Medication use in children from the 2015 Pelotas (Brazil) birth cohort aged between three months and four years

Uso de medicação em crianças da coorte de nascimentos de Pelotas, Rio Grande do Sul, Brasil, de 2015 com três meses a quatro anos de idade

Uso de medicación en niños, desde los tres meses hasta los cuatro años de edad, en una cohorte de nacimiento de 2015 en Pelotas, Rio Grande do Sul, Brasil

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Abstract

Medication use is an important part of the health process and prevalence of its use among infants can reach up to 65% in their first months of life. The excessive use of medication could lead to an increase in their potential harm, surpassing their benefits. Considering this, this study aimed to describe medication use in children aged 3, 12, 24, and 48 months. Standardized questionnaires were applied to assess patterns and covariables of medication use. Medication use was investigated as an outcome and defined as the receipt of any medication within 15 days before the interview. Prevalence of medication use and 95% confidence intervals (95%CI) were described using chi-squared tests. Prescription source and frequency of use were also reported, along with the most frequent medication in each follow-up. Medication use prevalence was 67.2% (95%CI: 65.8; 68.6), 68.2% (95%CI: 66.8; 69.6), 52.4% (95%CI: 50.9; 54.0), 47.2% (95%CI: 45.7; 48.8), at 3, 12, 24, and 48 months, respectively. We observed a decrease in the proportion of medically prescribed medications and an increase in self-medication over the years. Drugs for gastrointestinal disorders (A03), vitamins (A11), analgesics (N02), anti-inflammatories (M01), and nasal formulations (R01) were the most frequently used medications. We found that children under four years of age comprised over 50% of the total use of medications and self-medication. These results highlight the need to warn caregivers on the importance of proper professional examination and prescription before they administer medications to children.

Drug Utilization; Infant; Preschool Child; Longitudinal Studies; Child Care

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Introduction

If appropriately conducted, medication use is an important part of the health process. However, its inappropriate use can represent a harm to health that could be even greater than its potential benefits. Therefore, health policies have been implemented over the years to improve the Brazilian population's access to medication, as well as the quality and safeness of prescriptions [1].

About 66% of Brazilian adults report having taken one or more medications during a 15-day recall period [2]. In children, this prevalence is also high; about 65% at ages 3 and 12 months, about 55% and 35% at 24 and 48 months, respectively, during a 15-day recall period [3,4].

The use of over-the-counter medication in children and adolescents is a common practice, reaching almost 40% of those who report taking any medication [5]. This practice can lead to increased risks of adverse drug reactions that, in children, can result in hospital admission in 0.4% to 10.4% of the time [6].

In 2017, medication use was the main cause of intoxication in Brazil (27.1%), higher among children aged under one year (38.9%) and from one to four years (33.5%), representing almost 12 children intoxicated every day in the country [7].

Understanding children's medication use patterns can help to improve and implement existing policies to ensure safe medication access to children. Considering this, this study aimed to describe medication use in children aged 3, 12, 24, and 48 months from the 2015 Pelotas (Brazil) birth cohort.

Methods

In this study, we used data from the 2015 Pelotas (Brazil) birth cohort to describe medication use among children from childbirth to four years of age. Pelotas is a city with nearly 350,000 inhabitants located in the State of Rio Grande do Sul, in Southern Brazil [8]. In 2015, all live births, between January 1st and December 31, to mothers that lived within the urban area of Pelotas, were eligible to be included in the study as defined in the first Pelotas (Brazil) birth cohort 1982 [9]. Thus, mothers who gave birth in hospitals in Pelotas and lived in the Jardim América district (which currently belongs to the neighboring municipality of Capão do Leão) and the Z3 fishing village (which is no longer classified as urban) were invited to participate. A total of 4,387 live births that occurred in Pelotas in 2015 were eligible to be included in the cohort, out of which 4,275 were included in the study [10].

Included children's caregivers answered standardized questionnaires applied by trained interviewers to assess socioeconomic, demographic, and behavioral information. The study includes, so far, pre- and perinatal interviews, and 3-, 12-, 24-, and 48-month follow-ups. This study assessed medication use data from the four follow-ups conducted between ages three and 48 months with follow-up rates of 97.2% at three months and 95.4% at 12, 24, and 48 months. Further methodological information has been previously published [9,10].

Medication use was investigated as an outcome and defined as the positive response to the question "Did [the child] receive any medication in the last 15 days, including vitamins or fever medicine?" If so, the names of the medications were collected, what the medication was used for and for how long, and their packages and prescriptions, if available.

Besides the number of medications used, we also show the indication source (current medical prescription; previous medical prescription – reuse of a previously used medical prescription; other healthcare providers; child's parents; family or friend; or other); and use regularity, categorized as sporadic (irregular use in the last 15 days) or continuous (daily use for one month or more).

Covariates

The following maternal and children's characteristics, used to describe medication use in infants up to four years of age, were included in our sample: maternal age (full years), schooling level (full years), family income (minimum wages), skin color (white, black, mixed-race/yellow/other), and marital status (living with or without a partner). Maternal characteristics were collected by self-report. Children's sex (male or female), gestational age at birth (preterm < 37 weeks, early term 38 to 38 weeks,

full term 39 to 40 weeks, and late or post-term 41 to 42 weeks), type of delivery (vaginal or cesarean section), breastfeeding duration (≤ 6 months, 7 to 12 month or >12 months), and child's health status, according to maternal perception, were also included as covariates. Child's perinatal characteristics were collected via physical examination by trained personnel within 24 hours of birth and via medical records. Breastfeeding duration and child's health status were reported by mothers in all four follow-ups. To apply the questionnaires, at 3-, 12-, and 24-month follow-ups, data collection was performed using a software especially developed for this purpose. At the 48-month follow-up, data were collected using the REDCap Software (https://redcapbrasil.com.br/) [11].

