

Understanding of pediatric antimicrobial prescriptions among health units in a southern brazil city

ABSTRACT

The aim of the study was to evaluate the understanding of the antimicrobial prescriptions by children's accompanying adults, describing the medicine utilization profile among Health Units in a South Brazilian city. A cross-sectional study was carried out and its target was people accompanying children during consultations that resulted in antimicrobial prescription (n=209), from May to June, 2007. A score (4-12) was generated to evaluate the understanding based on correct and incorrect/unknown statements about the prescription. Understanding was considered adequate when the score was below 6.5. Schooling (p=0.05), income (p=0.03), skin color (p=0.007) of accompanying person and length of the visit in minutes (p=0.05) were associated to a better understanding of the prescription. Adequate understanding represented 58.9% of the prescriptions. The most prescribed antimicrobials were amoxicilin and the association Trimethoprim-Sulfamethoxazole. The results point out to a need for standardization of written information and educational measures such as oral and written orientation to assure a better understanding of the prescriptions. We therefore assure a better understanding of the prescription, which helps the treatment to succeed, also avoiding the phenomena of microbic resistance.

Key words: understanding; pediatric prescription; antimicrobial

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Funding: the researchers' own

Approved by the Research Ethics Committee of the Association of Charity Santa Casa do Rio Grande. Case No. 004 / 2007.

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INTRODUCTION

The indiscriminated and inappropriate use of antimicrobials may increase the development of multiresistant microorganisms¹. About 75% of these drugs are prescribed, inappropriately, and an average of 50% of the patients take these medicines incorrectly². Medication mistakes, expectations from the prescribers and patients and the lack of comprehension, or the lack of observation of the medicine therapy, are examples of factors that contribute to the irrational use of medicines, resulting in the increase of microbial resistance of drugs and unnecessary expenditures made by the public organs²⁻³.

The lack on comprehension of prescriptions information is common in health care services and its causes may be related to a complex language, unorganized or implicit information and an inappropriate handwriting that makes the written information unintelligible, making more difficult its understanding³⁻⁴.

The commitment of the child to the treatment becomes more complicated because it depends on the perspectives and on the relationship between the family and the doctor. Communication between the parents and the prescriber is a fundamental factor for the commitment to the treatment⁵. Factors related to the responsible for the person, such as the low socioeconomic level⁶ and the prescriber, the prescription with many medicines⁷, may make difficult the understanding of the written information and contribute for the treatment not to be fulfilled, risking the compliance of antimicrobial therapy child.

This study has as a goal to evaluate the understanding of antimicrobials prescription by the responsible for the child, after the pediatric consultation in Health Units, in a city in South Brazilian and to describe the profile of antimicrobials prescriptions.

METHODS

A transversal study in the city of Bagé,

state of do Rio Grande do Sul, which has, according to the 2007 census by Brazilian Institute of Geography and Statistics, approximately 112 thousand inhabitants, has been carried out. Such study has been done in all of the health posts of the average complexity level (03), which feature pediatric treatment and have 10 pediatricians. The gathering of data was done from May to July 2007. The target population consisted of people responsible for the children treated by the pediatricians, who got the prescription of at least one antimicrobial.

The calculation for the size of the sample for the study of association considered the different levels of study (less than 4 years old), with a statistical power of 80% and a confidence level of 95%, a relative risk equal to 2 and a reason not exposed/ exposed to 4/1. Considering a prevalence of 16% among non-exposed, the result was 360 individuals. 10% have been added to this number for losses and refusals and 15% for the control of confusion factors, resulting in a sample of 455 individuals. For logistic issues, it has been decided to have 50 interviews of people responsible for children after the consultation with the pediatrician (n=10), which resulted in 500 interviews. In the study, the people responsible for the children with ages ranging from 0 to 12 years old and who had medicine prescriptions during the study period were included. They have been interviewed in the beginning of the consultation time, daily, according to a sequence of odd-numbered appointments, up to 50 interviews for pediatrician, which assured that all patients that were treated had the same probability of participating in the study.

The data gathering was done through a questionnaire structured pre-coded (with information about the child, his/her responsible and questions about the understanding of the prescription) and a spreadsheet to gather information about the prescription (indicators of prescription and prescription drugs).

