Use of opioids in geriatric palliative care: analysis of a public hospital in Brazil's Federal District

Uso de opioides nos cuidados paliativos geriátrico: análise de um hospital público do Distrito Federal, Brasil

Priscilla Avelino Tavares¹ (10), Mariana do Nascimento Morais¹ (10), Jacksandra Farias de França Campos² (10), Emília Vitória da Silva³ (10), Débora Ferreira Reis² (10)

ABSTRACT

Introduction: Patients in Geriatric Palliative Care (GPC) complain of pain and opioids are the drugs used to manage it. This study aims to understand the sociodemographic, clinical and opioid use characteristics of GPC patients in a public hospital in the Federal District of Brazil.

Methods: This is a cross-sectional approach based on analysis of prescriptions. The results are shown in tables after descriptive and bivariate analysis. Fisher's exact test, Bonferroni's post hoc for categorical variables and Kendall's tau correlation coefficient for continuous variables were used.

Results: Four hundred and forty-four prescriptions for 49 patients were analyzed. Data showed a mean age of 80.4 years, a prevalence of women (57.1 %), the main diagnoses being Alzheimer's disease and neoplasia, and prevalent length of up to 7 days. Morphine was the most used medication (15.8 mg to 20.8 mg). The oral route was predominant at the beginning of hospitalization and the subcutaneous route at the end. There was a greater dose variation in degenerative disease of the nervous system and statistical significance between length of stay (1 to 7 days) and clinical diagnosis.

Discussion: The sociodemographic and clinical characteristics are in line with the Brazilian epidemiological profile. The use of opioids was equivalent to that recommended and is more associated with dyspnea control. Dose variation in degenerative nervous system disease probably occurred due to the variability of diseases included in this group. The statistical significance between length of hospitalization and diagnosis can be justified by the clinical severity of the patients hospitalized.

Keywords: Analgesics, Opioid; Palliative Care; Hospitals, Public; Geriatrics.

RESUMO

Introdução: Os pacientes em Cuidados Paliativos Geriátrico (CPG) queixam-se de dor e os opioides são os medicamentos usados para o manejo. Esse estudo visa conhecer as características sociodemográficas, clínicas e referentes ao uso de opioides nos CPG de um hospital público do Distrito Federal.

Métodos: Abordagem transversal a partir da análise de prescrições. Os resultados aparecem em tabelas após a análise descritiva e bivariada. Utilizou-se teste exato de Fisher, post hoc de Bonferroni para variáveis categóricas e o coeficiente de correlação tau de kendall para variáveis contínuas.

Resultados: Analisou-se 444 prescrições de 49 pacientes. Os dados mostram idade média de 80,4 anos, prevalência feminina (57,1%), diagnósticos principais de doença de Alzheimer e neoplasias, e tempo de internação prevalente de até 7 dias. A morfina foi o medicamento mais usado (15,8 mg a 20,8 mg). A via oral foi predominante no início da internação e a via subcutânea ao final. Houve variação de dose mais acentuada na doença degenerativa do sistema nervoso e significância estatística entre o tempo de internação (1 a 7 dias) com diagnóstico clínico.

Discussão: As características sociodemográficas e clínicas estão em conformidade com o perfil epidemiológico brasileiro. O uso de opioides mostrou-se equivalente com o recomendado e está mais associado ao controle de dispneia. A variação de dose na doença degenerativa do sistema nervoso provavelmente ocorreu devido a variabilidade de doenças incluídas neste grupo. A significância estatística entre o tempo de internação e o diagnóstico pode ser justificada pela gravidade clínica dos pacientes internados.

Palavras-chaves: Analgésicos Opioides; Cuidados Paliativos; Hospitais Públicos; Geriatria.

Escola Superior de Ciências da Saúde, Programa de Residência Multiprofissional em Cuidados Paliativos, Brasília, Distrito Federal, Brasil.

*Secretaria de Saúde do Distrito Federal, Programa de Residência Multiprofissional em Cuidados Paliativos, Brasília, Distrito Federal, Brasil.

³Universidade de Brasília, Faculdade da Ceilândia, Câmpus Ceilândia, Distrito Federal, Brasil.

Corresponding author: Priscilla Avelino Tavares; Email: priscilla8tavares@gmail.com.