Medicine classification

Medications were classified according to levels 1 (anatomical group) and 2 (therapeutic group) of the Anatomical Therapeutic Chemical Classification (ATC), following World Health Organization (WHO) criteria [12] and based on the reason they were used for. This system consists in classifying medications into groups according to the organ or system where they act on and to their chemical, pharmacological, and therapeutic properties.

Analyses

A description of the entire cohort at birth and samples at 3, 12, 24, and 48 months, according to maternal and child characteristics was carried out. Using the characteristics distribution of the same sample, an analysis was performed on the prevalence of medication use and their 95% confidence intervals (95%CI), in the four follow-ups, via Pearson's chi-square tests.

Relative frequencies of medication use at 3, 12, 24, and 48 months were described according to the number of medications used. Based on the total number of medications reported at each follow-up, the source of medicine indication and frequency of use were described.

The most used medicine groups were described according to the ATC2 classification, aiming to establish the most prevalent groups at each age stage and the variations between periods.

A description of all medicines reported according to ATC1 and ATC2, as well as a list of the most used medications at each follow-up, according to their chemical names, can be found in the Supplementary Material (http://cadernos.ensp.fiocruz.br/static//arquivo/suppl-e00117221_7157.pdf). Crude and adjusted analyses of the association of medication use (yes/no) at each follow-up with the independent variables is shown in Table 1.

Statistical analyses were performed using the Stata Statistical Software version 16.1 (https://www.stata.com)

Ethical considerations

The 2015 Pelotas (Brazil) birth cohort follow-ups were approved by the Research Ethics Committee of the Higher School of Physical Education (ESEF), Federal University of Pelotas (UFPel) with the approval number 26746414.5.0000.5313. All subjects provided written informed consent.

Table 1

Adjusted odds ratio (OR) of medication use association with maternal and child characteristics. The 2015 Pelotas (Brazil) birth cohort.

Characteristics	Medication use [OR * (95%CI)]			
	3 months [n = 4,110]	12 months [n = 4,018]	24 months [n = 4,014]	48 months [n = 4,010]
Maternal				
Age (years)	p = 0.838	p = 0.189	p = 0.419	p = 0.011
< 19	1.00	1.00	1.00	1.00
20-24	0.93 (0.75; 1.16)	1.12 (0.90; 1.40)	1.16 (0.94; 1.44)	1.23 (0.99; 1.52)
25-30	0.90 (0.72; 1.13)	1.26 (1.00; 1.57)	1.16 (0.94; 1.44)	1.31 (1.06; 1.62)
> 30	0.95 (0.76; 1.19)	1.23 (0.98; 1.53)	1.07 (0.86; 1.32)	1.43 (1.16; 1.78)
Educational attainment (years)	p < 0.001	p < 0.001	p < 0.001	p = 0.030
0-4	1.00	1.00	1.00	1.00
5-8	1.02 (0.80; 1.30)	1.21 (0.95; 1.55)	1.16 (0.91; 1.47)	1.06 (0.83; 1.36)
9-12	1.27 (1.00; 1.61)	1.54 (1.21; 1.97)	1.32 (1.04; 1.66)	1.14 (0.90; 1.45)
> 12	1.92 (1.49; 2.47)	2.13 (1.65; 2.76)	1.80 (1.42; 2.29)	1.34 (1.05; 1.71)
Family income (minimum wage)	p = 0.244	p = 0.570	p = 0.219	p = 0.565
≤ 1	1.00	1.00	1.00	1.00
1.1-3.0	1.05 (0.85; 1.29)	1.06 (0.86; 1.31)	1.10 (0.90; 1.35)	1.01 (0.82; 1.24)
3.1-6.0	1.10 (0.86; 1.40)	1.04 (0.81; 1.33)	1.25 (0.99; 1.57)	0.96 (0.76; 1.21)
6.1-10.0	1.38 (0.97; 1.96)	1.34 (0.93; 1.92)	1.35 (0.98; 1.86)	1.08 (0.78; 1.49)
Skin color	p = 0.007	p = 0.096	p = 0.520	p = 0.325
White	1.00	1.00	1.00	1.00
Black	0.75 (0.62; 0.90)	0.84 (0.70; 1.00)	0.92 (0.77; 1.10)	0.92 (0.77; 1.10)
Mixed-race/Yellow/Other	0.93 (0.76; 1.13)	0.86 (0.71; 1.06)	0.92 (0.76; 1.11)	0.89 (0.73; 1.07)
Living with a partner	p = 0.018	p = 0.079	p = 0.517	p = 0.698
No	1.00	1.00	1.00	1.00
Yes	0.80 (0.65; 0.96)	1.19 (0.98; 1.44)	0.94 (0.78; 1.13)	0.94 (0.80; 1.16)
Child				
Sex	p = 0.057	p = 0.001	p = 0.086	p = 0.623
Male	1.00	1.00	1.00	1.00
Female	0.88 (0.77; 1.00)	1.20 (0.70; 0.92)	0.90 (0.79; 1.02)	1.03 (0.89; 1.31)
Gestational age (weeks)	p < 0.001	p = 0.032	p = 0.552	p = 0.202
Preterm (< 37)	1.00	1.00	1.00	1.00
Early term (37-38)	0.60 (0.47; 0.75)	0.77 (0.62; 0.95)	0.97 (0.80; 1.17)	1.08 (0.90; 1.31)
Full term (39-40)	0.46 (0.37; 0.57)	0.75 (0.61; 0.93)	0.99 (0.82; 1.19)	0.93 (0.77; 1.13)
Late & post term (41-42)	0.44 (0.33; 0.59)	0.68 (0.51; 0.92)	0.83 (0.63; 1.10)	0.93 (0.71; 1.23)
Type of delivery	p = 0.190	p = 0.061	p < 0.001	p = 0.024
Vaginal	1.00	1.00	1.00	1.00
Cesarean section	1.10 (0.95; 1.27)	1.15 (0.99; 1.34)	1.29 (1.12; 1.47)	1.17 (1.02; 1.34)
Breastfeeding duration (months)	p = 0.007	p = 0.468	p = 0.276	p = 0.237
No breastfeeding	1.10 (0.90; 1.35)	0.90 (0.73; 1.10)	1.05 (0.86; 1.27)	0.95 (0.77; 1.17)
≤ 6	1.31 (1.11; 1.54)	1.05 (0.89; 1.24)	1.16 (1.00; 1.27)	1.08 (0.92; 1.25)
7-12	1.00 (0.82; 1.22)	0.95 (0.78; 1.17)	1.06 (0.88; 1.27)	1.17 (0.97; 1.41)
> 12	1.00	1.00	1.00	1.00
Maternal perception of child's health		p < 0.001	p < 0.001	p < 0.001
Excellent	-	1.00	1.00	1.00
Very good/Good	-	1.53 (1.33; 1.76)	1.66 (1.45; 1.90)	1.60 (1.40; 1.83)
Regular/Bad	-	4.08 (2.70; 6.16)	3.99 (3.02; 5.28)	4.54 (3.39; 6.01)