The independent variables of the responsible for the child were: gender, age

(in years completed), relationship with the child, skin color (white or non-white, based upon the observation by the interviewer, scholarship in years and family income (in real divided into quintiles, where the first refers to the poorest 20% and the fifth to the richest 20%). The child independent variables were: gender and age (in years completed).

The dependent variable were the prescription of antimicrobials (the most prescribed antimicrobials and indicators of prescription); the understanding of the pediatrician prescription about the details of the prescription drug, dose, interval of administration, duration of treatment, the prescription readability and an indicator of patient care. The topical use of antimicrobial prescriptions were considered in the study only for analysis of prescription understanding.

Indicators of prescribing and patient care, recommended by the World Health Organization (WHO), evaluated in the study, have been taken from the guide "Como investigar el uso de medicamentos en los servicios de salud" (1993)⁸. Among the indicators of prescription, it has been verified the percentage of appointments in which at least one antimicrobial of systemic use has been prescribed, the average number of for prescription of antimicrobials and the percentage of antimicrobials prescribed by their generic names. Among the indicators of patient care, it has been verified the consultant duration, which was obtained measuring the time and recording the period in minutes in which the child was in the consultation.

The medicines have been classified according to the Anatomical Therapeutic Chemical Classification System (ATC), suggested by the Drug Utilization Research Group (DURG) of WHO to the study of medicine use⁹.

The agreement with the information about the prescribed has been analyzed, being informed by the responsible for the child with the medical prescription, and the responses have been classified in right,

wrong or ignored information.

Considering that there isn't an appropriate instrument to measure the understanding of the recommended treatments, a score has been created to evaluate the understanding of the prescription, based on variables knowledge about the recommendations, dose, interval and duration of the prescribed treatment. The value of the score ranged from 4 (all correct answers) to 12 points (all wrong or unknown answers). Each correct answer added 1 (one) point to the score and each wrong or unknown answer added 3 (three) points. For the composition of the score, the wrong and unknown answers were considered as equivalent.

Once there isn't validated recommendations to evaluate this outcome, it has been decided to dichotomize it and classify the understanding as "appropriate" or "inappropriate". The understanding was considered "appropriate" when the score value was lower than 6.5, and above this value as "inappropriate". The cutoff point of 6.5 points was established for being the equivalent to the best punctuation (4 points) added by 1 (one) standard deviation of the score (2.5).

The prescription was considered readable when the responsible for the child was able to read the name of the antimicrobial, regardlessly of the scholarship level. People responsible for the children who informed they couldn't read were not considered for the analysis of readability.

The medical consultation duration, based on the average of the consultations times, has been categorizes in below and above 5 minutes.

The data was entered twice in the Epi Info 6.04 software. A validation has been done after its entering. The statistical analysis of the database were done with the statistic package Stata 9.2 (Stata Corp., College Station, TX: 2007).

The test for linear trend was used to evaluate the association of categorical variables with the outcomes. The T Test was used to analyze the averages of the understanding scores. Had been calculated by Poisson regression of the reasons of crud and adjusted

prevalence for proper understanding of the categories of variables studied.

This study has been approved by Ethics Committee the Association of Charity Santa Casa of the city of Rio Grande-RS, where this project has originally been conceived. The Municipal Secretariat of Health and Environment of Bagé-RS agreed in its realization, after being informed about the research goals and the lack of interest conflicts been declared. The goal of the study was explained to the responsible for the children and only after the agreement of the people interviewed and the signature of the consent terms, the interviews have been proceeded.

RESULTS

The consultation resulted in 1285 prescribed medicines, being 225 antimicrobials, 209 for systemic use. From the consultations included in the study, the percentage of prescriptions of at least one antimicrobial systemic was 41,8%. In prescriptions including antimicrobials, the average of medicines for prescription was 2,9.

Table 1 describes the distribution of consultations with prescriptions of antimicrobials, in the studied population, according to demographic characteristics of the child. The prescription of antimicrobials differs for age ($p = 0,003$) and is higher with older

children. The age average of the children assisted was 4 years old ($DP = 3,3$).

From the antimicrobials, 81,8% were prescribed by its generic name. Table 2 describes the profile of antimicrobials prescriptions according to the age of the child. The most frequent antimicrobials for systemic use were amoxicilin (53,9%) and the association trimethoprim-sulfamethoxazole (19,4%), and amoxicilin was the most frequent antimicrobial in all ages.

