Original Research
Community Dental Health

Prescriptions of analgesics and anti-inflammatory drugs in municipalities from a Brazilian Southeast state

Alex Júnio Silva da CRUZ[a]
Jacqueline Silva SANTOS[a]
Edmilson Antônio PEREIRA JÚNIOR[b]
Cristina Mariano RUAS[c]
Flávio de Freitas MATTOS[d]
Lia Silva de CASTILHO[e]
Mauro Henrique Nogueira Guimarães ABREU[d]

[a]Universidade Federal de Minas Gerais – UFMG, School of Dentistry, Graduate Programme in Dentistry, Belo Horizonte, MG, Brazil.

[b]Universidade Federal de Minas Gerais – UFMG, School of Education, Belo Horizonte, MG, Brazil.

[c]Universidade Federal de Minas Gerais – UFMG, School of Pharmacy, Department of Social Pharmacy, Belo Horizonte, MG, Brazil.

[d]Universidade Federal de Minas Gerais – UFMG, School of Dentistry, Department of Community and Preventive Dentistry, Belo Horizonte, MG, Brazil.

[e]Universidade Federal de Minas Gerais – UFMG, School of Dentistry, Department of Operative Dentistry, Belo Horizonte, MG, Brazil.

Declaration of Interests: The authors certify that they have no commercial or associative interest that represents a conflict of interest in connection with the manuscript.

Corresponding Author:
Mauro Henrique Nogueira Guimarães Abreu
E-mail: maurohenriqueabreu@gmail.com

https://doi.org/10.1590/1807-3107bor-2021.vol35.0011

Abstract: The objective of this study was to describe dental prescriptions of non-steroidal anti-inflammatory drugs (NSAID), opioids, and analgesics dispensed by the Brazilian National Health System (BNHS, *SUS* in Portuguese) of a Southeastern state from January to December 2017, and to analyze their association with socioeconomic and oral health care services' characteristics at municipal level. Data were collected from the Brazilian Integrated Pharmaceutical Care Management System. Medicines were grouped according to the Anatomical Therapeutic Chemical Classification System. The total number of Defined Daily Doses (DDD) and DDD per 1,000 inhabitants (inhab.) per year were presented and compared between groups of municipalities. Data analysis used the Classification and Regression Tree model performed with IBM SPSS 25.0. The total number of NSAID, opioids, and analgesics prescriptions was 70,747 and accounted for 354,221.13 DDD. The most frequently prescribed medicine was ibuprofen (n = 24,676; 34.88%). The number of dental practitioners in the BNHS per 1,000 inhab. ($p < 0.001$), first dental appointment coverage ($p = 0.010$), oral health teams per 1,000 inhab. ($p=0.022$), and the proportion of rural population ($p = 0.014$) were variables positively associated with the number of DDD of NSAID per 1,000 inhab. per year. *Bolsa Família* program coverage per 1,000 inhab. ($p = 0.022$) was negatively associated with NSAID prescription. Regarding analgesics, first dental appointment coverage ($p=0.002$) and *Bolsa Família* program coverage per 1,000 inhab. ($p = 0.012$) were positively associated with DDD per 1,000 inhab. per year. In conclusion, dental prescriptions of analgesics and NSAID in the BNHS were associated with socioeconomic and oral health care services' characteristics.

Keywords: Anti-inflammatory Agents, Non-Steroidal; Analgesics, Opioid; Dentistry; Pharmacoepidemiology.

Introduction

The prevalence of toothache in Brazilian adults was estimated in 21%.[1] It seems painful conditions are the most common reason for unscheduled visits to the dentist.[2] The correct management of dental pain includes clinical

Submitted: May 21, 2020
Accepted for publication: Jue 28, 2020
Last revision: August 21, 2020

treatment and, when necessary, the prescription of medicines.[2,3] Nonsteroidal anti-inflammatory drugs (NSAID), opioids, and analgesics are frequently prescribed by dental practitioners.[3,4,5]

Research shows an overall increase in the prescription of medicines to control pain.[6,7,8] It is recognized that millions of people suffer from untreated pain around the world.[9] Greater inequalities in the management of pain are found in low and middle-income countries, especially among the vulnerable population.[9] Some studies reported that poverty, imbalanced income distribution, and health service' characteristics could be associated with health services access and the use of pain relievers.[10,11]