95%CI: 95% confidence interval.

* Logistic regression. Multivariable analysis – 1st level: backwards selection: maternal age, schooling, skin color, marital status, and family income, 2nd level: children sex and gestational age, 3rd level: type of delivery, 4th level: breastfeeding duration and maternal perception of the child's health. Significance level: p-value < 0.05, p-value < 0.2 kept in the model for confusion control purposes.

Results

The number of participants, with information about the outcome, at 3, 12, 24, and 48 months of age was 4,106, 4,017, 4,005, and 3,994, respectively. The high follow-up rates of the cohort resulted in very similar samples at all follow-ups. About a third of mothers were aged 30 years or older and over 60% had nine or more years of formal education. Average family incomes ranged from one to six minimum wages and most women reported to be white and living with a partner. Less than 15% of children included in the cohort were born prematurely and about 65% of deliveries were cesarean sections. Over 80% of mothers reported breastfeeding their babies for at least three months and rated their children's health as excellent or very good/good. There were no differences among follow-up samples, except for breastfeeding duration and maternal perception of the child's health. Mothers included in the 48-month follow-up showed lower frequencies of "no breastfeeding" and higher frequencies of evaluating their infant's health as "very good or excellent" (Table 2).

Table 2

Description of the 2015 Pelotas (Brazil) birth cohort total population sample, and samples at three, 12, 24, and 48 months of age according to maternal and child's characteristics.

Characteristics	Total cohort [n = 4,275] %	3 months [n = 4,110] %	12 months [n = 4,018] %	24 months [n = 4,014] %	48 months [n = 4,010] %	p-value *
Maternal						
Age (years)						0.952
< 19	14.5	14.6	14.5	14.4	14.5	
20-24	23.7	23.7	23.6	23.7	23.8	
25-30	29.0	29.1	29.1	29.0	28.9	
> 30	32.8	32.6	32.8	32.9	32.8	
Educational attainment (years)						0.882
0-4	9.2	9.0	8.9	8.9	8.8	
5-8	25.6	25.7	25.5	25.8	26.0	
9-12	34.1	34.4	34.8	34.5	34.8	
> 12	31.1	38.9	30.8	30.8	30.4	
Family income (minimum wage)						0.698
≤ 1	12.6	12.6	12.5	12.5	12.4	
1.1-3.0	47.1	47.1	47.1	47.3	47.7	
3.1-6.0	26.4	26.5	26.6	26.5	26.5	
6.1-10.0	7.6	7.5	7.5	7.4	7.4	
> 10.0	6.3	6.3	6.3	6.3	6.0	
Skin color						0.751
White	70.9	70.8	70.9	70.7	70.3	
Black	15.6	15.7	15.8	15.9	16.0	
Mixed-race/Yellow/Other	13.5	13.5	13.3	13.4	13.7	
Living with a partner						0.991
No	14.2	14.2	13.9	14.0	14.2	
Yes	85.8	85.8	86.1	86.0	85.8	

(continues)

Table 2 (continued)

Characteristics	Total cohort [n = 4,275] %	3 months [n = 4,110] %	12 months [n = 4,018] %	24 months [n = 4,014] %	48 months [n = 4,010] %	p-value *
Child						
Sex						0.977
Male	50.6	50.5	50.9	50.6	50.6	
Female	49.4	49.5	49.1	49.4	49.4	
Gestational age (weeks)						0.994
Preterm (< 37)	15.5	14.7	14.6	14.7	14.7	
Early term (37-38)	37.1	37.2	37.4	37.4	37.2	
Full term (39-40)	39.7	40.2	40.1	39.9	40.2	
Late & post term (41-42)	7.8	7.9	7.9	8.0	7.8	
Type of delivery						0.973
Vaginal	34.8	35.1	35.0	35.1	35.2	
Cesarean section	65.2	64.9	65.9	64.9	64.8	
Breastfeeding duration (months)						0.013
No breastfeeding	18.6	16.7	15.8	15.3	13.3	
≤ 6	33.5	34.2	34.5	34.9	35.7	
7-12	16.4	16.9	17.2	17.1	17.5	
> 12	31.5	32.2	32.5	32.7	33.5	
Maternal perception of child's health						< 0.001
Excellent	-	-	47.8	40.0	38.0	
Very good/Good	-	-	47.4	52.8	55.1	
Regular/Bad	-	-	4.8	7.2	6.8	

* Chi-squared test for tendency from 3 to 48 months.

Cohort participants reported a total of 5,463 medications for the 4,106 children included in the 3-month sample. These numbers were 5,643 at 12 months, 4,128 at 24 months, and 3,321 at 48 months of age. In total, 67.2% (95%CI: 65.8; 68.6), 68.2% (95%CI: 66.8; 69.6), 52.4% (95%CI: 50.9; 54.0), 47.2% (95%CI: 45.7; 48.8) of all interviewed children at each respective follow-up were given at least one medication within 15 days before the interview (Table 3).

