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Pharmacoeconomic Analysis of the Use of Omeprazole by Elderly Patients in One of the Primary Healthcare Centers in Brazil

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Abstract

Omeprazole is the most prescribed proton pump inhibitor in Brazil and is indicated for the treatment of diseases caused by gastroesophageal reflux, peptic ulcer, erosive esophagitis, eradication of Helicobacter pylori, Zollinger-Ellison syndrome, gastrinomas, gastritis, and hypersecretory disorders, as well as peptic ulcer prevention. The indiscriminate and unnecessary use, mainly by the elderly, is an important public health issue to be addressed. Despite the existence of indiscriminate use of omeprazole being known, there is a need to verify how this medication is prescribed in the context of the Unified Health System (UHS) in Brazil. In addition, it is believed that studies that aim to analyze the prescription of omeprazole in a pharmacoeconomic way can contribute to the review or implementation of guidelines and protocols involving the use of this drug. The objective of this study was to characterize and perform a pharmacoeconomic analysis of the use of omeprazole in a Primary Healthcare Centers (PHC) in Minas Gerais, Brazil. This is a descriptive study analyzing the prescriptions of 41 elderly patients treated in the period of April/May 2018 and the following variables were identified: age, sex, dose, indication, endoscopy, other medications in use, and cost of treatment. In the pharmacoeconomic analysis, the average cost of the amount of omeprazole prescribed per patient was calculated and whether or not endoscopy was performed was considered. In the studied population, 29 (70.3%) were female with a median age: 69 years. Only in 4 medical records (9.8%) was there indication for use, and 18 (43.9%) patients had been using omeprazole for more than two years and 7 (17.1%) for more than five years. Only 3 (7.3%) patients underwent endoscopy, and 371 months-worth of omeprazole were used, totaling a financial value of R$35,657.23. The findings suggest long-term prescriptions and no record of their indication on medical records. The cost related to prescriptions could be optimized by performing endoscopy and discontinuing its use when no indication is found.

Keywords: Elderly. Omeprazole. Prescription. Medication Errors. Pharmacoeconomics.

INTRODUCTION

Population aging is a worldwide phenomenon characterized by reduced fertility rates, decreased mortality, and increased life expectancy, which is also observed in the Brazilian population[1,2]. Research indicates that the aging of the population is related to a greater number of diseases and disabilities, and consequently, increased use of healthcare services[3,4,5]. Treatments aimed at patients with chronic diseases last for years and require constant care, such as the administration of medications for a continuous period and periodic examinations[3]. The use of medication by the elderly requires

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pecific care, mainly due to the greater vulnerability of these patients to more serious damage resulting from the incorrect use of these products[6].

Studies and protocols have described the uses for Proton pump inhibitors (PPIs) highlighting: the treatment of gastroesophageal reflux disease; peptic ulcer, Helicobacter pylori eradication; Zollinger-Ellison syndrome; gastrinomas; esophagitis; gastritis; as well as preventing peptic ulcer disease in patients using non-steroidal anti-inflammatory agents (NSAIDs)[7]. This is a class of medication frequently used by the elderly that can cause numerous damages to health when used incorrectly[8,9]. There is a low incidence of adverse effects with short-term treatments using PPIs; however, the safety and lack of long-term toxicity have not been properly documented. Therefore, the unnecessary use of this class of drugs should be avoided[7].

Although some patients have a medical indication for the chronic use of PPIs, the period of treatment with these drugs should not exceed eight weeks[8]. Prolonged use of PPIs is related to several adverse reactions, such as: kidney disease, dementia, fracture and bone complications, acute myocardial infarction, alteration of the intestinal microbiota, spontaneous bacterial peritonitis, *Clostridium difficile* infection, pneumonia, nutritional deficiencies, and gastrointestinal cancer, among others[8,9,10,11,12,13,14, 15,16,17].

Omeprazole is the most prescribed PPI drug in Brazil and is among the five most prescribed drugs for the elderly[18]. Furthermore, it is part of the National List of Essential Medicines in Brazil (RENAME), making it one of the components of the List of Essential Medicines in Municipalities (REMUME)[10]. The deliberate use of PPIs, through self-medication, is still a major problem in Brazil. Added to this fact is the lack of knowledge, by most health professionals, of the potential consequences related to indiscriminate use and for long periods of time of PPIs[19].

