

The Pattern of Antibiotic Administration for Toddlers and Infants with Acute Respiratory Infections (Mashhad, Iran)

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ABSTRACT

Background: Acute Respiratory Infections (ARI) are the main cause for Antibiotic (AB) use in all age groups, specially during the first two years of life. The local information about the pattern of AB prescription in ARI is a necessary part of any program which aims for logical use of AB. The current study was designed to find the frequency and types of AB administration for ARI in young children (<2years) in Mashhad, Iran.

Methods: This is an observational cohort study which started in November 2005 and ended in May 2006. The study group was composed of 1000 infants between 6 month and 20 months old. The children were followed monthly via telephone calls (for up to six month after the first interview) and were surveyed on the signs and symptoms of Acute Respiratory Infection and systemic Antibiotic use during each month.

Results: The average monthly incidence of ARI was 34.5% in the study population; 66.3 % (mean) of the children with ARI were visited by a doctor, which resulted in AB prescription in 32.7 % (mean) of times. The frequency of injectable antibiotics was almost twice for oral ABs, and benzatin penicillin was the most prominent prescribed AB (54% of all ABs).

Conclusion: The rate of AB administration for infants with ARI is not very high in Mashhad city. However, the frequency of AB injections is unacceptable.

Keywords: Antibiotics, ARI, Infants, Respiratory Infections

Introduction

Antibiotic resistance is a serious and fast-growing problem in the world as well as our city (Mashhad, Iran). Group A β -hemolytic streptococcus is resistant to erythromycin in 73.7% of children (1).

Streptococcus pneumonia is resistant to erythromycin, cefixime and amoxicillin in 43%, 40% and 22% of children respectively. Cotrimoxazole, which was an effective broad-spectrum antibiotic 20 years ago, does not seem to be effective for respiratory, gastrointestinal and urinary infections in Mashhad (2).

Inappropriate use of antibiotics for Acute Respiratory Infections (ARI), as the most common childhood disorder, is the leading fuel for the expanding fire of antibiotic resistance. In this research, we have studied the pattern of antibiotic use among infants and young children (<2 years old) during influenza season in Mashhad.

Method

This is an observational cohort study which started in November 2005 and ended in May

2006. The study group was composed of 1000 infants aged between 6 month and 20 months old who were brought in for routine vaccination. Multistage sampling method was applied in order to select the participants. At first, 10 centers were randomly selected out of all 46 primary healthcare centers in Mashhad, Iran. Afterwards, 100 infants who were brought in for routine vaccination were randomly selected from each primary healthcare centre. Ten healthcare workers were educated to interview the parents. They called the caregivers of infants monthly (for up to six month) after the first interview and completed certain checklists. The checklists included information on the signs and symptoms of Acute Respiratory Infection (ARI), any visits by doctors concerning ARI and systematic antibiotic therapy during the last month. The follow-up period lasted for 6 months and each child was reassessed every month during this period. Two educated healthcare providers managed and facilitated the data collection phase for this study.

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Table 1. Sociodemographic characteristic of participants

	Mean	SD
Age	13.86	5.12
Weight(g)	9715.72	1777.03
Birth Weight(g)	3198.27	521.12
Mothers age	26.73	5.03
Fathers age	31.36	6.67
Mothers job	num	%
employed	58	5.3
housewife	932	94.7
Fathers job	num	%
governmental	378	38.2
Self employed	612	61.8
Day care nursery	31	3.1
Insurance coverage	422	42.7
lactation	num	%
Breast milk	930	94
formula	60	6
Visible disability	26	2.7
congenital disease	19	1.9

Neonate who showed more than one of the signs or symptoms of ARI were first thought to have influenza-like illnesses by their caregivers. The symptoms included fever, rhinorrhea, coughing, shortness of breath, otitis and bloodshot eyes. Otitis was defined as the cases were visited by a doctor and after getting history of earache, irritability and otorrhoea among neonates. This study was approved by the Ethics Committee of Mashhad University of Medical Sciences. Participation in the experiment was voluntary and based on informed consent. During each stage of the study, the parents were free to refuse to participate at any given point. No conflict of interest was declared.

SPSS 11.5 software (SPSS Inc., Chicago, Illinois, USA) was used for all statistical analyses. Standard descriptive statistics were applied to describe the

pattern of the data. Chi-square test was used to examine the significance of the association between categorical data. Normality of the data was checked with Kolmogorov-Smirnov test. When the test statistics follow a normal distribution, T-test is used. For the non-normal distributions Mann-Whitney-U test was applied. All tests were 2-tailed and the probability values < 0.05 were considered significant.

Results

One thousand infants were followed for a six-month period. During the study, ten infants (1%) were lost from follow-up. The mean age of the children was 13.86 months (± 5.12 M). Table 1 shows the demographic features of the study participants in detail. Table 2 depicts the frequency of flu-like illnesses during the study period. The monthly incidence of ARI varied from 35.3% to 49.9% (mean 34.5). The number of hospital admissions due to the severance or complications of the disease varied between 0 to 3 per month.