The interest in pharmacoepidemiology studies is growing lately.[6] However, most of the studies in this field were conducted in developed countries. This could be explained by the limited reliable data on drug consumption available in the Public Health System in some developing countries.[12] Furthermore, the majority and most recent populational research on analgesics prescriptions by dental practitioners does not evaluate the influence of social health determinants.[5-8] In this study, we aimed to describe dental prescriptions of NSAID, opioids, and analgesics dispensed by the Brazilian National Health System (BNHS, *SUS* in Portuguese) of a Southeastern state and to analyze their association with socioeconomic and oral health care services' characteristics at municipal-level from January to December 2017.

Methodology

Ethical considerations

The Ethics Committee of the Federal University of Minas Gerais approved this study under the protocol number CAAE- 88465118.8.0000.5149.

Sampling

This ecological cross-sectional study was based on data retrieved from the Brazilian Integrated Pharmaceutical Care Management System (*Sistema Integrado de Gerenciamento da Assistência Farmacêutica- SIGAF*) in the state of Minas Gerais from January to December 2017. This state-level system enables pharmaceutical service management and has been used since 2009.[13] The dataset was accessed after the state's formal permission and under approval of the local ethics committee.

Minas Gerais is one of the 27 states of Brazil. It is located in the southeast region with a total area of 586,521.12 square kilometers (km^2) and comprises 853 municipalities.[14] According to the 2010 Demographic Census, the state's population was 19,597,330. (rural population= 2,882,114; urban population= 16,715,216).[14] The state's demographic density was 33.41 inhab. per km^2.[14] The state's Human Development Index (HDI) is 0.731[14] and GINI index is 0.563.[15] In June 2017, 1,026,671 families were beneficiaries of the *Bolsa Família* (BF) program.[16] BF program is the national conditional cash transfer program directed to vulnerable families. Its main goals include ensuring the right to food and access to education and health.[16]

All medicines dispensed through dental prescriptions and registered at SIGAF were grouped according to the Anatomical Therapeutic Chemical (ATC) Classification System.[17] In this system substances are classified according to the physiological system or organ where they act.[17,18] Drugs belonging to the following ATC Classification System groups were included in the analyzes: M - Musculo-Skeletal System (M01A - Anti-inflammatory and Antirheumatic Products, Non-Steroids) N - Nervous System (N02A - Opioids and N02B - Other Analgesics and Antipyretics).

Measurements

To measure the dispensing process of the studied medicines in each municipality, the Defined Daily Dose (DDD) proposed by WHO was applied.[17] DDD is a unit of measurement defined as the average maintenance daily dose for a drug used for its main indication in adults.[17] Each chemical substance is assigned with a standard DDD that may vary due to the administration route (e.g. oral, parenteral, and rectal). This unit was created to enable the comparison of drug consumption trends across different regions and time.[17,18]

According to the 2019 Guidelines for ATC classification and DDD assignment[17] and the list of DDD for combined products[19], the DDD of all chemical substances dispensed by SIGAF were first converted

into the same unit of mass-milligrams. Then total DDD and DDD per 1,000 inhabitants (inhab.) per year were calculated for each municipality in the state of Minas Gerais. To calculate total DDD, the number of pharmaceutical forms (e.g., number of tablets) of each chemical substance was multiplied by its concentration in milligrams, and the result was divided by the drug-specific DDD.[18,20] To estimate DDD per 1,000 inhab. per year, the number of DDD was multiplied per 1,000 and then the figure was divided by population.[18,20,21] This calculation was independently performed by two of the authors of this paper. When discrepancies were noticed, a pharmacist with more than 10 years of experience in pharmacoepidemiology research was consulted.

The outcome variable in this study was the municipal mean DDD per 1,000 inhab. per year of prescribed NSAID, opioids, and analgesics, individually. Independent variables were organized into two groups of items: a) Municipal data: GINI Index,[15] HDI,[22] BF program coverage per 1,000 inhab.,[16] and proportion of rural population.[23] b) Oral health care services data: dental practitioners in the BNHS per 1,000 inhab.,[24] first dental appointment coverage,[24] oral health teams per 1,000 inhab.,[24] and proportion of individual clinical procedures[24] (Table 1).