Digestive endoscopy is the method of choice for the diagnosis of lesions caused by gastroesophageal reflux, characterizing the presence of complications of gastroesophageal reflux disease (Barrett's esophagus, stenosis, and esophageal ulcerations)[21].

In Brazil, digestive endoscopy is indicated for patients over 40 years of age and who have manifestations such as: dysphagia, weight loss, odynophagia, anemia, digestive hemorrhage, family history of cancer, nausea and vomiting, high-intensity symptoms, or nocturnal events[16]. In addition, previous history of gastric ulcer or gastric surgery, as well as the use of non-steroidal anti-inflammatory drugs suggest the indication for the performance of the endoscopic examination[17]. This test is the method of choice for diagnosing lesions caused by gastroesophageal reflux, allowing you to assess the severity of the esophagitis and perform biopsies where and when necessary. Therefore, it should be a priority in the evaluation of the patient.

With this in mind, it is increasingly necessary to install institutional protocols that standardize prescriptions for omeprazole, associated with carrying out pharmacoeconomic studies that analyze the costs of drug therapy for the health system and the population.

Although the existence of indiscriminate use of omeprazole is known, there is a need to identify how this drug is prescribed in the context of the Unified Health System (UHS) in Brazil. In addition, it is believed that studies that aim to analyze the prescription of omeprazole in a pharmacoeconomic way can contribute to the review or implementation of guidelines and protocols involving the use of this drug.

The present study aimed to characterize

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and carry out a pharmacoeconomic analysis of the prescription of omeprazole for the elderly in a Primary Healthcare Center (PHC) in Brazil.

MATERIALS AND METHODS

The present work is a pharmacoeconomic study carried out in a neighborhood PHC in the city of Congonhas, Minas Gerais, composed of a professional team of community health agents, health assistants, nurse technicians, a nurse, a doctor, a pharmacist, a physiotherapist, a social worker, a physical education instructor, a nutritionist, and an occupational therapist.

The study included patients over 60 years of age, considered elderly herein, of both sexes, attended at the PHC from April to May 2018, with a file in the medical records indicating the use of omeprazole for a period of up to six months before the data collection. In the city studied, 20mg of omeprazole the form of a capsule for oral use is standard. Patients whose prescriptions were not provided by physicians from the PHC under study were excluded from the study. The occurrence of death during the study of a patient who was in accordance with the inclusion criteria was considered to be a study sample loss. Identification of prescriptions for omeprazole occurred by consulting medical records. The following variables were identified: age, sex, prescribed dose, indication of time of use, specification of the reason for using the medication, endoscopy, and other medications in use. The other medications in use were classified according to the Anatomical Therapeutic Chemical (ATC) classification[20].

Data were recorded in a *Microsoft Excel®* spreadsheet and then a descriptive statistical analysis was performed using the MINITAB 18 program. To carry out the pharmacoeconomic analysis, the average cost of using omeprazole by patients was calculated, considering the prescribed dose and duration of use. To identify the cost of one omeprazole unit, the price list of medicines for public purchases by the Drug Market Regulation Chamber (DMRC) was considered[22]. As the drug dispensed at the Neighborhood PHC during the study period is similar, the discount generated for public purchases of similar drugs was added to the value identified in the DMRC, corresponding to 36%.

The project was approved by the Ethics Committee linked to the Faculty of Medical Sciences of Minas Gerais - FCM-MG through opinion CAAE 2.601.724, dated April 16, 2018.

RESULTS

In the analyzed period, 68 patients used omeprazole, of which 41 were included in the study, 25 were excluded, and 2 were included in the loss criteria. Among the 41 patients participating in the study, 29 (70.3%) were female, with a median age of 69 years old.

Twenty -seven (93.1%) female patients and 10 (83.3%) male patients did not specify the use of omeprazole in their medical records.

Of the 41 patients using omeprazole, 18 (43.9%) had used the drug for more than two years, of which 4 (9.8%) had used it for more than five years, as specified below in Table 1.