Conflict of interest: The authors declare no conflict of interest

Authors' contributions: PTA, DFR, JFFC, MNM, and EVS: substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the study. PTA, DFR, and EVS: redaction or critical review of the article for relevant intellectual content. PTA, DFR, and EVS: final approval of the version to be published. PTA, DFR, JFFC, MNM, and EVS: agree to be responsible for all aspects of the work to ensure that issues relating to the accuracy or completeness of any part of the work are properly investigated and resolved.

Received on January 26, 2023; Final version received on July 30, 2023; Accepted on October 23, 2023; Published on December 29, 2023.

Editor-in-chief: João Batista Santos Garcia; Scientific editor: Rudval Souza da Silva



INTRODUCTION

Geriatric Palliative Care (GPC) is the unification of geriatric medicine with palliative medicine. In other words, it is an approach focused on the elderly population and their families who face problems associated with life-threatening illnesses, aiming to improve patients' quality of life by preventing and relieving suffering^{1,2}. In recent years, GPC has gained more prominence due to the aging population associated with the involvement of chronic multimorbidities, such as cardiovascular diseases, diabetes, cognitive decline, and cancer³.

Among the main symptoms affecting patients in palliative care, pain is the most common complaint reported by elderly patients and opioids are the most indicated drugs for managing this symptom. However, pain in the geriatric population is often under-treated and opioids are used restrictively by health professionals due to their adverse reactions^{4,5}.

Proper use of opioids in the elderly requires attention to the physiological changes that are characteristic of this age group. For example, the metabolization and excretion of drugs by the body are processes that undergo significant changes with advancing age, as well as an increased sensitivity to the use of drugs. Despite this fact, the use of opioid analgesics is possible and should be used whenever necessary in order to achieve pain control, comfort, and better quality of life, commensurate with the elderly person's clinical condition^{3,4}.

Given the fact that GPC is an emerging field of study³ and considering that opioids are drugs that are little used in symptoms management in the elderly⁴, this study aims to understand the sociodemographic, clinical, and opioid-related characteristics in the geriatric palliative care unit of a public hospital in the Federal District of Brazil.

METHODS

This is a six-month cross-sectional study based on the analysis of patient prescriptions in the geriatric palliative care unit of a public hospital in Brazil's Federal District. The prescriptions of inpatients were analyzed, looking at the dose and route of administration of the following opioid analgesics: morphine, methadone, and fentanyl. The sociodemographic and clinical characteristics of the patients were also assessed, considering gender, age, International Classification of Diseases (ICD-10) and length of hospitalization.

Patients admitted to the hospital's geriatric unit between September 2021 and March 2022 took part in the study. Patients were included in the study according to the following criteria: age 60 or over with severe dementia confirmed by a doctor, urinary and faecal incontinence, absence of significant verbal communication, limited speech capacity; frail

elderly over 80 years old, characterized by multimorbidities, weight loss in the last year, low physical activity, exhaustion, weakness, decreased gait speed. Patients were excluded according to the following criteria: patients with a recent stroke (less than three months) or first episode of cerebrovascular accident vegetative states, patients on any form of dialysis, using mechanical ventilation, using parenteral nutrition, and using vasoactive drugs.

Data was collected by accessing patients' electronic medical records and prescriptions through the Trakcare® system, after prior approval by the Research Ethics Committee. The doses of methadone and fentanyl were converted into morphine-equivalent doses, based on the literature⁶, to enable comparison and analysis of the data. All doses presented in the results are in milligrams (mg).

With this information, a descriptive analysis was carried out on all the study variables, presented in absolute numbers, proportion, mean and standard deviation. Diagnosis, age and sociodemographic characteristics, clinical characteristics and opioid use were analyzed using Fisher's exact test, followed by Bonferroni's post hoc test for categorical variables and Kendall's tau correlation coefficient for continuous variables. Data was considered significant when p < 0.05. All analyses were carried out using the IBM SPSS program, version 19.0. There are no conflicts of interest related to the publication of the study.

RESULTS

The study analyzed 444 prescriptions from 49 inpatients between September 2021 and March 2022. The results are shown in Table 1, Table 2, Table 3, and Figure 1.

