

Antimicrobial distribution and costs in primary care

Distribuição e custo de antimicrobianos na Atenção Primária
Distribución y costo de antimicrobianos en la Atención Primaria

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Keywords

Anti-infective agents; Good distribution practices;
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Descritores

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Descriptores

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Abstract

Objective: To analyze antimicrobial distribution and costs in primary care of a capital city in the Northeast region of Brazil.

Methods: Cross-sectional, analytical study, developed in the city of Teresina, in the state of Piauí, Brazil. Data cover the period from June 2015 to July 2016. Descriptive statistics and the Kruskal-Wallis test were calculated to compare the medians of the independent data distributions.

Results: A total of 1,651,516 antimicrobials were distributed in 15 different types, with amoxicillin (500mg) being the most distributed (75%) in psychosocial care centers, and in the basic health units (47%). The total cost for the period was 98,705.00 BRL. There were no statistically significant differences among the costs medians in each zone of the studied municipality.

Conclusion: These drugs are irregularly distributed among the units, according to the demand. The supply does not follow a specific protocol, and a possible increase or reduction in demand is not investigated.

Resumo

Objetivo: Analisar a distribuição e custos de antimicrobianos na Atenção Primária de uma capital da Região Nordeste do Brasil.

Método: Estudo transversal, analítico, desenvolvido em Teresina, Piauí, Brasil. Os dados contemplam o período de junho de 2015 a julho de 2016. Calculou-se estatísticas descritivas e o Teste de Kruskal-Wallis para comparar as medianas das distribuições de dados independentes.

Resultados: Foram distribuídos 1.651.516 antimicrobianos de 15 tipos diferentes dos quais a amoxicilina (500mg) foi o mais distribuído (75%) nos Centros de Atenção Psicossocial e nas Unidades Básicas de Saúde (47%). O custo total no período foi de 98.705,00 reais. Não houve diferenças estatisticamente significante entre as medianas dos custos em cada zona do município estudado.

Conclusão: A distribuição desses medicamentos é realizada de forma irregular entre as unidades, de acordo com a demanda. O fornecimento não segue protocolo específico, e não se investiga um possível aumento na demanda ou redução.

Resumen

Objetivo: Analizar la distribución y costos de antimicrobianos en Atención Primaria de una capital del Noreste de Brasil.

Método: Estudio transversal, analítico, desarrollado en Teresina, Piauí, Brasil. Datos obtenidos entre junio de 2015 y julio de 2016. Se aplicó estadística descriptiva y el Test de Kruskal-Wallis para comparar las medianas de las distribuciones de datos independientes.

Resultados: Fueron distribuidos 1.651.516 antimicrobianos de 15 tipos diferentes, de los cuales la amoxicilina (500mg) fue el más entregado (75%) en Centros de Atención Psicossocial y en Unidades Básicas de Salud (47%). El costo total durante el período fue de 98.705,00 Reales. No hubo diferencia estadísticamente significativa entre las medianas de costos en cada zona del municipio estudiado.

Conclusión: La distribución de estos medicamentos se realiza de manera irregular entre las unidades, de acuerdo a la demanda. La provisión no cumple protocolos específicos, y no se investiga un posible aumento o reducción de demanda.

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Introduction

Antimicrobials are one of the most frequently distributed and used drugs in health services, accounting for almost a third of medical prescriptions. They are considered one of the most remarkable drugs to impact not only on the patient being treated, but on the whole ecosystem in which he/she is inserted,⁽¹⁾ because these drugs irrational use has contributed significantly to antimicrobial resistance (AMR), a global threat to public health.

The AMR phenomenon is complex, but it is a natural biological process that arose with the use of antibiotics in the treatment of infections, and was enhanced with the irrational use of antimicrobials. It is understood as the ability of microorganisms to multiply even in the presence of high concentrations of antimicrobials,^(2,3) and is related to the use of this medicine in all environments, either at home, in (primary, secondary or tertiary) healthcare settings, or in other sectors of activities, such as agriculture.