Except for the 3-month follow-up, at the 12, 24, and 48 months interviews, higher maternal age was associated with a higher prevalence of medication use [71.4% (95%CI: 68.9; 73.8) vs. 59.5% (95%CI: 55.4; 63.4), 53.8% (95%CI: 51.1; 56.4) vs. 46.3% (95%CI: 42.3; 50.4), and 51% (95%CI: 48.3; 53.7) vs. 39.4% (95%CI: 35.5; 43.4) at 12, 24, and 48 months, respectively]. Children of mothers with more years of formal education also received more medication than those of less-educated mothers [75.1% (95%CI: 72.7; 77.4) vs. 60.5% (95%CI: 55.4; 65.4), 76.4% (95%CI: 73.9; 78.6) vs. 57.1% (95%CI: 51.9; 62.2), 59.3% (95%CI: 56.5; 62.0) vs. 44.7% (95%CI: 39.6; 49.9), and 52.2% (95%CI: 49.4; 55.0) vs. 43.0% (95%CI: 37.9; 42.3, respectively]. A similar pattern was observed among richer mothers [77.2% (95%CI: 71.7; 81.9) vs. 62.1% (95%CI: 57.8; 66.2), 76.8% (95%CI: 71.2; 81.6) vs. 60.4% (95%CI: 56.1; 64.6), 60.5% (95%CI: 54.3; 66.3) vs. 46% (95%CI: 41.7; 50.4), and 56.7% (95%CI: 50.3; 62.8) vs. 43.5% (95%CI: 39.2; 48.0), respectively]. Children born to those women showed a higher prevalence of medication use. Living with a partner was not associated with the prevalence of medication use in three of the four follow-ups.

Medication use was higher among male infants only at 12 months [70.5% (95%CI: 68.5; 72.4) vs. 65.8% (95%CI: 63.7; 67.9)]. Children that were full or late/post-term showed a lower prevalence of medication use at all ages, with no significant difference at 24 months. Cesarean deliveries were associated with a higher prevalence of medicine use, whereas breastfeeding duration seems to be disassociated with medication use. Higher maternal perception of child's health were associated

Table 3

Prevalence of medication use according to maternal and child's characteristics at 3, 12, 24, and 48 months of age. The 2015 Pelotas (Brazil) birth cohort.

Characteristics	Medications use prevalence [% (95%CI)]			
	3 months [n = 4.106]	12 months [n = 4.017]	24 months [n = 4.005]	48 months [n = 3.994]
Maternal				
Age (years)				
< 19	64.3 (60.4; 68.1)	59.5 (55.4; 63.4)	46.3 (42.3; 50.4)	39.4 (35.5; 43.4)
20-24	65.6 (62.6; 68.5)	66.2 (63.1; 69.2)	52.3 (49.1; 55.5)	45.7 (42.6; 48.9)
25-30	66.9 (64.2; 69.6)	70.7 (68.0; 73.2)	54.2 (51.3; 57.0)	48.2 (45.3; 51.1)
> 30	69.9 (67.4; 72.3)	71.4 (68.9; 73.8)	53.8 (51.1; 56.4)	51.0 (48.3; 53.7)
Educational attainment (years)	60.5 (55.4; 65.4)	57.1 (51.9; 62.2)	44.7 (39.6; 49.9)	43.0 (37.9; 42.3)
0-4	61.1 (58.1; 64.0)	61.5 (58.5; 64.4)	48.3 (45.3; 51.4)	43.4 (40.4; 46.4)
5-8	66.4 (63.9; 68.8)	68.8 (66.3; 71.1)	51.5 (48.9; 54.2)	46.9 (44.3; 49.5)
9-12	75.1 (72.7; 77.4)	76.4 (73.9; 78.6)	59.3 (56.5; 62.0)	52.2 (49.4; 55.0)
> 12	60.5 (55.4; 65.4)	57.1 (51.9; 62.2)	44.7 (39.6; 49.9)	43.0 (37.9; 42.3)
Family income (minimum wage)				
≤ 1	62.1 (57.8; 66.2)	60.4 (56.1; 64.6)	46.0 (41.7; 50.4)	43.5 (39.2; 48.0)
1.1-3.0	64.8 (62.7; 66.9)	66.4 (64.3; 68.5)	50.2 (48.0; 52.5)	46.3 (44.0; 48.5)
3.1-6.0	69.0 (66.1; 71.6)	70.2 (67.3; 72.8)	55.6 (52.6; 58.6)	47.3 (44.3; 50.3)
6.1-10.0	76.4 (71.4; 80.9)	78.3 (73.2; 82.6)	60.0 (54.3; 65.5)	52.4 (46.6; 58.0)
> 10.0	77.2 (71.7; 81.9)	76.8 (71.2; 81.6)	60.5 (54.3; 66.3)	56.7 (50.3; 62.8)
Skin color				
White	69.2 (67.5; 70.8)	70.4 (68.7; 72.0)	53.9 (52.1; 55.8)	48.6 (46.8; 50.5)
Black	60.2 (56.4; 63.9)	62.8 (58.9; 66.5)	48.9 (45.0; 52.8)	44.6 (40.8; 48.5)
Mixed-race/Yellow/Other	64.9 (60.8; 68.8)	63.2 (59.0; 67.2)	48.8 (44.6; 53.0)	43.3 (39.2; 47.5)
Living with a partner				
No	31.3 (27.6; 35.2)	61.4 (57.3; 65.4)	50.7 (46.7; 54.8)	45.4 (41.3; 49.5)
Yes	67.0 (65.4; 68.5)	69.3 (67.8; 70.8)	52.8 (51.1; 54.4)	47.6 (45.9; 49.2)
Child				
Sex				
Male	68.8 (66.7; 70.7)	70.5 (68.5; 72.4)	53.9 (51.7; 56.0)	46.9 (44.8; 49.1)
Female	65.6 (63.5; 67.7)	65.8 (63.7; 67.9)	51.0 (48.8; 53.2)	47.6 (45.4; 49.8)
Gestational age (weeks)				
Preterm (< 37)	78.7 (75.2; 81.8)	73.1 (69.4; 76.6)	53.3 (49.3; 57.3)	47.4 (43.4; 51.5)
Early term (37-38)	69.6 (67.2; 71.8)	69.2 (66.8; 71.5)	53.3 (50.8; 55.8)	50.1 (47.6; 52.7)
Full term (39-40)	62.3 (60.0; 64.7)	66.6 (64.3; 69.9)	52.5 (50.0; 54.9)	45.1 (42.7; 47.5)
Late & post term (41-42)	59.4 (54.0; 64.7)	62.3 (56.8; 67.5)	46.7 (41.3; 52.2)	44.2 (38.8; 49.8)
Type of delivery				
Vaginal	63.3 (60.8; 65.8)	63.5 (60.9; 66.0)	46.8 (44.2; 49.4)	43.3 (40.7; 45.9)
Cesarean section	69.3 (67.5; 71.0)	70.8 (69.0; 72.5)	55.6 (53.6; 57.4)	49.4 (47.5; 51.3)
Breastfeeding duration (months)				
No breastfeeding	67.0 (63.4; 70.4)	65.3 (61.5; 68.9)	51.3 (47.3; 55.2)	44.8 (40.6; 49.1)
≤ 6	71.0 (68.6; 73.3)	69.4 (66.9; 71.8)	54.3 (51.7; 56.9)	47.6 (45.1; 50.2)
7-12	-	69.9 (65.4; 72.3)	53.2 (49.5; 56.9)	50.8 (47.1; 54.5)
> 12	-	68.0 (65.4; 70.4)	50.6 (47.9; 53.3)	45.9 (43.3; 48.6)
Maternal perception of child's health				
Excellent	-	64.1 (62.0; 66.2)	44.8 (42.4; 47.3)	39.4 (37.0; 41.9)
Very good/Good	-	70.6 (68.5; 72.6)	55.5 (53.3; 57.6)	49.5 (47.4; 51.6)
Regular/Bad	-	85.0 (79.1; 89.3)	72.8 (67.3; 77.6)	72.5 (66.9; 77.5)
Total	67.2 (65.8; 68.6)	68.2 (66.8; 69.6)	52.4 (50.9; 54.0)	47.2 (45.7; 48.8)