Table 1 shows the descriptive results of the sample relating to sociodemographic and clinical characteristics and opioid use. The study participants were on average 80.4 years old (SD \pm 9.6) and 57.1% were women. With regard to clinical characteristics, the majority had a diagnosis of Alzheimer's dementia (44.9%), followed by neoplasia (22.4%). The patients had been in the geriatric unit for up to 7 days (65.3%). Most of them used only one opioid (96%), with 98% using morphine. The opioid dose varied on average from 15.8 mg (SD \pm 13.0) to 20.8 mg (SD \pm 18.6) and changed for 53.1% of the participants. Regarding the route of administration, the oral route was the most used at the beginning of hospitalization (28.6%) and the subcutaneous route was the most used at the end of hospitalization (26.5%). In all, 32.7% of patients had their route of administration changed.

Figure 1 shows the variation in the opioids' doses taken by the participants according to their clinical diagnosis. There was an increase in doses on the first day of hospitalization and minimum doses, compared to doses on the last day of

Table 1. Sociodemographic, clinical, and opioid use characteristics of elderly patients admitted to a public hospital in Brazil's Federal District from September 2021 to March 2022.

Variables	N	Mean (SD) %
Sociodemographic characteristics		
Age	49	80.4 (9.6)
≤ 80 years	27	55.1
> 80 years	22	44.9
Gender		
Female	28	57.1
Male	21	42.9
Clinical characteristics		
Diagnosis		
Neoplasia	11	22.4
Dementia in Alzheimer's disease	22	44.9
Degenerative disease of the nervous system	8	16.3
Other diseases	8	16.3
Length of hospitalization	49	8.9 (9.6)
l to 7 days	32	65.3
8 to 14 days	7	14.3
≥ 15 days	10	20.4
Use of opioids		
Opioid		
Morphine	48	98.0
Methadone	2	4.1
Fentanyl	2	4.1
Number of opioids	49	1.1 (0.3)
	47	96.0
2	1	2.0
3	1	2.0
Dose (mg)		
Minimum	49	13.9 (10.8)
Maximum	49	22.2 (19.0)
Dose (mg)		
First day of hospitalization	49	15.8 (13.0)
Last day of hospitalization	49	20.8 (18.6)
Dose change		
Yes	26	53.1
No	23	46.9
Routes of administration		
Oral	15	30.6
Sublingual	5	10.2
Nasoenteral tube	13	26.5
Gastrotomy	9	18.4
Endovenous	10	20.4
Subcutaneous	15	30.6

Table 1. Cont.

Variables	N	Mean (SD) %
Change of routes of administration		
Yes	16	32.7
No	33	67.3
Number of administration routes		
1	34	69.4
2	12	14.5
3	3	6.1
Routes of administration on the first day of hospitalization		
Oral	14	28.6
Sublingual	5	10.2
Nasoenteral tube	5	10.2
Gastrostomy	7	14.3
Endovenous	4	8.2
Subcutaneous	9	18.4
Routes of administration on the last day of hospitalization		
Oral	9	18.4
Sublingual	3	6.1
Nasoenteral tube	8	16.3
Gastrostomy	8	16.3
Endovenous	8	16.3
Subcutaneous	13	26.5

Source: Trakcare® system, of Brazil's Federal Health Secretariat, 2021-2022.

Table 2. Sociodemographic, clinical, and opioid use characteristics of elderly patients admitted to a public hospital in Brazil's Federal District from September 2021 to March 2022, according to diagnosis.

Variables	Diagnosis				
	Dementia and deg	Dementia and degenerative diseases		l other diseases	
	N	%	N	%	р
Sociodemographic characteristic	cs				
Age					
≤ 80 years	15	50.0	12	63.2	0.36
> 80 years	15	50.0	7	36.8	
Gender					
Female	20	66.7	8	42.1	0.09
Male	10	33.3	11	57.9	
Clinical characteristics					
Length of hospitalization					
1 to 7 days	18	60.0	14	73.7	0.02
8 to 14 days	7	23.3	O*	0.0	
≥ 15 days	5	16.7	5	26.3	
Use of opioids					
Opioid					
Morphine	29	96.7	19	100.0	0.32

Table 2. Cont.

