Effect of Establishment of Treatment Guidelines on Antibiotic Prescription Pattern for Children with Upper Respiratory Tract Infection

Ghada. M. Khalil[1&2], Abdullah A Alghasham[3], Yasser F Abdelraheem[4&5]

[1]Department of Public Health Preventive and Social Medicine, Faculty of Medicine, Zagazig University, Egypt.
[2]Department of Community Medicine,College of Medicine, Qassim University)
[3]Department of Pharmacology and Therapeutics,College of Medicine, Qassim University
[4]Department of Pediatric, Faculty of Medicine, Assuit University, Egypt
[5]Pediatric Department, College of Medicine, Qassim University
ghadamahmoud1@hotmail.com, ghadamahmoud@qumed.edu.sa

Abstract: Background: Upper respiratory tract infection in childhood is a common cause of antibiotic description which increases the likelihood for emergence of antibiotics-resistant microorganisms leading to increased illness, deaths, and substantial economic loss. **Objective:** To evaluate antibiotics prescription pattern for children and to establish clinical practical guidelines for judicious antibiotic use in upper respiratory tract infection. **Methodology:** Randomized controlled trail, Pediatric cases of upper respiratory tract infection were studied for overall antibiotics and disease specific prescription rate and their relation to several risk factors. **Result**: Significant reduction of overall antibiotic prescription between intervention and control groups was 0.008 with odd ratio 1.2 and confidence interval CI 0.62-2.39. By using logistic regression models for antibiotic prescription as dependant outcome variable showed to be significant and influenced by; assignment to intervention and control groups, primary diagnosis, associated symptoms were cough, sputum and pain also discussion with parent before prescription. **Conclusion:** Using standardized guidelines for pediatric antibiotic prescription in upper respiratory tract infection as intervention method caused reduction in antibiotics' prescribing rates for some upper respiratory tract diseases, while maintaining a high level of prescription in others.

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Key words: Antibiotics, upper respiratory tract, pediatric, guidelines.

1. Introduction

Children are particularly challenging group of patients when trying to ensure the safe use of medication [(1)]. Upper respiratory tract infection in children is a common cause of health care visits and antibiotic prescription [(2)] that increases the likelihood for emergence of antibiotics-resistant microorganisms leading to increased illness, deaths, and substantial economic loss [(3)].

Antibiotic over prescribing is a major health problem worldwide, which contributes to antibiotic resistant bacteria. Antibiotics are frequently prescribed for the management of upper respiratory tract infections, in spite of the fact that the majority of these infections are viral in origin [(4)].

Children receive a significant proportion of the antibiotics prescribed each year and represent an important target group for effort aimed at reducing unnecessary antibiotic use [(5)]. Approximately 75% of all outpatient antibiotic prescriptions given to children are for upper respiratory tract conditions, such as viral upper respiratory tract infections (URTIs), bronchitis, pharyngitis, sinusitis and otitis media [(6)] which are mostly of viral origin, they resolve by their own, and antibiotics need not to be prescribed [(7)]. The main reasons for physician overprescribing of antibiotics for URTIs are due to diagnostic uncertainty in ill-appearing, febrile child and anxious parents, and fear of physicians to offer only symptomatic therapy. If the physicians were more certain that the infection is viral in origin, they may not prescribe broad spectrum antibiotics [(8)]. Other factors that affect prescription of antibiotics are physician characteristics, such as location of medical training, specialty, and number of years in practice, hospital affiliation and place of practice private or general settings [(9-10)]. Socioeconomic status and level of knowledge of the parents are factors for influencing physician prescribing of antibiotics [(11)]. the Centers for Disease Control and Prevention (CDC) established principles for the use of antimicrobial agents in children, which were later endorsed by the American Academy of Pediatrics [(12,13)]. Several studies have suggested interventions to improve the implementation of these recommendations, such as physician education by written guidelines, parental education, point-of-care evidence, and use of public media.[(14,15)]

Study objectives:

1. To evaluate the pattern of antibiotics prescribing for children younger than 18 years with upper respiratory tract infection.

2. To establish and implement evidence-based clinical practical guidelines for judicious antibiotic use in upper respiratory tract infection and train physician on its use.
3. To measure effectiveness of clinical practical guidelines in children with upper respiratory tract infection in term of changing diagnostic criteria, prevalence and pattern of antibiotic prescription.

2. Patients and Methods:

Subjects:

1- Four pediatric outpatient clinics affiliated to governmental health care center in Byreda city, Qassim Governorate, KSA were contracted to participate in this study all study done through four months. Each pediatric clinic had one full time pediatric specialist.
2- Pediatric cases: 6months to 18 years with primary diagnosis upper respiratory tract infection only.

Study design:

Randomized Intervention pre and after study:

1- Pre intervention measurement for antibiotic prescription rate in pediatric cases of upper respiratory tract infection in four pediatric outpatient clinics before randomization.
2- Assignments of pediatric clinics randomly into control and intervention groups, 2 control (B) and 2 interventions (A).
3- Intervention phase start when the two intervention clinics' physicians attended educational seminar provided by senior pediatrician –professor-and senior pharmacist-professor about how to develop standardized evidence based treatments guidelines, followed by adopted readymade ,evidence based, upper respiratory tract infection guidelines for pediatric population provided by center for disease and prevention CDC I2 , 13 then Post intervention measurements for antibiotic prescription rate in pediatric cases of upper respiratory tract infection in both control and intervention group.
4- Comparison between pre and post intervention measurements.