The socioeconomic and demographic characteristics of the people responsible for the children in the site of the study, as well as the prevailing of proper understanding for the whole sample are described in Table 3. A trend in the prescription being less understood among people responsible for the child with less than 4 years of education ($p = 0,001$), income between the first and the second quintile ($p = 0,02$) and non-white ($p = 0,03$) has been verified.

Evaluating only consultations where there has been prescription of antimicrobials ($n = 209$) with the variables these study (Table 4), it has been verified that, in crude analysis, the proper understanding was associated with people responsible for the child with higher income ($p = 0,03$), white ($p = 0,007$) and with higher levels of scholarship and consultation time, and such associations have borderline statistical

Table 1. Distribution of consultations with antimicrobial prescription ($N=209$) according to children's demographic characteristics in health clinics. Bage, RS – Brazil, 2007.

Variable	Consultations with prescription ATBs* N (%)	IC 95%	Value- p
Gender			
Men ($n = 263$)	110 (41.8)	35.8 – 47.8	1.00 **
Female ($n = 237$)	99 (41.8)	35.4 – 48.1	
Age			
1 year ($n=171$)	62 (36.3)	29.0 – 43.5	0.003 ***
Between 2 – 5 years ($n=178$)	74 (41.8)	34.4 – 49.1	
6 years ou more ($n=151$)	73 (48.3)	40.3 – 56.4	

* Antimicrobial

** Chi-square

*** Test for linear trend

Table 2. Antimicrobial prescription profile according to age group in health clinics. Bage, RS – Brazil, 2007, (N=209).

Antimicrobials ^a	Age (complete years)			Total
	1 year N(%)	2 – 5 years N(%)	6 years + N(%)	
Amoxicilin	25 (40.3)	42 (56.7)	44 (60.3)	111
Benzathine benzylpenicillin	7 (11.3)	8 (10.8)	5 (6.8)	20
Cefalexin	2 (3.2)	4 (5.4)	3 (4.1)	9
Tmp/Smx ^b	14 (22.6)	14 (18.9)	12 (16.4)	40
Others ATBs ^c	14 (22.6)	6 (8.1)	9 (12.3)	29
Total	62 (100)	74 (100)	73 (100)	209

^a Categorized according to ATC – Anatomical Therapeutic Chemical Classification System

^b *Trimethoprim/Sulfamethoxazole* association

^c ATBs = antimicrobials

Table 3. Socio-demographic characteristics of the person accompanying the child in health clinics and prevalence of pediatric prescription adequate understanding (N= 500). Bage, RS – Brazil, 2007.

Variable	N	%	Adequate understanding (%)	P
Gender				0.22 ^a
Women	433	86.6	53.7	
Men	67	13.4	61.7	
Age (years)				0.53 ^b
15 – 19	35	7.0	45.7	
20 – 29	180	36.0	63.3	
30 – 39	185	37.0	60.5	
40 – or more	100	20.0	61.0	
Skin color				0.03 ^a
White	341	68.0	63.9	
Non-white	159	31.8	53.5	
Degree of Kinship				0.02 ^b
Mother	432	86.4	62.5	
Father	31	6.2	48.4	
Grandmother/grandfather	23	4.6	52.2	
Uncle/ aunt	6	1.2	83.3	
Other	8	1.6	12.5	
Schooling (years)				0.001 ^b
0- 4	73	14.6	47.9	
5 – 8	205	41.0	57.6	
9 – or more	222	44.4	67.6	
Quintile of family income (R\$)				0.02 ^b
First (até 280,00)	102	20.4	55.9	
Second (281,00 – 370,00)	133	26.6	56.4	
Third (371,00 – 480,00)	98	19.6	61.2	
Fourth (481,00 – 670,00)	75	15.0	60.0	
Fifth (671,00- 4000,00)	92	18.4	71.7	

a: Chi-square

b: test for linear trend

Table 4. Adequate prescription understanding according to assessed variables and crude and adjusted Prevalence ratios obtained by Poisson regression. (N=209) Bage, RS – Brazil, 2007.