Rhinorrhea (79.6%), fever (76.8%), cough (66.8%), bloodshot eyes (11.9%), dyspnea (8.9%) and ear pain (4.6%) has been the most frequent symptoms (Table 3).

More than 60% of the children with ARI were visited in a doctor's office each month (monthly variation from 58.9% to 70.6%). Furthermore, 58.7% (53-60.7) of all contacts were with general practitioners and 41.3% (39.3-47) with pediatrician. On average, certain medication was prescribed for 94.1% of the cases 32.7 % of which (18.8%-39.8%) were antibiotics.

Table 2. Distribution of flu like illness, doctor's visit and drug prescription among study participants

Follow up schedule	Flu like illness N(%)	Doctor's visit			Hospital admission N(%)	Drug prescription* N(%)	Antibiotic prescription** N(%)	Dexamethasone**
		General practitioner N(%)	Pediatrician N(%)	Total N (%)				
1 st month	489(94.4)	175(60.1)	113(39.9)	288(58.9)	3	258(89.6)	103(39.8)	14(4.9)
2 nd month	486(49)	207(60.7)	134(39.3)	341(70.2)	1	307(90)	132(38.7)	10(2.9)
3 rd month	460(46.5)	183(58.1)	143(41.9)	326(70.9)	0	316(96.9)	103(31.6)	24(7.4)
4 th month	412(41.6)	176(60.3)	116(39.7)	297(70.9)	0	281(96.2)	110(37.7)	39(13.4)
5 th month	361(36.5)	124(53)	110(47)	234(64.8)	2	224(95.7)	44(18.8)	18(7.7)
6 th month	350(53.3)	130(59.9)	87(40.1)	217(62)	1	209(96.3)	65(29.6)	16(7.4)
mean	43.5	58.7	41.3	66.3		94.1	32.7	7.3

*percent among patients referred to doctor

** percent among drug recipients

Table 3. Distribution of flu like illness signs and symptoms among study participants

Follow up schedule	Fever N (%)	Rhinorrhea N (%)	Cough N (%)	Eye redness N (%)	Dyspnea N(%)	Earache N (%)
1 st month	253(51.7)	356(28.7)	299(61.1)	60(12.3)	37(7.6)	17(3.5)
2 nd month	314(64.6)	364(74.9)	328(67.5)	51(10.5)	43(8.8)	24(4.9)
3 rd month	346(75.2)	372(80.9)	328 (71.3)	67(14.6)	49(10.7)	25(4.9)
4 th month	305(74)	342(83)	304(73.8)	47(11.4)	41(9.9)	26(6.3)
5 th month	265(73.4)	300(83.1)	242(67)	53(14.7)	28(7.8)	16(4.4)
6 th month	238(68)	289(82.6)	208(59.4)	27(7.7)	24(8.9)	13(3.7)
mean	67.8	79.6	66.8	11.9	8.9	4.6

Table 4. Frequency of prescribed antibiotics according to follow up schedule

Antibiotic type	First month	Second month	Third month	Forth month	Fifth month	Sixth month
Co-trimoxazole	20	11	6	18	7	12
Amoxicillin	9	10	5	2	7	5
Erythromycin	2	3	1	0	0	0
Azithromycin	0	1	0	1	0	0
Cefalexin	2	0	2	2	0	0
Co-amoxiclav	0	0	2	2	2	1
Cefixime	0	1	0	1	1	2
	33(32.3)	26(27.1)	16(18.6)	26(30.9)	17(63)	20(44.4)
Ceftriaxone	2	2	0	11	2	5
Gentamicin	5	17	2	8	4	5
P 6.3.3	53	57	66	54	19	29
P 800	2	7	0	2	0	1
P 1200	0	0	1	2	0	0
Ampicillin	7	13	17	7	2	5
Sum*	69(67.7)	96(72.9)	86(81.4)	84(69.1)	27(37)	45(56.6)
total sum**	102	122	102	110	44	65

Table 5. Frequency of prescribed drugs according to follow up schedule

Antibiotic	1st month	2 ^d month	3 ^d month	4 th month	5 th month	6 th month	mean
Antibiotic	103	132	103	110	44	65	
	56.9	66.4	57.7	63.3	49.3	60.6	59
	43.1	33.6	42.3	36.7	50.7	39.4	41
Dexamethasone	14	10	24	29	18	16	
	75	55.6	64.3	66.7	41.7	50	58.9
	25	44.4	35.7	33.3	58.3	50	41.1

Benzathine penicillin 54%, cotrimoxazole (suspension) 14.9%, ampicillin (ampoule) 10.2%, gentamicin 8.2% and amoxicillin 7.6% were among most commonly prescribed antibiotics (Table 4). It is worth mentioning that 64% of the prescribed antibiotics were injective and 36% were oral. Among the oral antibiotics, gentamicin and azithromycin were the most and the least frequent respectively. Among the injective antibiotics, penicillin (6.3.3) and benzathine penicillin (1.200) were the most and the least frequent respectively. For another thing, 59% (49.3-66.4) of the antibiotics were prescribed by general practitioners and 41% (33.6-50.7) by pediatricians. Overall, the rate of antibiotic injection was 1.89 times higher than the oral administration.