Data from a multicenter study in 28 European countries point to an association between increased antimicrobial resistance and managerial quality of the government, suggesting that countries where the quality control of this class of drugs in humans and in other animals is poor show increased rates of microbial resistance and dissemination.⁽⁴⁾

Although hospital care is heavily responsible for increased AMR, the literature provides evidence that primary care can lead to an irrational distribution of antimicrobials, increasing costs and contributing to increased resistance. In addition, due to the large number of units that provide outpatient care in Brazil, it is believed that antimicrobial use can be compared to that of hospitals. For instance, a study carried out in the state of Rio de Janeiro, Brazil, found that most antimicrobial costs came from primary rather than hospital care.⁽⁵⁾

The non-hospital environment in Brazil does not have a specific surveillance system on the rational use of drugs, including antimicrobials, which limits monitoring and controlling this drug, and favors its empirically exacerbated use. In addition, an irregular and non-directed distribution can lead to AMR and potentiate unnecessary expenses. Thus,

the analysis of the distribution and costs related to the use of antimicrobials in primary care becomes pertinent because it characterizes its representativeness in the context explored.

Therefore, the objective of this study was to analyze the distribution and costs of antimicrobials used in primary care in a capital city of the Northeast region of Brazil.

Methods

This is a cross-sectional, analytical, retrospective collection study carried out in the city of Teresina, capital city of the state of Piauí. The database used was that of the essential medicines distribution center of the Pharmaceutical Assistance Management, linked to the Municipal Health Foundation (FMS) of Teresina, which is in charge of the Pharmaceutical Assistance Cycle, including planning, receiving, storing and distribution of medicines, medical-hospital supplies, and medical-dental products to basic health units (UBS) and psychosocial care centers (CAPS) under the responsibility of FMS.⁽⁶⁾

In the municipality, UBSs are subdivided into zones, namely: the East/Southeast Zone, which comprises 36 UBSs; the North Zone, with 25 units; and the Southern Zone, with 27. CAPS are divided into three models, each with its particularities: four CAPS II, one CAPS III, one CAPS AD and one CAPS for children and adolescents.⁽⁶⁾ Of the four models, only the CAPS for children and adolescents did not receive antimicrobials during the study period. Therefore, CAPS models II, III and AD were part of the study.

Among the models of CAPS studied, CAPS II are for daily care of adults with severe and persistent mental disorders in their coverage population. CAPS III are for adult daily and nocturnal care, seven days a week, serving the reference population who has severe and persistent mental disorders, and CAPS AD units are for alcohol and drug users, for daily care for the population with disorders resulting from the use and dependence on psychoactive substances such as alcohol and other drugs.⁽⁶⁾

Data on the distribution of antimicrobial drugs between June 2015 and July 2016 (14 months)

were investigated in this study. The temporal cut-off is based on Ordinance no. 04/2015, dated July 9, 2015,⁽⁷⁾ issued by the Municipal Health Department of Teresina-PI, which determines that the minimum filing time of a prescription for control purposes is two years, so according to the estimated period of data collection (January 2017), the period described above was defined.

A form with information about the distribution of antimicrobial drugs was used to collect the data, which contained information on the amount of these drugs distributed per month, by zone, by UBS and by CAPS; the name; and the cost of these distributed products. The form was validated (face-content) by field experts, and tested in a pilot phase.

Data were processed in the software Statistical Package for the Social Sciences (SPSS), version 21.0. Descriptive statistics were calculated for quantitative variables, and frequencies for qualitative variables, as well as the Kruskal-Wallis test to compare the medians of independent data distributions (distributions formed by data from different sources: different units).

The study complied with the principles of Resolution no. 466, of December 12, 2012, and was approved with the report no. 1.806.553. To guarantee the anonymity of the health units evaluated in the study, only their initials were used.

Results

In the period comprised for the research (14 months), 1,651,516 antimicrobials were distributed to primary care units in the capital city. Of these, 1,638,009 belonged to the UBS and 13,507 to the CAPS.

The area of the city that received the most amount of medications was the Eastern/Southeastern. As for CAPS units, CAPS II received the most part. The three antimicrobials most widely distributed in the UBS divided by zones were: Amoxicillin (500mg) in tablets, Metronidazole (250mg), and the combination of Sulfamethoxazole + Trimethoprim (400mg + 80mg) in tablets. Amoxicillin (500 mg) is the antimicrobial that is in evidence in the CAPS, as shown in table 1.