Variables -	Diagnosis				
	Dementia and degenerative diseases		Neoplasia and	l other diseases	
	N	%	N	%	p
Methadone	1	3.3	1	5.3	0.74
Fentanyl	1	3.3	1	5.3	0.74
Number of opioids					
1	29	96.7	18	94.7	0.24
2	1	3.3	0	0.0	
3	0	0.0	1	5.3	
Dose (mg)					
Minimum	0.07	0.54			
Maximum	0.22	0.07			
Dose (mg)					
First day of hospitalization	0.12	0.29			
Last day of hospitalization	0.17	0.16			
Dose change					
Yes	14	46.7	12	63.2	0.25
No	16	53.3	7	36.8	
Routes of administration					
Oral	9	30.0	6	31.6	0.91
Sublingual	2	6.7	3	15.8	0.31
Nasoenteral and gastrostomy tube	16	53.3	6	31.6	0.13
Endovenous	5	16.7	5	26.3	0.41
Subcutaneous	7	23.3	8	42.1	0.17
Change of route of administration					
Yes	8	26.7	8	42.1	0.26
No	22	73.3	11	57.9	
Number of administration routes					
1	22	73.3	12	63.2	0.56
2	7	23.3	5	26.3	
3	1	3.3	2	10.5	
Routes of administration on the first day of hospitalization					
Oral	8	26.7	6	31.6	0.05
Sublingual	2	6.7	3	15.8	
Nasoenteral and gastrostomy tube	13	43.3	4	21.1	
Endovenous	4	13.3	0	0.0	
Subcutaneous	3	10.0	6	31.6	
Routes of administration on the last day of hospitalization					
Oral	5	16.7	4	21.1	0.31
Sublingual	2	6.7	1	5.3	
Nasoenteral and gastrostomy tube	13	43.3	3	15.8	
Endovenous	4	13.3	4	21.1	
Subcutaneous	6	20.0	7	36.8	

^{*}Significant, considering p < 0.05. Source: Trakcare® system of Brazil's Federal Health Secretariat, 2021-2022.

Table 3. Sociodemographic, clinical, and opioid use characteristics of elderly patients admitted to a public hospital in the Federal District from September 2021 to March 2022, according to age.

Variables	Age				
	≤ 80 years		> 80 years		
	N	%	N	%	p
Sociodemographic characteristics					
Gender					
Female	13	48.1	15	68.2	0.15
Male	14	51.9	7	31.8	
Clinical characteristics					
Diagnosis					
Dementia and degenerative diseases	15	55.6	15	68.2	0.36
Neoplasia and other diseases	12	44.4	7	31.8	
Length of hospitalization					
1 to 7 days	16	59.3	16	72.7	0.18
8 to 14 days	3	11.1	4	18.2	
≥ 15 days	8	29.6	2	9.1	
Use of opioids					
Opioid					
Morphine	27	100.0	21	95.5	0.20
Methadone	1	3.7	1	4.5	0.88
Fentanyl	0	0.0	2	9.1	0.06
Number of opioids					
1	26	96.3	21	95.5	0.25
2	1	3.7	0	0.0	
3	0	0.0	1	4.5	
Dose (mg)					
Minimum	-1.00	0.41			
Maximum	-0.13	0.28			
Dose (mg)					
First day of hospitalization	-0.14	0.25			
Last day of hospitalization	-0.10	0.40			
Dose change					
Yes	14	51.9	12	54.5	0.85
No	13	48.1	10	45.5	
Routes of administration					
Oral	6	22.2	9	40.9	0.16
Sublingual	2	7.4	3	13.6	0.48
Nasoenteral and gastrostomy tube	13	48.1	9	40.9	0.61
Endovenous	5	18.5	5	22.7	0.72
Subcutaneous	9	33.3	6	27.3	0.65
Change of routes of administration					
Yes	8	29.6	8	36.4	0.62
No	19	70.4	14	63.6	

Table 3. Cont.

Variables		Ag	ge		
	≤ 80 years		> 80 years		
	N	%	N	%	р
Number of administration routes					
1	20	74.1	14	63.6	0.64
2	6	22.2	6	27.3	
3	1	3.7	2	9.1	
Routes of administration on admission					
Oral	6	22.2	8	36.4	0.65
Sublingual	2	7.4	3	13.6	
Nasoenteral and gastrostomy tube	11	40.7	6	27.3	
Endovenous	2	7.4	2	9.1	
Subcutaneous	6	22.2	3	13.6	
Route of administration on the last day of hospitalization					
Oral	5	18.5	4	18.2	0.91
Sublingual	1	3.7	2	9.1	
Nasoenteral and gastrostomy tube	10	37.0	6	27.3	
Endovenous	4	14.8	4	18.2	
Subcutaneous	7	25.9	6	27.3	

^{*}Significant, considering p < 0.05.