Statistical analysis

In the first study stage, descriptive statistics including medicines, number of pharmaceutical forms, and prescribed DDD were performed by calculating frequencies, measures of central tendency, and variability. In the second stage, the Classification and Regression Tree (CART)[25] was used to identify factors that best discriminated the outcome variable. CART is a decision tree based on the outcome and a set of independent variables. The tree analyzed in this study was the regression type, as it presented a numerical outcome variable.

The great advantage of CART is the intelligibility of the results, as it allows to understand the structure of the classification performed and to present all the

Table 1. Description of the independent variables.

Variables	Description	Reference year	Source
Municipal data			
GINI index	A measure used to calculate the inequalities on income distribution. Range: 0 to 1- 1 corresponds to maximal inequality.	2010	DATASUS
HDI	A summary measure of three dimensions: income, education, and life expectancy. Range 0 to 1- the closer to 1 the greater human development.	2010	Atlas of Human Development in Brazil
BF program coverage per 1,000 inhab.	**Formula**: (number of families benefited by the BF program X 1,000 inhab.) / population.	2017	Ministry of Citizenship
Proportion of rural population	Percentage of the rural resident population by municipality. **Formula:** (rural population / total population) X 100.	2010	IBGE
Oral health care services data			
Dental practitioners in the BNHS per 1,000 inhab.	The proportion of dental practitioners working in the BNHS per municipality per 1,000 inhab. **Formula:** (number of dental practitioners in the BNHS/ population) X 1.000 inhab.	December 2017	DATASUS
First dental appointment coverage	Evaluation of general health conditions and oral clinical examination for diagnostic purposes and development of a preventive-therapeutic plan. **Formula:** (number of first dental appointments / population) X 100.	2017	DATASUS
Oral health teams per 1,000 inhab.	Multidisciplinary work teams composed by a dental practitioner, dental office assistance, and/ or a dental hygienist. **Formula:** number of oral health teams / (population) X 1.000 inhab.	2017	DATASUS
Proportion of individual clinical procedures	**Formula:** (number of preventive and restorative clinical procedures)/ total number of dental procedures X 100.	2017	DATASUS

BF: Bolsa Família; BNHS: Brazilian National Health System; HDI: Human Development Index; IBGE: Instituto Brasileiro de Geografia e Estatística; inhab: inhabitants.

subdivisions generated. The logic of this technique lies in the fact that trees are built by subdividing groups into subgroups and so on.[25] To the successive divisions of the whole dataset was applied Chi-square Automatic Interaction Detection (CHAID). In the development of CART, some criteria were established. First, each node - the name given to each subset resulting from the application of a division rule - had a minimum of 50 observations to proceed with the subdivisions. Second, each terminal node needed a minimum of 30 observations. Third, the model did not consider subdivisions with a probability of significance (p-value) equal to or greater than 0.05.

Results

Data on dental prescriptions from 375 cities in the state of Minas Gerais, Brazil, in 2017 were analyzed. Of all patients, 41,847 (59.15%) were female (data not tabulated). A total of 145,598 dental prescriptions were issued. NSAID, opioids, and analgesics accounted for 49.10% (n = 71,499). The sum of 752 (1.05%) was excluded from the analysis because the number of pharmaceutical forms and the municipalities where medicines were dispensed were not informed in the database. As a result, 70,747 prescriptions were included in this study: NSAID (n = 39,153; 55.34%), analgesics (n = 31,451; 44.46%), and opioids (n = 143; 0.20%). The highest prescription frequencies were observed for ibuprofen (n = 24,676; 34.88%), metamizole sodium (n = 20,003; 28.27%), and paracetamol (n = 11,437; 16.17%). Prescriptions of morphine, tramadol, tramadol combinations, acetylsalicylic acid, and paracetamol combinations were the least frequent, with 1 prescription for each substance (Table 2). The municipal-level socioeconomic and oral health care service' characteristics of the 375 municipalities are presented in Table 3.