Moreover, dexamethasone was prescribed for patients 7.3% per month on average (Table 3), 58.9% of which was prescribed by general practitioners and 41.1% by specialists (Table 5).

Discussion

Most ARIs are upper respiratory infections and also viral in etiology which do not respond to antibiotics. Inappropriate prescription or giving extra doses of antibiotics for ARI is a global problem.

Our study indicated that more than 60 percent of the children with ARI were visited in a doctor's office every month. Nearly half of contacts were with general practitioners and the other half with

pediatricians. In general, medication was prescribed for approximately all cases. One third of the medications were antibiotics.

Nearly half of the prescribed antibiotics were Benzathine and penicillin. Other common prescribed antibiotics were cotrimoxazole (suspension), ampicillin (ampoule), gentamicin and amoxicillin. Most of the prescribed antibiotics were injectable. Among the oral antibiotics, gentamicin and azithromycin were the most and the least frequent respectively. On the other hand, among the injective antibiotics penicillin (6.3.3) and benzathine penicillin (1.200) were the most and the least frequent respectively. More than half of the antibiotics were prescribed by general practitioners and less than the other half were prescribed by pediatricians.

In Australia, 23% of the children (<5 years old) with ARI are treated with antibiotics (3). In Saudi Arabia, the rate of antibiotic usage for ARI is 87.8% in approximately 1200 prescriptions for all age groups (4).

Nguyen prospectively followed 823 Vietnamese children for 28 days to collect information regarding ARI and their use of any medications. During this period, 62% of the children received antibiotics which was only in case of mild ARI in 63% of the patients. This particular study is comparable to ours in the sense that both are patient-based while most of the previously mentioned studies are prescription-based. Additionally, we are aware of the fact that

many people might purchase the medication (antibiotics or cold medicine) directly from pharmacies without any prescription from any doctors (5). In Spain, antibiotics are given to 58.7% of the children with ARI who are visited in emergency rooms (bronchiolitis, 11.5%; bronchitis, 40.2%; pharyngitis, 80.9%; pneumonia, 92.4%; otitis, 93.4%; sinusitis, 92.6%). Amoxicillin/clavulanate (33.2%), amoxicillin (30.2%), cefuroxime axetil (8.5%) and azithromycin (6%) are the most commonly prescribed antibiotics, which is in contrast with our results in that injective antibiotics (mainly benzathine penicillin) are used almost twice (64/36) as oral antibiotics. Co-trimoxazol (64 cases) and Amoxicillin (38 cases) are the leading oral antibiotics in that regard. The fact that benzathine penicillin (in the form of 6.3.3 penicillin ampule) is by far the most frequent single antibiotic which is prescribed for infants with ARI in Mashhad, Iran is rather disappointing (6). The cost of inappropriate antibiotic use for children with ARI in Pakistan accounts for about 10% of the country's public health budget. In Multan, Pakistan, antibiotics are prescribed for 72% of the ARI patients. Meanwhile, a community study in four villages of Pakistan claimed that 80% of the ARI patients can successfully be managed without antibiotics (7). In 2004, in order to decrease antibiotic use and resistance in children, American Academy of Pediatrics recommended symptomatic treatment without antibiotics for non-sever Acute Otitis Media (AOM) in children of 24 months or older. In 2013, they expanded the recommendation to non-sever unilateral AOM in children of 6-23 months (8). In its Guideline for Bacterial Sinusitis, Infectious Diseases Society of America rules out any antibiotic treatments for non-sever acute sinusitis lasting for less than 10 days (9). Meropol reported trends in antibiotic prescription for ARIs in the UK (from 1990 to 2004) and made a 30.8% decline in the antibacterial usage for ARI children (10). On the other hand, Steinman studied the patterns of outpatient antibiotic use in the United States and noticed that antibacterial use for children with ARI dropped from 41% in 1991 to 21% in 1999 (11).

World Health Organization (WHO) recommends antibiotics for the treatment of pneumonia, acute streptococcal pharyngitis, AOM and mastoiditis. However, it is not advisable for the treatment of non-specific types of ARI (7). Hazir and colleagues conducted a double-blind, randomized, equivalence trial among 900 children (2-59 months) in accordance with WHO's defined

non-severe pneumonia. They realized that the clinical outcome in these children is not different when treated with antibiotic (amoxicillin 45mg/kg/day) or placebo (12).

In summery, the rate of antibiotic use in non-hospitalized children (< 2 years) with ARI in Mashad, Iran is much lower (32.7%) than that of other developing countries such as Saudi Arabia (87%) and is quite close to that of the developed countries such as the US (21%). However, the high rate of antibiotic injection in this group is a major concern of the medical society.

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