Variável	%	% Adequate understanding	Crude analysis RP (IC 95%)	p*	Adjusted analysis RP (IC 95%)	p*
Schooling				0.05		0.33
0 – 4 years	36.4	50.0	1.00		1.00	
5 – 8 years	37.8	55.0	0.90 (0.59-1.37)		0.96 (0.62-1.47)	
9 years +	25.8	67.1	0.66 (0.41-1.06)		0.79 (0.47-1.33)	
Income (quintiles)				0.03		0.18
1	22	52.2	1.00		1.00	
2	27.3	52.6	0.99 (0.66 – 1.49)		1.10 (0.74 – 1.64)	
3	19.6	58.5	0.87 (0.54 – 1.39)		0.94 (0.58 – 1.55)	
4	13.4	64.3	0.75 (0.42 – 1.34)		0.84 (0.46 – 1.54)	
5	17.7	73.0	0.56 (0.31 – 1.04)		0.71 (0.37- 1.34)	
Skin color				0.007		0.02
White	66.0	65.2	1.00		1.00	
Non-white	34.0	46.5	1.53 (1.12 – 2.11)		1.44 (1.05 – 2.00)	
Time for consultation				0.05		0.03
< 5 minutes	41.2	53.2	1.00		1.00	
> 5 minutes	58.9	67.1	0.70 (0.49-1.00)		0.68 (0.48 – 0.97)	

*Wald's test

significance ($p= 0,05$). After adjusting the variables analyzed to each other, the proper understanding kept associated only to skin color ($p= 0,02$) and consultation time ($p= 0,03$). This difference in the adjusted analysis has probably been attributed to the decrease of the sample size, when we consider only prescriptions with antimicrobials.

The average consultation time with the pediatricians was 5 minutes and 30 seconds (DP = 2' 30"; amplitude of 1-19). The consultations longer than 5 minutes had better understanding of the prescription by the responsible for the child, for the total number of assisted consultations ($p = 0,004$) as well for the ones with at least one prescription antimicrobial ($p = 0,03$). The average consultation time for the scholarship level between 0 and 4 years; 5-8 years and 9 or more years was, respectively, 5'13"; 5'14" and 5'51", and there was a trend in the increase in the consultation time when scholarship increased ($p= 0,02$).

It has been considered proper understanding 58,9% of the prescriptions including at least one antimicrobial, which means with valor do score lower than 6,5 points.

From the consultations where an anti-microbial has been prescribed, 97,8 % of the prescriptions included one dose; 93,3%, the interval of medicine administration and 87,5%, the duration of the treatment specified. About the readability, 30,1% of the responsible for the child couldn't read the name of the antimicrobial, being the prescription considered unintelligible. Only 2,4% of the people interviewed said they were illiterate and so couldn't read the name of the medicine. About the agreement information on antimicrobials informed by the responsible for the child with the contents of the prescription (Table 5), almost half of the people have informed, wrongly, or haven't known to inform, the dose, and the same was verified for a third about the administration interval variable.

Approximately 30% have informed wrongly or haven't know to inform the duration of the treatment.

DISCUSSION

Lapses in following the drug therapy are among the main factors that contribute

Table 5. Antimicrobial information as reported by the person accompanying the child (N=209). Bage, RS – Brazil, 2007.

Reporting of information to prescribed antimicrobial	Indication		Dose		Interval of administration		Duration of treatment	
	N	%	N	%	N	%	N	%
	Correct	166	79.4	119	57	134	64.1	148
Incorrect	12	5.8	26	12.4	26	12.4	21	10.1
Do not know	31	14.8	64	30.6	49	23.5	40	19.1
Total	209	100	209	100	209	100	209	100

to an antimicrobial resistance process to drugs, which compromises the population's health and brings expensive public expenditures^{5,10}.

The percentage of consultations in which at least one antimicrobial has been prescribed, (41,8%) shows that the indicator of rationality is out of the ranges suggested by the OMS (20-30%)⁸. Other papers, in Brazil, done in basic health units with infants, have found values between 29- 44,6%¹¹⁻¹². There are evidences that, in the context of the use of antimicrobials, the medical specialty that prescribes this drugs the most is pediatrics¹³⁻¹⁴.

Some researchers have mentioned that the mother's age and her education level, are also conditioning factors for the higher level of prescription of antimicrobials to their kids^{15,16}.

The consultations with prescriptions of systemic antimicrobials have shown a high average of the number of prescribed medicines (2,9), which can be considered a potential risk to drug interactions¹² and drugs prescriptions misunderstandings⁷. A study carried on in Araraquara (SP), with children with ages ranging from 1 to 5, has showed a similar value (2,7)¹¹. According to the WHO, the acceptable average of medicines for medical prescription would be between 1,3 – 2,2⁸.