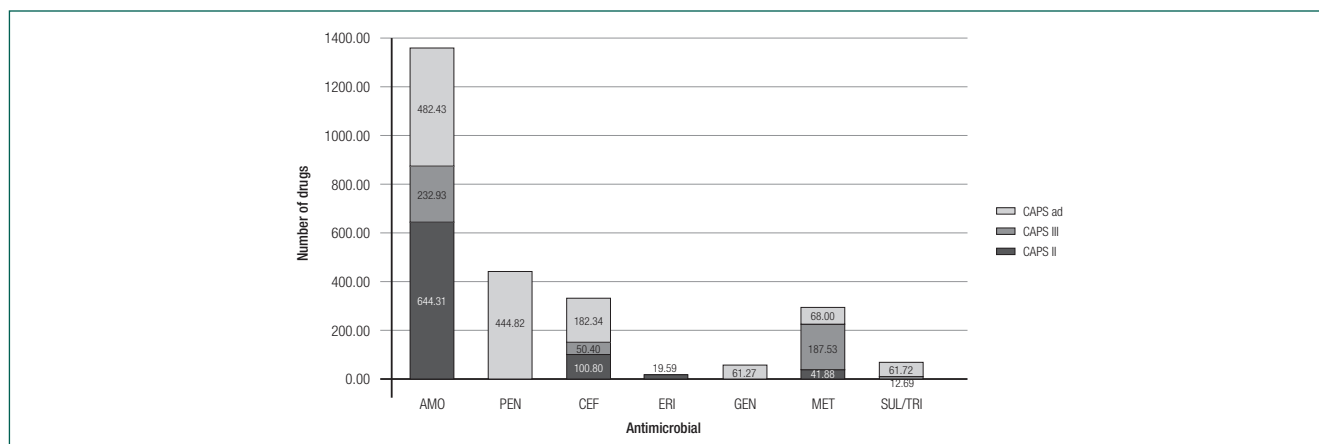
A total of 2,590.71 BRL was spent in the CAPS units of the city, and 98,705.00 BRL with antimicrobials distributed in the UBS units of the three city zones analyzed (Figure 1) (Table 2).

For the following table, the three UBSs that received the greatest amount of antimicrobials were chosen from each zone of the municipality in decreasing order. Based on the Kruskal-Wallis test, the medians of costs in each zone of the municipality were compared. The result showed that there were no statistically significant differences, that is, the costs for each unit (within the same region) in the evaluated period, although high, were almost the same (Table 2).

Table 1. Amount of antimicrobials distributed to primary care units according to the service demand (n=1,651,516)

Antimicrobial	E/SE	S	C/N	CAPS II	CAPS III	CAPS AD	Total
Amoxicillin 500mg	276,090	308,154	185,703	5,775	945	3,360	780,027
Amoxicillin suspension	7,990	7,900	5,880	0	20	0	21,790
Metronidazole 250mg tablet	199,280	166,920	162,780	600	260	0	529,840
Metronidazole 200mg suspension	7,960	6,801	6,950	0	0	0	21,711
Metronidazole 100mg cream	7,200	7,119	5,100	0	50	20	19,489
Sulfamethoxazole 200mg + Trimethoprim 40mg suspension	2,316	2,549	1,410	0	10	0	6,285
Sulfamethoxazole 400mg + Trimethoprim 80mg tablet	74,500	55,140	39,600	0	100	800	170,140
Cephalexin 500mg	29,950	17,680	23,100	400	200	900	72,230
Cephalexin suspension	853	597	587	0	0	0	2,037
Benzylopicillin 1.200.000	3,961	3,632	2,602	50	0	0	10,245
Benzylopicillin 600	1,330	879	880	0	0	0	3,089
Benzylopicillin 300.000	568	580	213	0	0	0	1,361
Erythromycin 500mg	3,833	2,330	3,270	0	0	0	9,433
Erythromycin 250mg suspension	1,707	985	485	0	7	0	3,184
Gentamicin 5mg	272	217	156	0	0	10	655
Total	617,810	581,483	438,716	6,825	1,592	5,090	1,651,516

Notes: E/SE: East/Southeast; C/N: Center/North; S: South. CAPS: psychosocial care center



AMO: amoxicillin; PEN: benzylpenicillin; CEF: cephalaxin; ERI: erythromycin; GEN: gentamycin; MET: metronidazole; SUL/TRI: sulfamethoxazole and trimethoprim

Figure 1. Costs with antimicrobials in the Psychosocial Care Centers in the period of the study (n=13,507)

Table 2. Costs of antimicrobials at the basic health units that showed the highest distribution in the study period according to the city zone