95%CI: 95% confidence interval.

with lower medication prevalence, when compared to those whose mothers reported their children's health status to be bad or regular (Table 3).

The number of children receiving at least one medication 15 days before each interview decreased as children grew older. The proportion of children who received four or more medications also decreased at every follow-up (Figure 1).

The main source of prescription for these drugs was current medical indication, although we observed a marked reduction over time. We also found an increase in reported previous medical prescription and paternal medication indication as children's age progressed. We observed a 4.1% frequency of parent's indication at three months and 14.8% at 48 months of age. Chronic medication use peaked at 12 months; 42.3% of medication were used for longer than a month, compared to 38.9% at three months. In following years, these figures started to decrease: 19.3% and 16.4% at 24 and 48 months, respectively (Figure 2).

The most frequently used medications at three months were "Drugs for functional gastrointestinal disorders" (A03), showing an important decrease over the years. They comprised 26% of all taken drugs at 3 months, but only 2.6%, 2.2%, and 1.9% at 12, 24, and 48 months, respectively. Analgesics (N02) were the second most used group at three months (21.1%) and its use remained above 15% for all age groups (17.3% 22.4%, and 16.4% at 12, 24, and 48 months, respectively). Another frequently administrated group was vitamins (A11), comprising 14.2% of all medication used at three months, peaking at 12 months. Vitamins were 16.2% of all medication children used at that age. At 24 and 48 months, proportions decreased markedly to 5.5% and 2.9%, respectively. Nasal formulations (R01) were nearly 10% of all medication used in every follow-up (11.2%, 6.2%, 8% and 9.3%, respectively). Anti-inflammatory medication (M01) increased from 3.6% to 8.8% in the three to 12-month period, remaining at about 15% at 24 (14.1%) and 48 months (14.5%). (Figure 3).

Figure 1

Medication use frequency according to the number of drugs taken at 3 [n = 4.106], 12 [n = 4.017], 24 [n = 4.005], and 48 months [n = 3.994] of age. The 2015 Pelotas (Brazil) birth cohort.
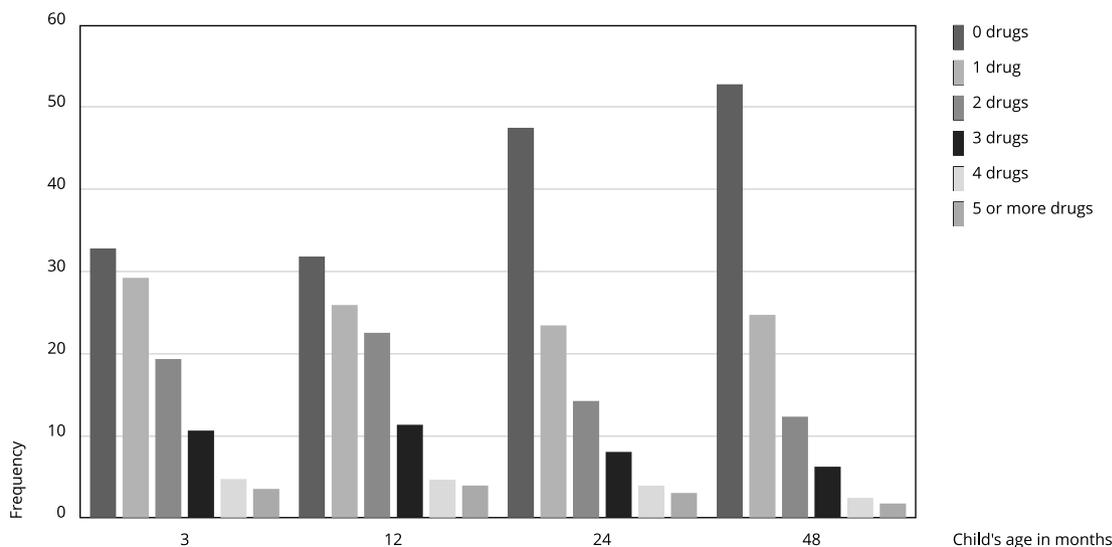
Figure 2

Medication prescription source and continuous or sporadic use at 3 [n = 5.462), 12 [n = 5.642], 24 [n = 4.128], and 48 months [n = 3.321] of age. The 2015 Pelotas (Brazil) birth cohort.