The CART analysis for the municipalities that dispensed NSAID (Figure 1) showed the influence of the variable dental practitioners in BNHS per 1,000 inhab. ($p < 0.001$) on the Root Node ([N0] n = 319;

Table 2. Pain relievers dispensed by dental prescriptions in the Brazilian National Health System in the state of Minas Gerais, 2017.

ATC Code	ATC Name	Frequency	Percentage (%)	Number of units dispensed	Number of DDD
Non-steroidal anti-inflammatory drugs					
M01AB05	Diclofenac	4,16	5.88	72,330.50	36,244
M01AB16	Aceclofenac	41	0.06	474	237
M01AC01	Piroxicam	5	0.01	53	53
M01AC06	Meloxicam	102	0.14	1,066	1,061
M01AE01	Ibuprofen	24,676	34.88	357,369.50	177,703.33
M01AE02	Naproxen	94	0.13	1,491	1,088.50
M01AE03	Ketoprofen	3	0	72	24
M01AX17	Nimesulide	10,072	14.24	109,092.50	57,588.25
Opioids					
N02AA01	Morphine	1	0	90	9
N02AJ06	Codeine and paracetamol	140	0.20	1,528	509.33
N02AJ13	Tramadol and paracetamol	1	0	10	2.50
N02AX02	Tramadol	1	0	20	3.33
Analgesics					
N02BA01	Acetylsalicylic acid	1	0	30	6
N02BB02	Metamizole sodium	20,003	28.27	193,498	50,391.17
N02BB52	Metamizole sodium, combinations excluding psycholeptics	9	0.01	131	15.17
N02BE01	Paracetamol	11,437	16.17	161,846.50	29,283.75
N02BE51	Paracetamol, combinations excluding psycholeptics	1	0	12	1.80
Total		70,747	100	899,114	354,221.13

Table 3. Socioeconomic and oral health services' characteristics from the 375 municipalities in the state of Minas Gerais, 2017.

Variables	Mean	SD	Median
GINI index	0.48	0.05	0.48
HDI	0.67	0.05	0.67
BF program coverage per 1,000 inhab.	77.48	40.14	67.71
Proportion of rural population (%)	31.78	18.85	29.46
Dental practitioners in the BNHS per 1,000 inhab.	0.63	0.47	0.52
First dental appointment coverage (%)	12.57	31.13	7.67
Oral health teams per 1,000 inhab.	0.93	7.35	0.29
Proportion of individual clinical procedures (%)	89.34	10.99	91.13

mean = 91.159 DDD per 1,000 inhab. per year). The influence of this variable divided the cities into two groups: N1 (n = 191; mean = 66.116) and N2 (n =1 28; mean = 128.529). First dental appointment coverage (p = 0.010) subdivided N1 into three subgroups: N3 (n = 50; mean = 32.313), N4 (n = 84; mean = 58.594), and N5 (n = 57; mean = 106.853). The subdivision of N2 by BF program coverage per 1,000 inhab. (p = 0.022) originated N6 (n = 80; mean = 161.209) and N7 (n = 48; mean = 74.062). The interaction of number of oral health teams per 1,000 inhab. (p = 0.022) and the proportion of rural population (p = 0.014) with N4 and N6, respectively, produced the terminal nodes N8 (n = 52; mean = 38.159), N9 (n = 32; mean = 91.799), N10 (n = 35; mean = 92.260), and N11 (n = 45; mean = 214.836).

Mean opioid prescription per city per 1,000 inhab. was 5.414 DDD (SD =1 0.759). The small number of municipalities that dispensed opioids (n= 20) impaired the use of CART. Among the 357 municipalities that dispensed analgesics, first dental appointment coverage (p = 0.002) divided N0 into 2 subgroups: N1 (n = 107; mean = 12.948) and N2 (n = 250; mean = 28.557). The interaction of the variable BF program coverage per 1,000 inhab. (p = 0.012) with the cities in N1 originated the terminal nodes N3 (n = 57; mean = 6.947) and N4 (n = 50; mean = 19.788) (Figure 2).