Among the total number of patients, 6

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(14.6%) used only omeprazole, and the others used an average of 3.3 (SD-standard deviation: 2.4) additional medications, as specified below in Table 2.

During the analysis of the medical records, it was detected that only 3 patients had undergone the endoscopy exam, and in none of the cases were the results of the exam described in the medical records. Below, Table 3 provides the description of the variables: specification of use, time of use greater or less than two years, performance of endoscopy and continuous use of more than five medications, according to gender.

Specifications for the use of omeprazole were found in 4 (9.8%) charts analyzed, which were for the following indications: epigastric pain, treatment of Helicobacter pylori, and endoscopic gastritis (in two charts).

Based on the price list of medicines for public procurement by the Drug Market Regulation Chamber (DMRC), the cost of omeprazole per pack with 14 capsules in the city of Congonhas was R$ 18.64, which, plus the discount of 36% for similar drugs totaled R$ 11.92, with each capsule having a final cost of R$ 0.85. The total cost over time of use of omeprazole is described below in Table 4.

Table 1 – Specification of the time of use of omeprazole in 41 patients at the Neighborhood PHC – Minas Gerais, April and May 2018.

Time of Use (years)	Female	Male	Total
Less than one year	1 (2.4%)	1 (2.4%)	2 (4.9%)
Between one and two years	14 (34.1%)	7 (17.1%)	21 (51.2%)
Between three and five years	10 (24.4%)	4 (9.8%)	14 (34.1%)
Over five years	4 (9.8%)	0 (0.0%)	4 (9.8%)
TOTAL	29 (70.7%)	12 (29.3)	41 (100%)

Table 2 - Specification of drugs in use according to ATC classification (2018) in 41 patients from the Neighborhood PHC - Minas Gerais, April and May 2018.

Medication	ATC Classification	Frequency of Use (n/%)
Losartan	Angiotensin II antagonist	26 (74.3%)
Acetylsalicylic acid	Antithrombotic agent	13 (37.1%)
hydrochlorothiazide	Thiazide diuretic	12 (34.3%)
Metformin	Blood glucose reducer	11 (31.4%)
Glibenclamide	Blood glucose reducer	9 (25.7%)
Furosemide	Diuretic	7 (20.0%)
Simvastatin	Lipid modifying agent	7 (20.0%)
Captopril	ACE inhibitor	4 (11.4%)
Cilostazol	Antithrombotic agent	3 (8.6%)
Digoxin	Cardiac glycoside	2 (5.7%)
Spironolactone	Potassium sparing agent	2 (5.7%)
Others *		18 (52.2%)

* others: 18 drugs cited only once: amiodarone – class I and III antiarrhythmic; atorvastatin – lipid modifying agent; carvedilol – beta blocking agent; citalopram – antidepressant; cholecalciferol – vitamin A and D; diazepam – anxiolytic; diosmin/hesperidin – hair stabilizing agents; enalapril – ACE inhibitor; glimepiride – blood glucose reducer; insulin – insulin and analogues; levodopa – dopaminergic agent; memantine – anti-dementia; methyldopa – centrally acting antiadrenergic agent; nifedipine – elective calcium channel blocker with mainly vascular effects; propranolol – beta blocking agent; quetiapine – antipsychotic; rosuvastatin – lipid modifying agent; sertraline – antidepressant.

ATC: Anatomical Therapeutic Chemical, ACE: Angiotensin Converting Enzyme; n: number

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Table 3 - Description of variables according to gender in 41 patients from Neighborhood PHC - Minas Gerais, April and May 2018.

Variable	Female (n=29)		Male (n=12)	
	Yes	No	Yes	No
Indication of Use Specification	2 (6.9%)	27 (93.1%)	2 (16.7%)	10 (83.3%)
Usage time greater than two years	14 (48.3%)	15 (51.7%)	4 (33.3%)	8 (66.7%)
Use time less than two years	2 (6.9%)	26 (89.7%)	1 (8.3%)	11 (91.7%)
Performed endoscopy	7 (24.1%)	22 (75.9%)	3 (25.0%)	9 (75.0%)
Continuous use of more than five medications	8 (27.6%)	21 (72.4%)	2 (16.7%)	10 (83.3%)

Table 4 - Acquisition cost (in reais) of omeprazole for the city of Congonhas, Minas Gerais, 2018.