2a) Medications prescription source
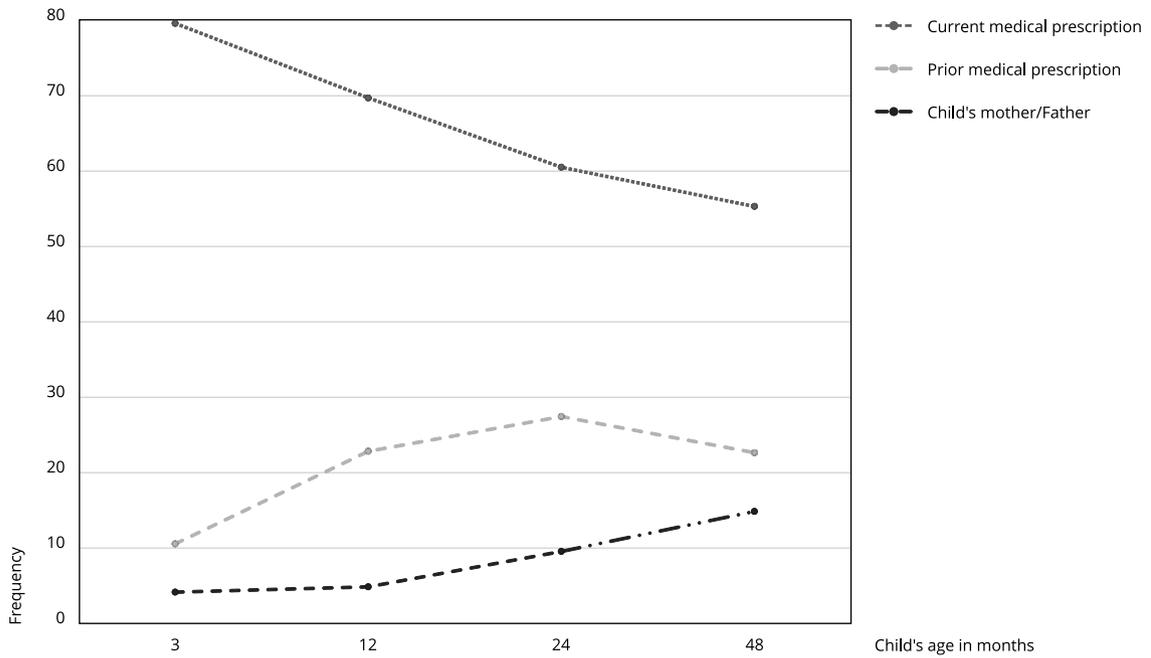
2b) Medications continuous or sporadic use
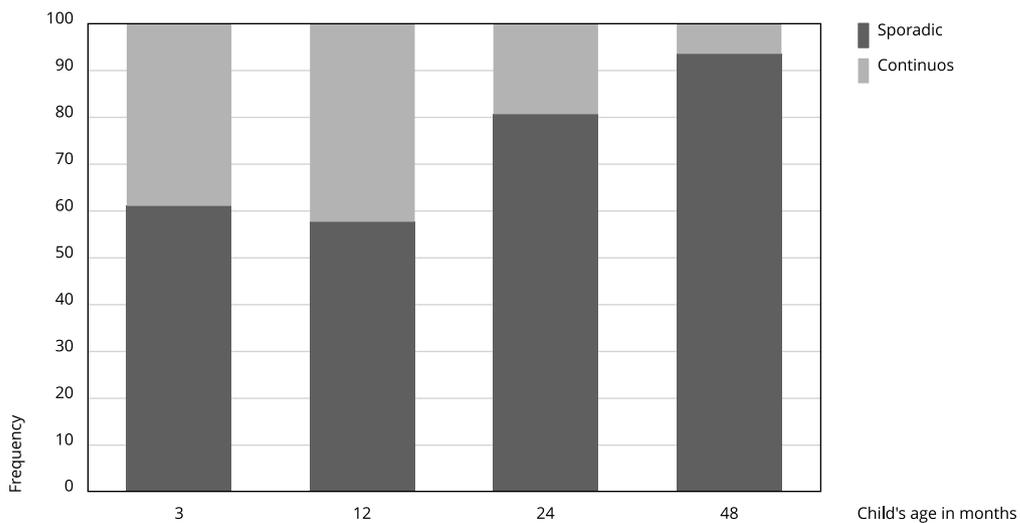
Figure 3