Discussion

At city-level, there was an association between social and health care services variables with mean DDD per 1,000 inhab. per year suggesting the influence of social disparities. Based on the reviewed literature, this is the first population-based study developed in Brazil on prescribing patterns of dental practitioners in BNHS.

Together, ibuprofen, metamizole, and paracetamol accounted for the majority of all dental pain prescriptions in the state of Minas Gerais in 2017. In a nationwide survey, paracetamol, metamizole, and ibuprofen were the 7th, 8th, and 12th medicines most used by the Brazilian population.[26] The high prescription frequency of such chemicals is related to the fact that they are included in the national list of essential medicines. They are also easily available in health units throughout Brazil.[27] In Australia[6,8] and Germany,[7] ibuprofen was also the most prescribed NSAID, probably because of its efficacy in a large range of painful inflammatory conditions and its price.[28]

In 2016, dental prescriptions of NSAID and analgesics in Australia reached 15.60 DDD per 1,000 inhab. per year.[8] In our study, there were higher prescription means for NSAID. These different findings may be explained by the characteristics and comprehensiveness of public health care systems in both countries, kinds of medicines subsidized by governments (either free of charge or under copayment) and the variety of chemical substances included in each country's list of essential medicines, and national prescribing guidelines and oral health conditions in Brazil. In a previous study,[11] DDD of opioids per 1,000 inhab. per year in the state of Minas Gerais was higher than our findings. This discrepancy is related to methodological differences. While in this study we focused on medicines dispensed in BNHS facilities, Lino et al.[11] assessed medicines dispensed in private drugstores. Opioids are strong analgesics but have significant side effects, thus they should be reserved to manage severe pain only.[2] Procedures that might induce these levels of pain, such as osseointegrated dental implants, are performed