Number of patients	Time of Use (months)	Total expense (R$)
2	2	102.17
8	12	2,452.11
13	24	7,969.37
5	33	4,597.71
6	48	7,356.34
3	60	4,597.14
3	72	5,517.25
1	120	3,065.14
Total	371	35,657.23

DISCUSSION

The results showed that 95.1% of the patients used omeprazole for more than one year, this period of treatment was regulated only to promote the healing of gastric and/or duodenal ulcers and to treat gastroesophageal reflux disease (GERD), including erosive esophagitis[19]. None of the 41 medical records analyzed showed a record of one of the causes cited as a justification for the use of omeprazole, suggesting that the elderly included in the study appeared to take the drug for a longer period than was actually necessary. It is understood that patients using the drug for more than one year may be unnecessarily exposed to undesirable effects.

It is noteworthy that the concern about the use of omeprazole in the elderly population subgroup is greater due to a probable lower elimination of the drug, with a consequent increase in bioavailability, which can potentiate the occurrence of undesirable effects[10]. In the elderly, which represent more than 50% of patients who regularly take the drug, about 40 to 60% have no indication for prolonged use[12].

In relation to the other drugs in use, according to Pimenta (2016), the concomitant use of omeprazole can cause an increase in the absorption of antihypertensive calcium channel blockers (such as nifedipine) and digitalis (such as digoxin), which are drugs used by some se-

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niors in this study. Omeprazole, by causing acid suppression, can also contribute to a decrease in the absorption of some drugs, such as ketoconazole and itraconazole, reducing their effectiveness. Thus, practices that promote shorter use of omeprazole by elderly people who have no indication for use would also contribute to the prevention of drug interactions and, consequently, would provide greater safety for patients.

Of the total number of medical records evaluated, only three of them (7.7%) had reported an endoscopy. According to recommendations of the endoscopy request protocol of the municipality under study, the patient starts using omeprazole after a specific complaint, remaining in use for two to three months. If there is no improvement, an endoscopy is indicated to evaluate the use of this medication. By identifying the number of patients using omeprazole for a period of more than three months and the number of endoscopies performed, it is possible to identify the difficulties of the study site in recommending the performance of this examination within the recommended period.

In Brazil, digestive endoscopy should be performed in patients aged over 40 years old and with alarming manifestations (dysphagia, weight loss, anemia, digestive hemorrhage, family history of cancer, nausea and vomiting, symptoms of great intensity or nocturnal events)[21]. In addition, a previous history of gastric ulcer or gastric surgery and the use of NSAIDs suggest endoscopic examination. Digestive endoscopy is the method of choice for the diagnosis of lesions caused by gastroesophageal reflux, characterizing the presence of complications of gastroesophageal reflux disease (Barrett's esophagus, stenosis, and esophageal ulcerations)[21].

For the city, an endoscopy has a cost of R$ 100.00 per patient. If all patients in the study had undergone the test, the total cost would have been R$ 4,100.00, an amount even lower than that spent by patients with continuous use of the drug for more than three months (R$ 35,657.23). The amount spent on dispensing the drug would be enough to carry out the endoscopy exam in about 350 patients. Endoscopy could contribute to the safer use of the drug, in addition to avoiding unnecessary health expenses. It is relevant to consider that, during the period in which this study was carried out, the dollar exchange rate was around R$ 3.8750[24].

The medical record is defined as the single document, consisting of a set of information generated based on facts, events, and situations about a patient's health and the care provided to them of a legal, confidential, and scientific nature, which enables communication between members of the multidisciplinary team and the continuity of care provided to the individual. Despite this importance, in Brazil, the literature has been pointing to a poor quality of health records[23]. As previously mentioned, during data collection, only three medical records were observed containing the specified indication for the use of omeprazole. The other medical records (38; 92.7%) of all those analyzed did not contain a specification of use for this medication, nor reports of requests for tests or complaints referring to the use of omeprazole. The absence of this information makes it even difficult for other professionals to recognize the real clinical needs of each patient.