Most used medication frequency at 3 [n = 5.462], 12 [n = 5.642], 24 [n = 4.128], and 48 months [n = 3.321] of age according to ATC level 2 classification. The 2015 Pelotas (Brazil) birth cohort.
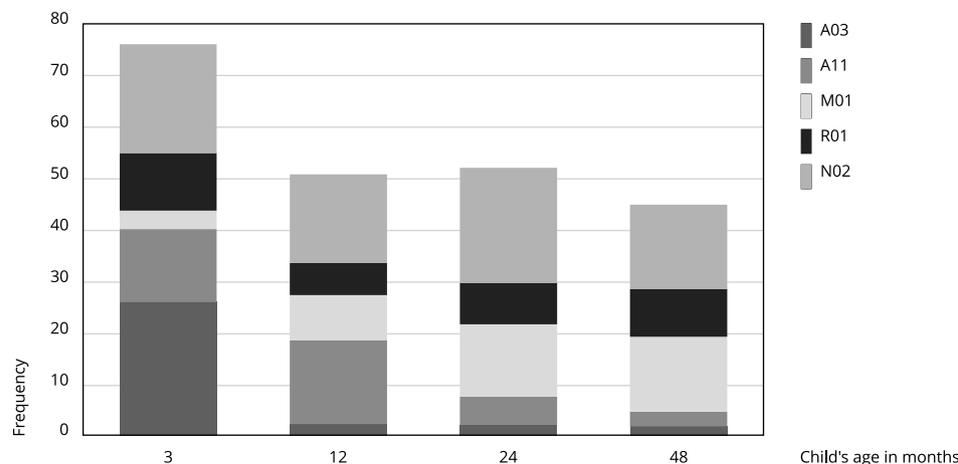
ATC: Anatomical Therapeutic Chemical Classification System, level 2 classifies drugs according to Anatomical or Pharmacological groups (ATC1) and Pharmacological or Therapeutic subgroup (ATC2).
A03: drugs for functional gastrointestinal disorders; A11: Vitamins; M01: anti-inflammatory and antirheumatic products; N02: Analgesics; R01: nasal preparations.

Supplementary Material (http://cadernos.ensp.fiocruz.br/static//arquivo/suppl-e00117221_7157.pdf) describes all medications used at each follow-up, according to levels 1 and 2 of the ATC. The Supplementary Material also describes the 10 most used drugs at each follow-up, according to their chemical name, and crude and adjusted associations of medication use with maternal and child characteristics (Table 1).

Discussion

About two-thirds of the children included in the study used at least one medication 15 days before the interview at three and 12 months of age. At ages 24 and 48 months, half the children met that criteria. These results are similar to previous national and international studies that evaluated medication use in children younger than 12 years of age [3,13,14,15,16,17,18].

Data from the *Brazilin National Survey on Access, Utilization and Promotion of Rational Use of Medicines* (PNAUM), a nationwide household survey of a representative sample of the Brazilian urban population [17], showed a 42% prevalence of medication use from children aged zero to four years. The higher prevalence found in our results might be due to methodological differences between the studies. Although both have the same recall period, in the PNAUM, chronic and sporadic medication use are collected separately since chronic drugs are often linked to chronic morbidities. Also, for children aged 15 or younger, PNAUM questionnaires are answered by the adult indicated as the guardian for the child's medication use who may not necessarily be the child's main caregiver [19], which could possibly lead to an underestimated prevalence.

Medication use was more frequent among children of older, white, higher-educated women. When testing for potential confounding factors, only maternal schooling level was associated to infant medication use at all ages (Table 1). Maternal education seems to confound the association between medication use and other maternal characteristics. Women with higher schooling level

and family incomes have more access to health-related information and resources. Medication use depends on access, which is directly linked with public services supply and purchasing power [20].

Prematurity is associated with infants' health issues, such as infections, motor delay, and respiratory illness like asthma [21]. This may relate to an increased need for medication use to treat such conditions. Also, preterm births are associated with higher hospitalization rates, when compared to full-term children, in the first five years of life, which also affects drug administration [22].

Cesarean deliveries have been associated with an altered immunological development due to an ineffective mother-child microbiome transfer, exposure to prophylactic antibiotics and synthetic hormones, and reduced exposure to mechanical forces and stress hormones that occur during vaginal childbirth [23]. An impacted immune system could make children more vulnerable to morbidities, hence increasing medication use during infancy.

Very good or excellent maternal perception of the child's health improved over the years. Children aged under five years are responsible for most of childhood morbidity and mortality cases [24]. As age progresses, lower frequencies of health events are expected to happen. This is consistent with mothers' better health evaluation of their children and the lower frequency of medication use in older children from the Pelotas cohort.

In this study, the main source of prescription was current medical indication. In Brazil, childcare routines include monthly medical appointments during children's first year of life. This enables parents to have periodic access to healthcare providers and guidance on medicine prescriptions to infants. Parents' self-medicating their children also increased with infants' age. A previous study, using data from the 1993 Pelotas (Brazil) birth cohort, reported an increase of self-medication until the age of three months, followed by a continued decrease until early adolescence [4]. Considering the wider access to information parents have nowadays, and that children's most common health complaints, such as colds and fevers, are medicated by a group of drugs which are easy to obtain and have become familiar to parents, this could make them confident to self-prescribe medications over time. Self-medication is especially concerning among children, in comparison to adults, due to the lower evidence on dosage, efficacy, and safety of medications in this group. This unavailability of information can be related to lower interest in conducting studies in this age group, probably due to ethical considerations and concerns with pediatric research, which is only conducted if its information is relevant for pediatric public health [25].

The lack of information about pediatric patients also applies to drug-to-drug interactions and is especially concerning in the presence of polypharmacy, defined as the daily use of five or more medications [26]. Although decreasing after 24 months, about 4% of our sample frequently used five or more drugs. A limited number of studies have characterized drug-to-drug pharmacokinetics in infant patients, often establishing it by extrapolating adult recommendations [27], which can lead to incorrect predictions of the effects of drug interactions, making polypharmacy especially concerning among children.

The age in which vitamins are preemptively prescribed coincides with the higher frequency of chronic medication use and larger total number of medicines used. Most medical professionals will follow the updated Brazilian Pediatric Association recommendation of initiating iron and vitamin supplementation at three months of age. Another possible cause for the higher proportion of medicine use in the first three months of life could be episodes of colic. Although the etiology of colic remains unclear, it has been associated with gastrointestinal issues, such as constipation, gastroesophageal reflux, and gas, among others [28]. Drugs that can relieve colic symptoms are commonly used at this stage of the infant's life, explaining the high frequency of drug use in three-month-old children. After this period, this prevalence is drastically reduced, as gastrointestinal symptoms tend to decrease and even disappear. Many drugs in the analgesic category are over-the-counter medications. This makes it easier for parents to purchase and to keep them at home for use as required. Also, their use is associated with mild symptoms that fail to lead to medical attention seeking, which maybe a possible reason for the maintenance of their elevated prevalence.