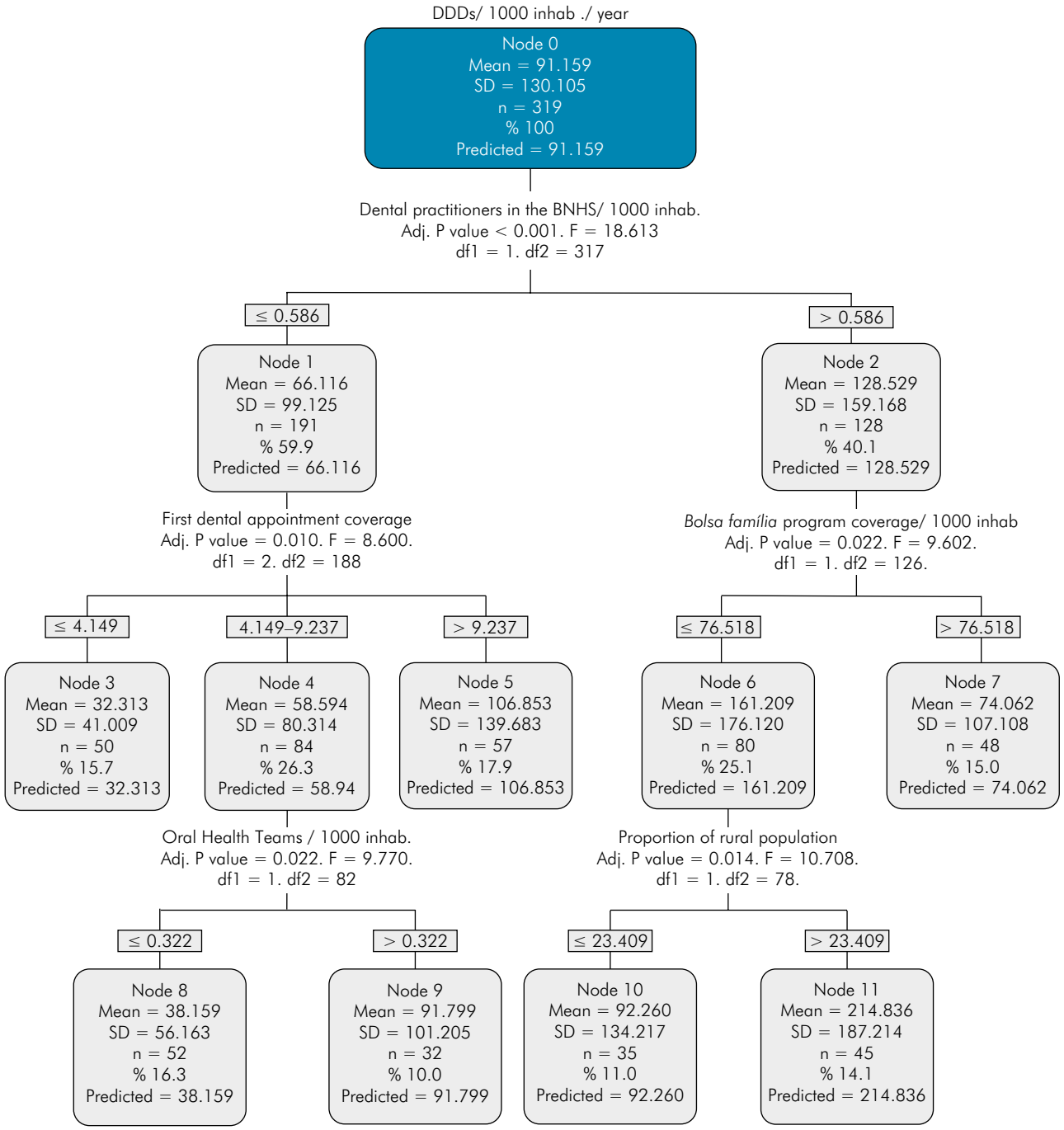

Figure 1. CART analysis for non-steroidal anti-inflammatory drugs.

rarely by the BNHS.[29] This could be a reason for the low DDD of opioids found in this research.

The process of prescribing, dispensing, and using medicines is closely related to the drugs availability in health services. The greater availability of NSAID and analgesics was positively associated with the number of professionals prescribing them in Brazilian health units.[27] Although there is not a direct relationship, cities with higher number of prescribing professionals may present higher rates of medicines' availability and, consequently, higher rates of prescription and consumption. Taking into account