It is essential that omeprazole be prescribed only when there is a correct indication for its use and for a determined period of time, contrary to what was observed during this study, in which elderly patients used the drug for up to 10 years in a row, without having been at least subjected to a specific assessment for such use. The rational use, especially related to omeprazole, can generate great savings for the city, making it possible to carry out investments in other areas of demand that stimulate the health of elderly patients in the city of Congonhas, Minas Gerais. It is noteworthy to point out that there was no shortage of 20 mg omeprazole, the standard dose in the city during the study period.

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As limitations of the present study, it was impossible to identify the occurrence of undesirable effects related to the use of omeprazole in patients who used the drug in the long term, in addition to the impossibility of validating the use of the drug by measuring adherence and persistence to the treatment. The data found in this study are limited to a specific public and cannot be extrapolated to patients other than the elderly. Furthermore, a specific reality of the Neighborhood PHC was identified, and it is possible that other health centers may present a different profile in relation to the use of omeprazole, varying due to the prescribing physician and the patients' complaints.

CONCLUSION

Most of the patients in the study (93%) had no indication for the use of omeprazole recorded in their medical records, which points to the need to strengthen reporting practices. The findings suggest the use of omeprazole in the long term without formalizing the reason for indication in the medical records. The pharmacoeconomic analysis showed an annual cost with the prolonged use of omeprazole corresponding to R$ 35,657.23 which could be optimized with the performance of endoscopy exams and suspension of the use of the drug in the long term in patients without indication.

Author statement CRediT

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All authors have read and agreed to the published version of the manuscript.

REFERENCES

1. Closs VE, Schwanke CH. A evolução do índice de envelhecimento no Brasil, nas suas regiões e unidades federativas no período de 1970 a 2010. Rev Bras Geriatr Gerontol. 2012;15(3):443-458. doi: 10.1590/S1809-98232012000300006.
2. Simões CCS. Relações entre alterações históricas na dinâmica demográfica brasileira e os impactos decorrentes do processo de envelhecimento da população. Rio de Janeiro: IBGE; Coordenação de População e Indicadores Sociais. 2016. Disponível em: https://biblioteca.ibge.gov.br/visualizacao/livros/liv98579.pdf .
3. Veras R. Population aging today: demands, challenges and innovations. Rev Saude Publica. 2009 maio;25(3):548-554. doi: 10.1590/S0034-89102009005000025.
4. Brito MC, Freitas CA, Mesquita KO, Lima GK. Envelhecimento Populacional e os Desafios para a Saúde Pública: Análise da Produção Científica. Rev Kairos. 2013;16(2):161-178. doi: 10.23925/2176-901X.2013v16i2p161-178.
5. Kernkamp CL, Costa CK, Massuda EM, Silva ES, Yamaguchi UM, Bernuci MP. Perfil de morbidade e gastos hospitalares com idosos no Paraná, Brasil, entre 2008 e 2012. Cad Saude Publica. 2016;32(7). doi: 10.1590/0102-311X00044115.
6. Marin MJS, Rodrigues LCR, Druzian, S, Cecílio LCO. Diagnósticos de enfermagem de idosos que utilizam múltiplos medicamentos. Rev Esc Enferm USP. 2010;44(1):47-52. doi: 10.1590/S0080-62342010000100007.
7. Braga MP, Silva CB, Adams AI. Inibidores da bomba de prótons: revisão e análise farmacoeconômica. Saúde (Santa Maria, Rio Grande do Sul, Brazil). 2011;37(2):19-32. doi: 10.5902/223658342963.
8. Oliveira MG, Amorim WW, Oliveira CR, Coqueiro HL, Gusmão LC, Passos LC. Consenso brasileiro de medicamentos potencialmente inapropriados para idosos. Geriatr Gerontol Aging. 2016;10(4):168-181. doi: 10.5327/Z2447-211520161600054.
9. Yang YX, Lewis JD, Epstein S, Metz DC. Long-term Proton Pump Inhibitor Therapy and Risk of Hip Fracture. JAMA. 2006;296(24):2947-