Source: Trakcare® system of Brazil's Federal Health Secretariat, 2021-2022.

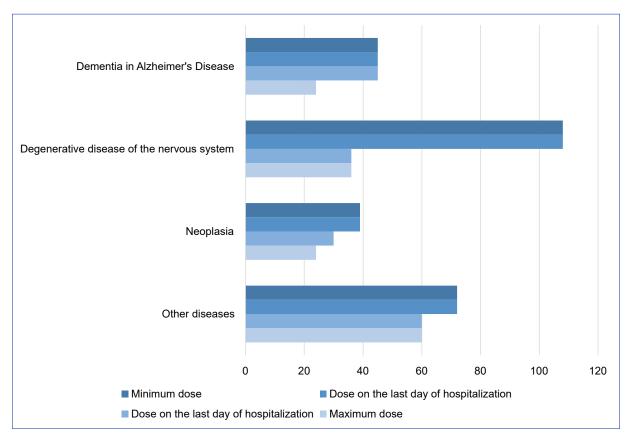


Figure 1. Doses of opioids used according to the clinical diagnosis of elderly patients admitted to a public hospital in Brazil's Federal District. Unit: mg

Source: Trakcare® system of Brazil's Federal Health Secretariat, 2021-2022.

hospitalization and maximum doses used by the participants. The graph shows that this difference was greater among patients diagnosed with degenerative diseases of the nervous system, with a variation of approximately 60 mg.

Table 2 shows the bivariate analyses between the variables and the main clinical diagnoses, dementia and degenerative diseases, and neoplasia and other diseases, showing that there was statistical significance between the length of time patients were hospitalized (1 to 7 days) and clinical diagnosis (p < 0.05). There was a marginal association between diagnosis and the maximum dose of opioids used (p = 0.07), as well as a higher percentage of patients using the oral route of administration (p = 0.05). The other patient's characteristics were not significantly different.

The bivariate analysis between the variables and age showed that there was no statistically significant difference in the percentage of patients aged 80 or over with sociode-mographic, clinical, and opioid use-related characteristics (Table 3).

DISCUSSION

The descriptive results of the sociodemographic characteristics indicate an average age of 80.4 years, varying by 9.6 years, and a higher prevalence of women (57.1%) (Table 1). This profile corresponds to the projected life expectancy estimated by the Brazilian Institute of Geography and Statistics (IBGE) for 2021/2022 of \simeq 80 years for women and \simeq 70 years for men. The descriptive results of the sociodemographic characteristics indicate a mean age of 80.4 years, varying from 9.6 years to more or less, as well as showing a higher prevalence of women (57.1%) (Table 1). This profile corresponds with the life expectancy projection estimated by IBGE for 2021/2022 of \simeq 80 years for women and \simeq 70 for men⁷.

The clinical characteristics related to diagnosis showed a prevalence of dementia as Alzheimer's disease (44.9%), followed by neoplasia (22.4%) and degenerative diseases of the nervous system (16.3%) (Table 1). These pathologies make up the World Health Organization ranking published in 2020 of the main causes of death in the world, highlighting the relevance of chronic non-communicable diseases⁸. It is also described in Brazilian epidemiology, which cites neoplasia and diseases of the nervous system among the main causes of mortality in the elderly^{9,10}.

Regarding clinical characteristics, 65.3% of participants were hospitalized for between 1 and 7 days and 20.4% for more than 15 days (Table 1). The bivariate analyses indicated that the length of hospitalization (1 to 7 days) showed a relevant result (ρ < 0.05) when correlated with the diagnosis (Table 2). It is likely that the profile of the study participants, which mainly

included frail elderly people with functional dependence and severe cognitive decline, combined with the fact that invasive and disease-modifying measures were not indicated, influenced this result. In other words, the clinical severity of patients in palliative care may have favored a shorter length of stay¹¹. Moreover, patients with longer hospitalization periods may have had pain that was difficult to control¹².