The most frequently used medication groups were vitamins (A11), nasal preparations (R01), drugs for functional gastrointestinal disorders (A03), anti-inflammatory and antirheumatic products (M01), and analgesics (N02). Vitamins were more frequent among 12-month-old children. The Brazilian

Pediatric Association recommends vitamin D supplementation starting at birth until 12 months of age [29], explaining the marked decrease in its prevalence in infants aged from 12 to 48 months.

Nasal obstruction is commonly observed in infants, mostly caused by allergies or infections. Nasal saline irrigation is frequently used to alleviate nasal obstruction symptoms and to help to eliminate mucus, improving the child's breathing [30]. Easy, over-the-counter access to these formulations, associated with their easy handling, could explain the prevalence of nasal preparations in infants' first years of life.

Anti-inflammatory drugs are commonly used for antipyretic, analgesic, and anti-inflammatory effects. Like analgesics, anti-inflammatories have many simple applications for common childhood morbidities and symptoms. Therefore, parents could have used previous medical prescriptions to treat their children following their health complaints, thus explaining the rising frequencies shown in this study as children get older.

Medication use in the first years of life must balance potential benefits and risks. The lack of evidence on maximum dosage and possible side effects on this group demand more attention from management of medicine administration [31].

Strength and limitations

This was a population-based cohort study with follow-up rates of over 90%. Its short recall period (15 days) makes it less likely for caregivers' information to be biased.

As limitations for this study, we must highlight that, although the interviewers were trained to collect all medication used, underreporting is still a possibility. However, asking for participants to bring medicine prescriptions or packaging aimed to minimize this risk. Also, as Pelotas is a city located in the Southernmost state of Brazil, and given the large extension of the country, drug use profiles may vary among children from different regions.

Conclusion

We found a high prevalence of medicine use and a high proportion of parental self-medication in children younger than four years of age. These results highlight the need to further spread information on proper medicine administration to children, as well as medical examination before any drug prescription. Understanding children's medication use profile can help guide the design and implementation of health policies that seek to reduce unnecessary and/or inappropriate medication use in young children.

Contributors

Additional informations

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Resumo

O uso de medicação é parte importante do processo de saúde, e a prevalência de uso entre lactentes pode chegar a 65% nos primeiros meses de vida. O uso excessivo de medicação pode levar a um aumento dos danos potenciais em relação aos benefícios. Levando isso em conta, o estudo atual buscou descrever o uso de medicação em crianças aos 3, 12, 24 e 48 meses. Foram aplicados questionários padronizados para avaliar os padrões de uso de medicação e covariáveis. O uso de medicação foi investigado enquanto desfecho, e definido como história de ter recebido qualquer medicação nos 15 dias anteriores à entrevista. A prevalência do uso de medicação e os intervalos de 95% de confiança (IC95%) foram descritos através do teste de qui-quadrado. Também foram relatadas a fonte da prescrição e a frequência de uso, junto com a medicação mais frequente em cada consulta. A prevalência do uso de medicação foi de 67,2% (IC95%: 65,8; 68,6), 68,2% (IC95%: 66,8; 69,6), 52,4% (IC95%: 50,9; 54,0) e 47,2% (IC95%: 45,7; 48,8), aos 3, 12, 24 e 48 meses, respectivamente. Ao longo dos anos, foram observados uma diminuição na proporção de medicamentos com prescrição médica e um aumento na automedicação (indicação pelos pais ou responsáveis). Os medicamentos mais frequentes eram para transtornos gastrointestinais (A03), vitaminas (A11), analgésicos (N02), anti-inflamatórios (M01) e formulações nasais (R01). Encontramos mais de 50% de uso total e de automedicação (indicação pelos pais/responsáveis) em crianças abaixo de 4 anos de idade. Os resultados destacam a necessidade de alertar os cuidadores sobre a importância do exame profissional e prescrição adequados antes da administração de medicamentos a crianças.

Uso de Medicamentos; Lactente; Pré-Escolar; Estudos Longitudinal; Cuidado da Criança

Resumen

El consumo de medicamentos es una parte importante del proceso de salud y la prevalencia de su uso entre bebés puede llegar a un 65% durante los primeros meses de vida. El excesivo consumo de medicamentos podría conducir a un incremento en sus perjuicios potenciales frente a sus beneficios. Teniendo esto en cuenta, el objetivo de este estudio fue describir el uso de la medicación en niños de 3, 12, 24, y 48 meses. Se aplicaron cuestionarios estandarizados para evaluar los patrones de uso de la medicación y sus covariables. Se investigó el uso de la medicación como un resultado y se definió como haber recibido alguna medicación en los últimos 15 días antes de la entrevista. Se describieron la prevalencia del uso de la medicación y los intervalos de 95% de confianza (IC95%), usando tests chi-cuadrado. También se informó de la fuente de prescripción y frecuencia del consumo, junto a la medicación más frecuente en cada seguimiento. La prevalencia en el uso de la medicación fue de un 67,2% (IC95%: 65,8; 68,6), 68,2% (IC95%: 66,8; 69,6), 52,4% (IC95%: 50,9; 54,0), 47,2% (IC95%: 45,7; 48,8), a los 3, 12, 24, y 48 meses, respectivamente. Se observó una disminución en la proporción de medicamentos recetados médicamente y un incremento en la automedicación a lo largo de los años. Los medicamentos más frecuentemente usados fueron los destinados para desórdenes gastrointestinales (A03), vitaminas (A11), analgésicos (N02), antiinflamatorios (M01), y preparados nasales (R01). Descubrimos que más de un 50% del total y automedicación en el consumo de medicinas en niños menores de 4 años. Estos resultados subrayan la necesidad de avisar a los cuidadores sobre la importancia de un examen profesional apropiado y la receta antes de la administración del medicamento a niños.

Utilización de Medicamentos; Lactante; Preescolar; Estudios Longitudinales; Cuidado del Niño