REVISTA O MUNDO DA SAÚDE

DOI: 10.15343/0104-7809.202347e1452020I

2953. doi: 10.1001/jama.296.24.2947.
10. Pimenta LR, Soares RS, Castro PF, Freitas JG, Nielson SE. Uso indiscriminado de omeprazol em idosos e a importância da atenção farmacêutica. Rev Universo. 2016;1(3):303-318. Disponível em: http://revista.universo.edu.br/index.php?journal=3GOIANIA4&page=article&op=view&path%5B%5D=3113.
11. Freedberg DE, Kim LS, Yang YX. The risk and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from The American Gastroenterological Association. Gastroenterology. 2017;154(4):706-715. doi:10.1053/j.gastro.2017.01.031
12. Linsky A, Gupta K, Lawler EV, Fonda JR, Hermos JA. Proton Pump Inhibitors and Risk for Recurrent Clostridium difficile Infection. Arch Intern Med. 2010;170(9):772-778. doi: 10.1001/archinternmed.2010.73
13. Yanagihara GR, Paiva AG, Pacheco Neto M, Torres LH, Shimano AC, Louzada MJQ, Annoni R, Penoni ACO. Efeitos da administração em longo prazo do omeprazol sobre a densidade mineral óssea e as propriedades mecânicas do osso. Rev Bras Ortop (Sao Paulo). 2015;50(2):232–238. doi: 10.1016/j.rbo.2014.05.012
14. Morschel CF, Mafra D, Eduardo JCC. Inibidores da bomba de prótons e sua relação com a doença renal. J Bras Nefrol. 2018;40(3):301-306. doi: 10.1590/2175-8239-jbn-2018-0021.
15. Kuller LH. Do proton pump Inhibitors Increase the risk of dementia? JAMA neurol. 2016;73(4):379-381. doi: 10.1001/jamaneurol.2015.4931
16. Filho JPPM, Hashimoto CL. II Consenso Brasileiro da Doença do Refluxo Gastroesofágico. Departamento de Gastroenterologia da Faculdade de Medicina da Universidade de São Paulo. 2003: 43-59. Disponível em: http://universidadefbg.com.br/arq/consensos/u3_r1.pdf
17. Forgacs I, Fox M. Clinical review: Gastrooesophageal reflux disease. BMJ 2006; 332:88-93. doi: 10.1136/bmj.332.7533.88
18. Moraes EM, Reis AMM, Moraes FL. Manual de terapêutica segura no idoso. Belo Horizonte: Folium, 2019:362-365. Disponível em: https://www.ivcf20.com.br/produto/78/MANUAL-DE-TERAPEUTICA-SEGURA-NO-IDOSO.
19. Lima APV, Neto Filho MA. Efeitos em longo prazo de inibidores bomba de prótons. Braz J Surg Clin Res. 2014;5(3):45-49. Disponível em: https://www.mastereditora.com.br/periodico/20140301_1352032.pdf
20. ANVISA (Agência Nacional de Vigilância Sanitária). Índice ATC. Disponível em: http://www.anvisa.gov.br/datavisa/Substancia/ATC.htm. Organização Mundial de Saúde (OMS). Índice ATC / DDD 2020. [Acessado 2018 ago 25]. Disponível em: https://www.whocc.no/atc_ddd_index
21. Psendziuk C, Nuñez MR, Nicoleit AR, Rodrigues DF, Pereira SW, Galvani GC. Prevalência de sintomas de doença do refluxo gastroesofágico em pacientes com indicação de endoscopia digestiva alta. ACM. Arquivos catarinenses de medicina. 2010;39(1):62-69. doi: http://www.acm.org.br/acm/revista/pdf/artigos/787.pdf
22. ANVISA (Agência Nacional de Vigilância Sanitária). Agência Nacional de Vigilância Sanitária (ANVISA). Listas de preços de medicamentos. [Acessado 2018 ago 25]. Disponível em: http://portal.anvisa.gov.br/cmed.
23. Vasconcellos MM, Gribel EB, Moraes IHS. Registros em saúde: avaliação da qualidade do prontuário do paciente na atenção básica. Cad Saude Publica. 2008;24(1):173-182. doi: 10.1590/S0102-311X2008001300021.
24. BCB (Banco Central do Brasil). Cotação do dólar. [Acessado 2021 mar 07]. Disponível em: https://www.bcb.gov.br/estabilidadefinanceira/historicocotacoes.

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