City zone	Antimicrobial	UBS SAT	UBS CSR	UBS PMR	p value*
East/Southeast	Amoxicillin	1,892.15	3,264.53	2,508.07	0.932
	Benzylpenicillin	4,159.16	2,058.38	4,780.85	
	Cephalaxin	555.12	442.23	650.08	
	Erythromycin	223.86	-	139.86	
	Gentamycin	30.89	97.35	61.74	
	Metronidazole	2,977.01	2,506.19	2,450.10	
	Sulfamethoxazole and trimethoprim	385.41	331.32	260.97	
	Total	10,223.6	8,7	10,851.61	
South	Amoxicillin	8,397.66	5,537.80	3,752.75	0.904
	Benzylpenicillin	3,355.55	3,873.53	3,796.44	
	Cephalaxin	423.02	601.94	568.67	
	Erythromycin	275.64	-	559.72	
	Gentamycin	-	-	411.43	
	Metronidazole	2,778.66	5,595.80	2,252.01	
	Sulfamethoxazole and trimethoprim	691.28	730.66	290.63	
	Total	15,921.81	16,339.73	11,631.65	
Center/North	Amoxicillin	3,916.35	3,403.14	3,431.92	0.911
	Benzylpenicillin	890.35	1,907.78	2,438.97	
	Cephalaxin	367.33	215.74	267.61	
	Erythromycin	-	-	288.34	
	Gentamycin	-	97.35	94.19	
	Metronidazole	2,248.56	2,963.51	1,574.42	
	Sulfamethoxazole and trimethoprim	372.44	248.97	309.57	
	Total	7,795.03	8,836.49	8,405.02	

Notes: SAT: Satellite. CSR: Centro de Saúde do Renascimento. PMR: Padre Mário Rocchi. CSKm-7: Centro de Saúde do km-7. CSVID: Centro de Saúde da Vila Irmã Dulce. VJWB: Vermelha - Dr. José Wilson Batista. CSMC: Centro de Saúde de Santa Maria da Codipi. CSAM: Centro de Saúde da Água Mineral. VAF: Vila Anita Ferraz.

*p: Kruskal-Wallis test significance

Discussion

The distribution of antimicrobials in the primary health care network of the municipality studied is irregularly performed among the health units, and does not follow a specific protocol. It was noticed that it relies on each zone's demand, without a system of analysis to guide the distribution. This situation involves an exacerbated use of the drug, which burdens the health care system due to the search of broad-spectrum antimicrobials to supply the demand that was not met with the previous drug, as well as the consequences to the patient's clinical evolution because it increases healing time of infection, and potentiates the need for other levels of health care.

Brazil was ranked by the Intercontinental Marketing Services Health (IMS Health) as one of the nations representing two-thirds of global pharmaceutical growth, with antimicrobials being a wide portion of that percentage, representing one of the most used drugs in the country. This motivated the Brazilian Health Regulatory Agency (ANVISA) to extend the measures for regulation and control related to sales, by demanding prescriptions for this class of drugs, which had been, thus far, sold freely; to require some data in the prescription, such as information about the patient, the issuer, the drug, and the prescription's date of issue; to insert them in the list of drugs when establishing guidelines regarding the distribution of drugs included in the Brazilian List of Essential Drugs (RENAME)

and in the Municipal List of Drugs (REMUME), among other regulations involving products containing antimicrobials in their composition.⁽⁸⁾

Drugs are still one of the main therapeutic instruments in the health-disease process, reflecting a historically hospital-based and curative care model. Pharmacological treatment of infectious diseases is a valuable ally in healing. However, irrational use and consequent antimicrobial resistance may hinder therapy progression. Therefore, its prescription, distribution, and disposal are necessary activities at all levels of health care, and are part of the set of services and actions called pharmaceutical assistance.⁽⁹⁾

The cycle of pharmaceutical assistance in primary care in Brazil consists of the selection of medicines, programming, acquisition, storage, material management, drug distribution, and disposal, respectively. The distribution stage consists of the supply of drugs to the health units in adequate quantities, with quality and timing. Purchase and distribution are performed through the regular and automatic, fund-to-fund transfer of federal resources, in the form of an added incentive to the Basic Care Price Ceiling.^(10,11)

The use of drugs, in general, is influenced by a number of factors, such as demographic structure, morbidity profile, socioeconomic, behavioral and cultural factors, characteristics of the pharmaceutical market, and government policies directed to the sector.⁽¹²⁾

The authors of this study found that the distribution of antimicrobials in the city studied is performed only according to the demand of the health units. Thus, it is possible to state that the areas of activity of the units are related and have repercussions on the profile of drug use, which is influenced by social, population and economic issues. For instance, a study carried out in the same city showed that respiratory infections were the most frequently diagnosed in the UBSs (52.2%), and that their treatment involved empirical antibiotic therapy in 95.5% of the time, with no previous request of antimicrobial culture, and emphasis on the use of amoxicillin (85%).⁽¹³⁾ This approach aims at the prevention of more severe complications, such as rheumatic fever and/or periamyglossal abscesses,

and has a direct impact on antimicrobial use and distribution.