With regard to the use of opioids, it was found that most patients used at least one opioid (96%), with morphine being prescribed for 98% of patients (Table 1). The use of morphine is indicated to control moderate to severe pain and dyspnea¹³. This result may indicate adequate management of GPC, considering morphine as an indicator of quality of death^{14,15}. In addition, the list of Potentially Inappropriate Medications for the Elderly, or Beers Criteria, allows for the prolonged use of morphine and other strong opioids in the elderly, in cases where palliative care is indicated or for the management of moderate chronic pain^{16,17}.

The average dose of opioids ranged from 15.8 mg (SD \pm 13.0) to 20.8 mg (SD \pm 18.6), 53.1% of participants adjusted their dose throughout their hospitalization and a small percentage of patients (2%) used up to three opioids (Table 1). Comparing these results with those recommended, the average dose values found are lower than those expected for opioid-naive patients for pain control (30 mg to 60 mg per day) and are in line with the doses indicated for dyspnea control (15 mg to 30 mg per day). This may indicate a greater use of opioids for dyspnea control than for pain among the study participants. Moreover, it is also recommended to re-evaluate the opioid prescribed and adjust the daily doses according to the need to control symptoms, which would justify changing the dose in 53.1% and the use of up to three opioids in 2% of the participants 6,13,18,19 .

The maximum dose showed a marginal association (p = 0.07) with diagnosis (Table 2) and the variation of doses according to diagnosis shows an increase of opioid doses on the first day of hospitalization and minimum doses, in relation to doses on the last day of hospitalization and maximum doses used mainly among patients diagnosed with degenerative diseases of the nervous system, a variation of approximately 60 mg (Figure 1). It is likely that the complexity and diversity of the diagnoses is related to the management and use of opioids found in the analysis. The term "degenerative disease of the nervous system" groups together many other diseases, such as frontotemporal dementia, progressive supranuclear palsy, corticobasal degeneration, Parkinson's disease, dementia with Lewy bodies, and others that would require their own drug management in each case, which would explain the greater variation of doses taken by the study participants²⁰.

Regarding the route of administration, it was found that the oral route was the most used at the beginning of hospitalization (28.6%) and the subcutaneous route was the most used at the end of hospitalization (26.5%), with 32.7% of the participants changing their route of administration (Table 1). There was also a marginal association between the diagnosis and the percentage of patients who used the oral route of administration (p = 0.05) (Table 2). This data can be explained by the suggestion of the most physiological route (oral) whenever possible, as well as the subcutaneous route being indicated as the most comfortable injectable route for patients in palliative care. Likewise, a change of route is recommended whenever necessary, depending on the worsening of the clinical condition 6.18.19.

The correlation with age did not yield any relevant results, i.e., there was no significant association between the patients' age and the variables analyzed (Table 3). It is possible that the sample size evaluated in the study was not enough to establish an association²¹.

In general, the study revealed that the conduct related to opioid management in the hospital evaluated is in line with recommendations^{6,18,19}, considering the dosage and characteristics of the prescription of opioid analgesics in palliative care, standing out in comparison with the use of opioids in Brazil. Brazil ranks low in the world ranking of quality of death due to, among other indicators, the small amount of opioids prescribed¹⁴. On the other hand, it was not possible to assess pain management in comparison with the doses in use and the fact that the sample size was insufficient to establish a greater number of associations²¹. It is therefore very important to encourage more research into the use of opioid analgesics in palliative care and geriatrics, in order to expand knowledge on the subject, and consequently, the use of opioids.

ACKNOWLEDGMENTS

The authors wish to thank the Escola Superior de Ciências de Saúde, especially the Multiprofessional Residency Program in Palliative Care, for encouraging them to carry out this research, and the Health Secretariat of the Federal District of Brazil for providing the data analyzed in the study, and for the cordiality and assistance provided during its development.