It has been verified a high percentage of antimicrobials prescription by their generic names (81,8%), compared to other studies carried on in health services with pediatric care (32% - 45,2%)¹¹⁻¹². However, this indicator is not in compliance with the legislation,

which demands in the context of National Health System that 100% of the medicines are prescribed according to the Brazilian Common Denomination or, in its absence, the International Common Denomination¹⁷. The standardization in the prescribing habits according to the generic naming may bring the responsible for the child a better understanding of the medicine name and its clinical indication.

In this study 13 distinct antimicrobials have been prescribed. The group drug penicillin represented more than half the prescriptions. The most prescribed antimicrobials were amoxicilin, followed by the combination trimethoprim-sulfamethoxazole, both with broad spectrum of action. Many studies have shown the widespread use of these two antimicrobials at the community level, where variations in the frequency of use values comprise between 35,8 to 54% and from 12,1 to 26,8%, respectively^{11,14,15,18}. The antimicrobials not standardized by the List Municipal Standardization, prescribed were cefadroxil, the combination amoxicilin + clavulonic acid, chloramphenicol and azithromycin, also considered of broad spectrum. The excessive use of antimicrobials of broad spectrum increases the risks of selective pressure for several pathogens^{15,19}.

There was a trend if the antimicrobials be more prescribed with older ages, showing an inverse relation to the ones found in other studies, where it has been observed a decrease in the prescription for older children^{15,18}. Researches show that the use of antimicrobials in children is twice as higher compared to the use in adults and

that in ages below five years get a significant prescription of antimicrobials^{18,20}. Some hypothesis may be according to the trend of the antimicrobials to be more prescribed as the age increases: weaning from the first year of life, leading to decrease of immunoglobulins, favoring thus the emergence of infections and increased contact with the outside world as the child grows, providing contact with infectious agents, especially in day care centers and nursery schools²¹.

Most of the people responsible for the children were young mothers, with enough education level to be able to read. However, it has to be taken into consideration that, in Brazil, 59% of the students with up to four years of education do not show reading skills compatible with the level of literacy and are classified as functional illiterate, since they don't use the writing language as an essential element in their lives²².

Almost all of the information about dose (97,85%), interval of administration (93,3%) and treatment duration (87,5%) was present in the contents of the antimicrobials prescriptions. Abrantes e col. (2007) have observed in a study in a basic health unit, similar results with values of 99.6%, 98.9% and 89.3%, respectively¹⁴.

Information omitted from the contents of prescriptions may become a problem, especially for people with low levels of education or when a multiple scheme of drugs have been prescribed, besides representing one of the most commons medication mistakes, contributing to the non-compliance to the treatment⁵ and make difficult the dispense of medicines in the health service¹⁴. The prescription is a document given by a skilled professional that determines the conditions in which the medicine must be used²³. The quality of the medical prescription is one of the factors that determine how the users of the health services, in this case the people responsible for the children, use the medicines⁵.

The consequence of the lack of information in a medical consultation may have had influence the agreement of the information given by the responsible for the child with

the prescription of the antimicrobials. About half of the people have informed, wrongly, or didn't know to inform the dose (43%); the same thing happened for a third concerning the variable administration interval (36%) and about 30% did not inform correctly the duration of the treatment. The lack of understanding of the technical information in the prescription is concerning, since the prescription indicator of antimicrobials shows values higher than what is demanded by WHO, which may lead to medication mistakes and be an increase in the phenomenon of microbial resistance. Besides that, the data suggests that communication pediatrician-child's responsible person has been limited, emphasizing the need to develop, in the health service, educational methodologies that assure a transmission and reception of information. This hypothesis is confirmed by other researches, which mention that one of the factors in the misunderstanding of the prescriptions is the relation patient-prescripitor and that the patients should be encouraged to have all of their questions answered in a medical consultation^{4,24,25}. An appropriate understanding of the prescription helps the success of the treatment and may avoid the phenomenon of the microbial resistance.

When associated, the understanding of the pediatrician prescription to the level of education and income of the person responsible for the child, in all of the consultations or only in the ones with prescription of antimicrobials, it has been verified more occurrence of appropriate understanding by whom had a higher level of education and a higher income. However, in adjusted analyses, the power of this association has decreased in the prescriptions including antimicrobials, probably because of the smaller size of the sample, but this difference is not statistically significant.