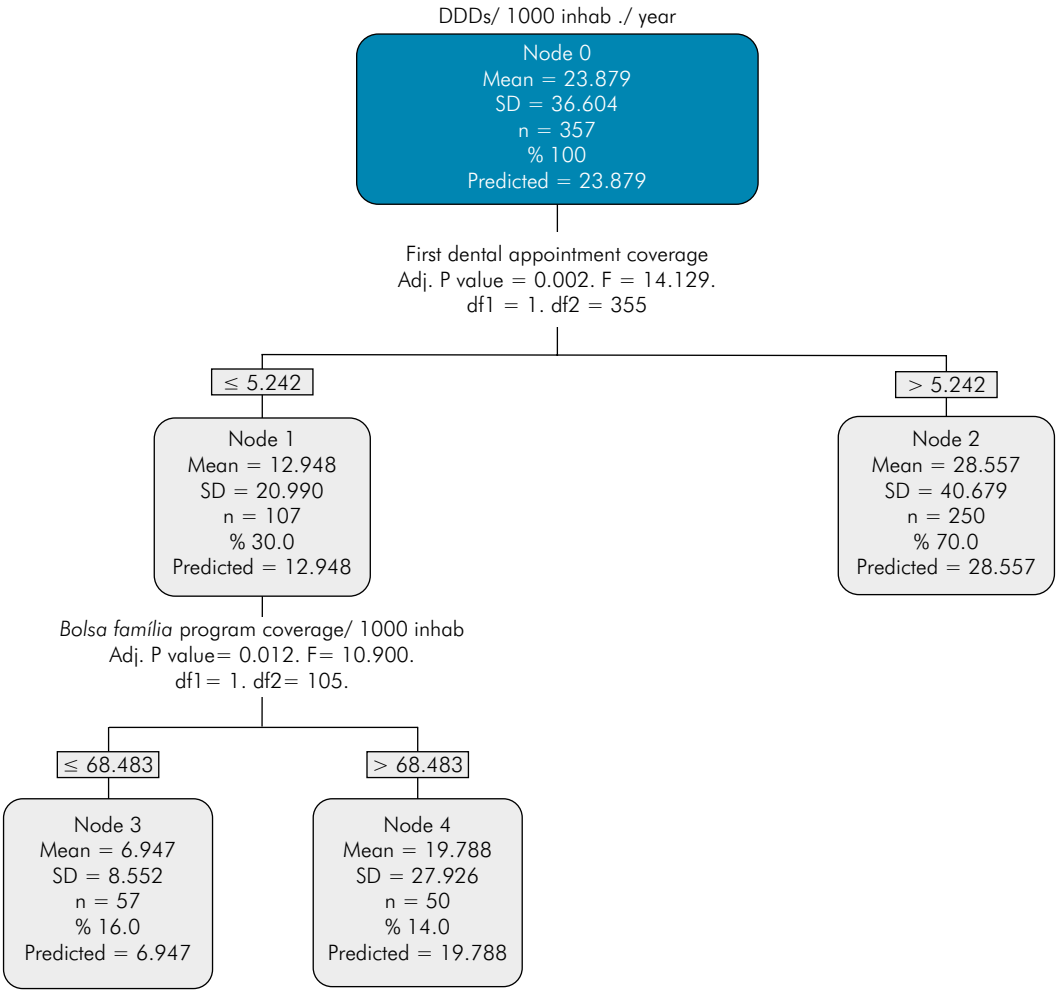

Figure 2. CART analysis for analgesics.

the cross-sectional design of the study, the direction of the relationship is not easy to be determined, and an inverse relationship could exist, *i.e.* higher rates of medicines' availability could stimulate professionals to prescribe them more often.

The development of oral health policies increased the number of public oral health teams in BNHS in the past decades.[30] As a consequence, both population access to treatment and the number of oral procedures grew considerably.[30] The first dental appointment coverage indicates population access to dental services.[31] It is expected that oral health teams in cities with higher service access rates perform more clinical procedures, including surgeries, endodontics, and dental trauma management. These procedures might induce inflammatory response and pain and the consequent prescription of NSAID and analgesics.

There is a close relationship between inequalities and the burden of oral diseases, poverty, and access to and utilization of oral health care services.[32] In this matter, conditional cash transfer programs such as BF tackle social disparities and improve some health outcomes.[33,34] BF program directly transfers income to families living in poverty and extreme poverty under compliance with some conditions, such as children's school enrollment and regular health checkups.[34] BF was designed for vulnerable people, therefore there is a proxy between the number of its beneficiaries and the proportion of poor people in each city.[35] In this study, there was a relationship between BF coverage and DDD per 1,000 inhab. for NSAID and

analgesics. NSAID are known to be more expensive than analgesics.[36] Health managers in poor cities may tend to purchase more of the latter, and consequently NSAID are less available for prescription by dental practitioners. It may explain the lower NSAID mean DDD and the higher analgesic mean DDD in cities with higher BF coverage. However, there are very few studies relating BF program and oral health outcomes in the general population and these results must be interpreted with caution.

A higher NSAID mean DDD per 1,000 inhab. per year was observed in cities with higher proportions of rural population. Evidence suggests there is a link between living in rural areas and poorer access to quality health care services.[37] Also, dental care is likely to be delayed by people from rural communities.[37,38] As a consequence, oral diseases are diagnosed in advanced stages and increase the demand for dental extractions and emergency services. The delay in receiving dental care and the search for emergency dental treatment explain higher prescription rates in cities with higher proportion of rural population.

This study has some limitations that should be addressed. The cross-sectional methodology has low analytical power. Data for the analyzed variables were collected from different datasets and reproducibility could not be assessed. Inferences in individual level also could not be achieved. Nevertheless, ecological studies allow the analysis of the impact of contextual variables on the outcome and this approach can be useful, especially to evaluate health care policies.

Conclusions

Dentists' prescription of NSAID and analgesics were associated with municipal characteristics, such as socioeconomic and organization of oral health care services.

Acknowledgments

We thank *Secretaria de Estado de Saúde* for providing access to the database. Mauro Henrique Nogueira Guimaraes de Abreu is fellow of CNPq. We would like also to thank *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior* (CAPES) (financial number 001).

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