REFERENCES

- Voumard R, Truchard ER, Benaroyo L, Borasio GD, Bula C, Jox RJ. Geriatric palliative care: a view of its concept, challenges and strategies. BMC Geriatr. 2018;18:220. https://doi.org/10.1186/ s12877-018-0914-0
- World Health Organization. Palliative care [Internet]. 2020 [cited 2020 Aug 5]. Available from: https://www.who.int/news-room/ fact-sheets/detail/palliative-care/

- World Health Organization. Palliative care for older people: Better practices [Internet]. 2011 [cited 2020 Aug 5]. Available from: https://www.who.int/europe/publications/i/item/9789289002240
- Borsheski R, Johnson QL. Pain management in the geriatric population. Mo Med. 2014;111(6):508-11.
- Naples JG, Gellad WF, Hanlon JT. The Role of Opioid Analgesics in Geriatric Pain Management. Clin Geriatr Med. 2016;32(4):725-735. https://doi.org/10.1016/j.cger.2016.06.006
- Ferreira GD, Mendonça GN. Cuidados Paliativos: Guia de Bolso.
 São Paulo: Agência Nacional de Cuidados Paliativos; 2017.
- Instituto Brasileiro de Geografia e Estatística. População Projeção [Internet]. 2022 [cited 2022 Dec 21]. Available from: https://www.ibge.gov.br/apps/populacao/projecao/index.html
- World Health Organization. The top 10 causes of death [Internet].
 2020 [cited 2020 Dec 09]. Available from: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death/
- 9. Romero D, Maia L. A epidemiologia do envelhecimento: novos paradigmas? Rio de Janeiro: Fundação Oswaldo Cruz; 2022.
- Ministério da Saúde (BR) Secretaria de Vigilância em Saúde: Análise epidemiológica e vigilância de doenças não transmissíveis [Internet]. 2023 [cited 2023 Jul 29]. Available from: https://svs.aids. gov.br/daent/centrais-de-conteudos/paineis-de-monitoramento/ saude-brasil/mortalidade-geral/
- Andrade FLJP, Jerez-Roig J, Ferreira LMBM, Lima JMR, Lima KC. Incidência e fatores de risco para hospitalização em pessoas idosas institucionalizadas. Rev Bras Geriatr Gerontol. 2020;23(4): e200241. https://doi.org/10.1590/1981-22562020023.200241
- Sampaio SG dos SM, Motta LB da, Caldas CP. Dor e internação hospitalar em cuidados paliativos. Rev Bras Cancerol. 2021;67(3): e-131180. https://rbc.inca.gov.br/index.php/revista/article/view/1180
- Wiermann EG, Diz MdPED, Caponero R, Lages PSML, Araujo CZ, Bettega RT, et al. Consenso brasileiro sobre manejo da dor relacionada ao câncer. Rev Bras Onc Clín. 2014;10(38):132-43. https://www.sboc.org.br/sboc-site/revista-sboc/pdfs/38/artigo2. pdf
- World Health Organization. Assessing the development of palliative care worldwide: A set of actionable indicators [Internet].
 2021 [cited 2023 Jul 29]. Available from: https://www.who.int/ publications/i/item/9789240033351/
- Finkelstein EA, Bhadelia A, Goh C, Baid D, Singh R, Bhatnagar S, Connor SR. Cross country comparison of expert assessments of the quality of death and dying 2021. J Pain Symptom Manage. 2022;63(4):e419-e429. https://doi.org/10.1016/j. jpainsymman.2021.12.015
- Oliveira MG, Amorim WW, Oliveira CRB, Coqueiro HL, Gusmão LC, Passos LC. Consenso brasileiro de medicamentos potencialmente inapropriados para idosos. Geriatr Gerontol Aging. 2016;10(4):168-81. https://doi.org/10.5327/Z2447-211520161600054
- 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019;67(4):674-94. https://doi.org/10.1111/ jgs.15767
- Castilho RK, Pinto CS, Silva VCS. Manual de Cuidados Paliativos.
 3rd ed. São Paulo: Academia Nacional de Cuidados Paliativos;
 2021.
- Zoccoli TLV, Ribeiro MG, Fonseca GM, Ferrer VC. Desmistificando cuidados paliativos. Brasília: Oxigênio; 2019.
- Erkkinen MG, Kim MO, Geschwind MD. Clinical neurology and epidemiology of the major neurodegenerative diseases. Cold Spring Harb Perspect Biol. 2018;10:a033118. https://doi.org/10.1101/ cshperspect.a033118
- Miot HA. Tamanho da amostra em estudos clínicos e experimentais. J Vasc Bras. 2011;10(4):275-8. https://doi.org/10.1590/ S1677-54492011000400001