National⁶⁻²⁶ and international^{3,7} researches that relate the understanding of the written form, indicate that the level of education as a important factor for a good understanding. These papers, by verifying the understanding of the users of the health

units about the information included in labels of medicines or in medical prescriptions after the consultations, have showed a prevailing in misunderstandings of the written information between 29 - 63%^{26,3,6,7}.

In this study, the inappropriate understanding corresponded to 41.1%. It needs to be taken into account that, although the individual declares correctly the instructions for the medicine use, sometimes he does not understand them, showing a cognitive deficiency.

A study that analyzes the medicine directions understanding has shown that 70.7% of the users of the service, with low level of education, have declared appropriately the directions. On the other side, only 34.7% have shown the right number of pills to be taken on a daily basis⁷.

There is a consensus, made from many evidences, that the level of education of positively related to income. In Brazil, the illiteracy rate in homes where the income is higher than ten minimum salaries is only 1.4% and, in which whose income is lower than a minimum salary, it's almost 29%, what shows that income has influence in access to education²². Likewise, data shows that non-white individuals have less financial resources and, consequently, less opportunities of study²⁷. This way, it can be seen a relationship with the more difficulty of understanding the information provided by the health service.

The medical consultation time has been below the demands (15 minutes)⁸. This study could demonstrate that this variable is a determining factor in understanding the pediatrician prescription, because even being far from what is demanded, the time average, the prevailing of the proper understanding was the time average above 5 minutes. The consultation time was directly proportional to the level of education, being the highest consultation time averages for the people responsible for the children having highest levels of education. However, it could be the opposite, because young mothers, with less experience and lower educational level need more consultation

time e support from the pediatrician¹⁶. It would be necessary qualitative studies to evaluate the factors that influence the consultation time.

In the places in the study, all of the prescriptions were hand written, and this factor increases the problems concerned with readability and contributes for the misunderstanding of the prescription. Electronic systems for medical prescriptions have been developed to reduce prescription mistakes and to better the readability by the person responsible for the child²⁸.

Readability influences communication and can interrupt or alter the process of assistance to the patient²³. Mistakes in the reading and misunderstanding of the information may contribute for medication mistakes, so it is necessary that such information be given in uppercase letters, in an organized, logical and appropriate way to the reading skill to facilitate the treatment understanding⁴.

A limitation in the study was that it was realized in only three Units of Health, due to the fact that only these had the pediatric specialized service, with a professional pediatrician. Besides that, although it has been estimated a sample that was big enough for the associations between variables and their outcomes, it was considered a prevailing in the insufficient use of antimicrobials for the adjusted analysis, masking the determining factors to the understanding of antimicrobials prescriptions. It is suggested the reproduction of this work in all of the Public Health Units of the city so that there is a right representation of the antimicrobials pediatrics prescriptions understanding and, consequently, a bigger sample size.

FINAL CONSIDERATIONS

In this study, it was verified that the level of education, income and skin color of the person responsible for the child, as well as the consultation time, were directly associated to the understanding of the medicine prescription and that the higher the education level and income of the child's

responsible person and the consultation time, the better the understanding, being this higher for white individuals.

The understanding of the antimicrobials prescription could have been better if all of the medicines had been prescribed by its generic name, making easier to become familiar with the treatment, medicine name and its indication; also if the hand writing were appropriate to a total readability and if the index of polytherapy were reduced in prescriptions including antimicrobials.

Mistakes in drug therapy can be avoid with the correct understanding of the antimicrobial therapy by the responsible for the child, since factors related to the prescriber, such as the clearness of the oral and written information, provided during the medical consultation and the ones referred to the person who is responsible for the child,

such as the difficulty in questioning during the consultation, may interfere in the prescription understading. Because of this, health professionals should be prepare to promote ways of health education, such as giving verbal and written guidance about the right way to use antimicrobials during the consultation and dispense of medicines. So, it can be assured a correct understanding of the information given to the service users, regardelessly of their education levels.

The written information standardization in Units of Health can also be a strategy that increases the consistency of the information contents and improves the understanding of the pediatrician prescription, avoiding medication mistakes, contributing for a better adherence to the treatment and also minimizing the phenomenon of the antimicrobials resistance.

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