Studies of UBS pharmacies in three other Brazilian municipalities support the information that amoxicillin is the predominant antimicrobial drug among the most prescribed drugs.⁽¹³⁻¹⁵⁾ This profile of high consumption is due to its broad spectrum characteristics, low toxicity, oral administration, good tolerability, and great experience of clinical use favoring its selection in the basic care units.^(13,16) Amoxicillin is a beta-lactam antibiotic that has a bactericidal action against gram-positive and gram-negative microorganisms, being indicated for upper airways infections and urinary tract infections, clinical conditions that are prevalent in primary care.⁽¹⁷⁾

Studies in Ghana and Nigeria also show amoxicillin as the most prescribed drug (26.7%; 18.2% respectively), followed by metronidazole (25.4%; 20.1%). Together, these drugs are considered the main antimicrobial agents used in primary care in these countries.^(18,19) Metronidazole is an antimicrobial with bactericidal activity against gram-negative anaerobic bacilli, all anaerobic cocci, and sporulated Gram-positive bacilli. It is recommended in wounds to control the odor caused by anaerobic bacteria,⁽²⁰⁾ besides the treatment of some protozoal infections (*Giardia lamblia*, *Trichomonas vaginalis*), which justifies its high demand in primary care.⁽²¹⁾

In the case of distribution of antimicrobials to the CAPS, this data is scarce in the literature, reinforcing the pioneer character of this study. These centers are health units dedicated to specialized psychosocial health care and often use specific drugs for the treatment of mental disorders. However, the care provided in these establishments demands the integration of mental and physical care, that is, the user needs treatment for the disorder, but should also have his/her other needs met, such as an infection, so that resolute and holistic assistance is provided.⁽²²⁾

In terms of costs, pharmaceutical costs with antibiotics for primary care are high, a finding that is supported by other studies in Malaysia⁽²³⁾ and in the United States of America.⁽²⁴⁾ According to data from the Integrated System of General Services

Administration (SIASG), from 2006 to 2013 there was a significant increase in pharmaceutical expenditures by the Brazilian government, with total expenditure tripled (2.72 times), while the amounts purchased only doubled (1.99) during the same period.⁽²⁵⁾ The irrational use related to uncertainty in the diagnosis and the lack of devices to specify the appropriate therapy, as well as the lack of a system of surveillance of community infections in Brazil can be pointed out as factors that collaborate for the irrational use of antimicrobials, and consequently impact on high costs and unnecessary expenses.⁽²⁶⁻²⁸⁾

The management of community-based infections in primary care is still empirically conducted, based on the observation of signs and symptoms presented by the patient, rather than on the bacterial culture or antibiogram.⁽²⁹⁾ The lack of Brazilian legislation and regulations aimed at the prevention and control of infection in out-of-hospital environments that may guide clinical practice require adaptations of professionals, which may result in unnecessary interventions and high expenditures to the health system.⁽³⁰⁾

This study has some limitations. The first regards the fact that it was performed in a single municipality, which makes it difficult to generalize its findings. The use of secondary data that may be imprecise should also be considered. It is worth emphasizing the need for replication of studies of this magnitude in other Brazilian regions in order to consolidate the profile of the distribution of antimicrobials in Brazil and subsidize interventions at the local and national levels for the rational distribution of these drugs.

Conclusion

The analysis of antimicrobial distribution and costs in primary care of the municipality studied presented an irregular distribution based on the demand presented by each zone of the municipality. The capital city does not have any specific protocol or system to investigate a possible increase or reduction in demand. The costs are proportional to the drug distribution, so if there is no distribution sys-

tematization, there is no financial management of expenditures.

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Collaborations

Lima HKS, Carvalho HEF, Sousa AFL, Moura MEB, Andrade D, and Valle ARMC declare that they contributed with the project design, data analysis, and interpretation, relevant critical review of the intellectual content and approval of the final version to be published.

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