption: *Number of episodes where medication was prescribed.

The mean time to obtain NVS zero was two days, this control was attained in until 24 hours in the majority of the episodes. This finding was above to the described by other authors. Lima et al.[21] observed 70% of pain without control at the hospitalization and 15% still had pain in the eighth day of hospitalization. In Korea, 17% did not have controlled pain in the seventh day of hospitalization[23]. In a study in Thailand, the mean time of pain control was seven days and, in only 42% of the patients, it was described NVS=<4 in the seventh day of treatment [24]. In this last study, it draws the attention that the mean NVS in the last day of hospitalization was 3.7, above the mean observed in the seventh day of hospitalization (2.3).

Two methodological differences between the present study and the other studies mentioned need to be distinguished. The first is the value of NVS where pain was defined as controlled: 0 in the present study, =<3[21], =<4[23]. The second difference is that in the present study, when the patient was not capable of quantifying the pain, but the professional reported absence of pains complaint, it was attributed NVS 0. In the other studies, these patients were excluded.

Being the control of the symptoms one of the principles of palliative care, in the case, pain, it is desirable that it is obtained as quick as possible. Given the frequency of the symptom observed when hospitalized, an earlier control of the pain may lead to an earlier release.

Still comparing the present study with the findings of Lima et al.[21], the proportion of the use of analgesics was similar (89% and 90%). The use of strong opioids was discrepant(82% and 51%), just like the use of adjuvants (90% and 31%). These differences may justify the earlier control of the pain observed in this work.

Considering the use of bisphosphonate regardless of the indication, the frequency of use is similar (10% and 13%). On the other hand, if considered only the use of bisphosphonates for pain, the percent of the current study drops to 0.4%. This data is not described in the other study.

Although there is progression of the disease to the bone in 23.6% of the patients, only in 21 episodes (4.9%) were utilized bisphosphonates to control the pain. Some possible justifications for this discrepancy are: patient using bisphosphonates regularly with monthly or quarterly cycle with hospitalization out of the period of administration of the drug, KPS very low or expectation of evolution to death in short time (which makes a therapeutic futility the use of medication), since the objective is symptoms control [25].

Relating the drug profile in the day when the pain was considered controlled with the work of Wangnamthip et al.[24], the use of opioids was bigger than in the present study (93% and 71%), with lower use of weak opioid (17% and 46%). The current study utilized less non-hormone anti-inflammatory (2% and 23%) and antidepressants (19% and 51%). The difference in this drug profile justifies the better control of the pain observed in the present study.

A study in Italy observed distribution per the analgesic ladder different from the current study: 17% in the first step, 63% in the second and 20% in the third. The population presented KPS much higher and the majority of the patients did not present the symptom pain.

The use of antidepressant was equivalent to the encountered by Janberidze et al.[26] (14.5% and 14% respectively). The fact that 75% of the patients using antidepressant failed to meet the criteria of depression may indicate the use of this drug class as adjuvant.

The benefit of the gabapentinoids for pain control is well defined in the literature, either in monotherapy or as adjuvant[27]. The current study showed that 20% of the episodes gabapentin or pregabalin was prescribed, being more frequent its association with strong opioid (32%). There is no record of its use as monotherapy.

The mean daily dose of oral morphine (opioids converted according to analgesic equipotency) observed in the present study (117 mg/day) was close to the value of 120 mg/day in the study of Lundorff et al.[22] and lower than 117 mg/day in the study of Janberidze et al.[26] The frequency of use of common analgesic concomitant to the opioid was also similar to the findings of Lundorff et al.[22] (85% and 83%) and higher than of Janberidze et al.[26] (28%). The association with adjuvants (excluding neuroleptic and corticosteroids) was bigger in this study than in the other two (34, 25 and 11%).

Although the association of opioid, anxiolytic and antipsychotic is feared in the treatment of the general population [28], it is used frequently in patients in palliation for symptoms control, especially in end of life caring[29]. Golčić et al.[30] conducted a retrospective study with 765 patients comparing the survival of patients with different associations of these classes of drugs in a hospice in Croatia. They observed extended survival in the opioid, antipsychotic and anxiolytic group simultaneously than in the other combinations. The mean dose of haloperidol was 4.5 mg/day (0.2 to 20 mg/day) and was administered to 15% of the patients. Midazolam was utilized by 26% of the patients with mean dose of 15 mg/day (7.5 to 30 mg/day) and diazepam in 21% of the mean dose of 10 mg/day (2 to 45 mg/day). The mean equivalent dose of morphine was 129.3 mg/day (+/-145.9, median 80 mg/day). The biggest mean doses encountered by Golčić et al.[30], when compared to the current study may be justified because they have included only patients in the final phase of the life.

Some drugs have multiple indications in palliative care. For instance: corticosteroids are also prescribed for fatigue, hyporexia and tumor edema[31,32]; neuroleptic for *delirium*[33] and nausea[34]; benzodiazepines for palliative sedation[35] and insomnia[36]. The analysis of its importance for pain control in this study was quite hindered. The investigator attempted to identify the indication of these drug classes but the information found in the charts failed to clarify the large majority of the cases. The indication of pain control appeared in only 5% of the cases for dexamethasone, 2% for haloperidol, 11% for midazolam and 1% for diazepam. It remained clear through charts analyzes that, very rarely, pain was the main indication, although in several episodes was one of the indications.

The fact of the dose of dexamethasone was similar in the two groups (with and without pain) and bigger when only dyspnea was reported, corroborates the previous hypothesis. The dose of midazolam, orally or parenterally was bigger when only the symptom dyspnea was present. As the use for pain control was not emphasized, it is possible that higher doses have also been motivated by dyspnea and *delirium* in the group of pain. Similarly, the relatively higher doses of haloperidol utilized must have been motivated by *delirium* (frequent symptom, especially in the last days of life). Accurate conclusions were not reached because this information was not clearly detailed.

The action of a trained palliative care team fosters a better control of the symptoms and quality of life of the patients in oncologic palliation. In the systematic review and meta-analysis conducted by Kassianos et al.[10], it were encountered positive results in every article selected, with emphasis to the importance of the multi-professional team. The differences observed in the drug profile may reflect the expertise of the prescribers at the unit and, consequently, improved control of the symptoms.

The bigger limitation of this study was the collection of data restricted to the chart. It should be pursued the elaboration of a complementary study with the quantification of the pain collected straight from the patient and the identification of the type of pain instead of chart review to confirm the results obtained.

CONCLUSION

This manuscript met the necessity of knowing better the best drug treatment for pain applied at the unit of oncologic palliative care studied. With populational profile similar to other studies, although the methodological differences, the practice of using adjuvants and the safe management of strong opioids appear to be the factors associated to the favorable findings. Continued team training and monitoring of indicators are essential to improve the services offered at the unit.

CONTRIBUTIONS

All the authors participated of the conception and design of the study, analysis and interpretation of data, wording and review of the manuscript and approved the final version.

DECLARATION OF CONFLICT OF INTERESTS

There are no conflict of interests to declare.

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