Measuring variables:

The main measurable variables for both intervention and control groups are:

1- The overall antibiotics' prescription rate for children with upper respiratory tract infection.
2- Upper respiratory disease specific antibiotics prescription rate.
3- Association between several risk factors as disease category, signs and symptoms such as fever, cough, sputum, pain and general condition, parent educational level, presence of treatment guidelines and parents' discussion with physician.

Intervention method:

Physician training work shop on how to develop standardized evidence based acceptable clinical guidelines, at the end of workshop pediatrician agreed on adopted standardized guidelines and apply it on their daily practice CDC/AAP [12,13]

Study time limit:

Four months: one month for pre intervention measurement, two months for 4 intervention seminar sessions and one month for post intervention measurements.

Sample size:

A total of 370 cases: 185 before and 185 after implementation of clinical practical guidelines, 110 cases intervention group (A)before intervention and 110 cases for same group after intervention, 75 cases control group (B) before intervention and 75 for same group after no intervention.

Sample selection:

Pediatric cases visiting pediatric clinics 6 month to 18 year age according to CDC guidelines [(12,13)] during study period complaining of upper respiratory tract infection which defined as presence of one of the following: Otitis Media, rhinitis, sinusitis, pharyngitis, non specific cough illness/bronchitis.

Total number of upper respiratory tract infection cases visited the four contracted clinics were 831 cases only 370 cases agree to participate in this study.

Exclusion criteria:

Patients had other acute or chronic health problems, other than upper respiratory tract infection and patient who had more than one diagnosis of upper respiratory tract infection diseases like otitis media plus pharyngitis or patient with upper respiratory tract disease associated with complication such as presence of pharyngeal abscess, perforated drum etc…

Data was collected using*:*

Variable measurement designed checklists measuring:

1- Socio demographic data: age, gender, father and mother occupation, education.
2- Clinical history, sign and symptoms: general condition, primary diagnosis, pain, fever, cough, sputum, rash, illness duration, presence of any complication
3- Treatment prescription: antibiotic prescription, type, duration, first or second time prescription, discussion before prescription

Statistical analysis:

Statistical Package for social science **S**PSS 11 was used. Comparison made using appropriate

statistical test. Logistic regression we used block entry with removal of non significant variables.

Ethical consideration:

Patient parents who shared in study were asked for consent, patient' parent who refused participation not considered in sample size, all study data considered highly confidential.

3. Result:

Table I: shows mean age of patients under study in pre intervention period was 4.58± 2.83 years and 96% of their parents were employed and 58.4% were male patients.

Table II : shows categories of patients according to their diagnosis, most of patient in intervention group (A) before and after intervention were diagnosed with acute pharyngitis 33 and 35 from total of 110 orderly, they were 10 cases before intervention and 17 cases after intervention period in control group (B).Common cold cases were 37 and 35 respectively in control group (B) before and after intervention compared to 4 and 7 cases in group (A) before and after intervention respectively but in control group (B) most frequent diagnosis was common cold 37 and 35 from 75 totals for both pre and after intervention period.

Table III, shows that overall antibiotic prescription before intervention in group (A) it was 42.7 % compared to 27.2% post intervention with significant difference. In group (B) the control group the overall rate in pre-intervention period was 30.66 which increased to 37.3% in post intervention period. Most frequent diagnosis categories showed 100% prescription was acute tonsillitis in both intervention and control groups before intervention but decrease to 50%in intervention group (A) after intervention with high significant difference and acute pharyngitis showed 60.6% prescription in intervention group (A) before intervention but decrease to 51.42% without significant difference considering control groups (B) in pre-intervention period it was 50% increased to 64.7% in post - intervention period significant difference.

Common cold showed 0% prescription in both groups in pre-intervention period, it still 0% in intervention group after intervention and increased to 5.7% in control group in post intervention period. Running nose showed 0% prescription rate in group (A) before and after intervention compared to 57.14% in group (B) in pre-intervention period which increased to 100% in post intervention period with significant difference, while non specific URTI showed prescription rate 11.4% which decreased to 3.4% for intervention group (A) pre and post intervention respectively with significant difference and in group (B) non specific URTI showed prescription rate was 12.5% increased to 33.3% in post intervention period with significant difference.

Table IV, comparing overall antibiotics prescription in post intervention period which showed no significant difference in-between intervention and control groups 0.09 with odd ratio 1.84 and confidence interval CI (0.94-1.43).

Table V showed risk model using logistic regression models for antibiotic prescription as dependant with assignment to intervention and control groups, primary diagnosis ,associated symptoms were cough, sputum and pain also discussion with parent before prescription of antibiotics which all founded to be significantly influence dependant variable.

Table I: Basic data for pediatric patients before intervention

variables	Total population 175
Age Mean ±SD	4.5869 ± 2.839 years
Father occupation	Manual worker :20.5% Employee :46.5% Professional: 28.1% Not working:4.9
Gender	Male : 58.4% Female: 41.6%

Table II: Numbers of diagnosed cases at pediatric clinic before and after intervention in both intervention and control groups.

Diagnosis	Intervention group A before	Control group B before	Intervention group A after	Control group B after	Total
Acute pharyngitis	33	10	35	17	95
Nonspecific upper respiratory tract infection (non specific cough)	35	8	28	9	80
Otitis media	5	6	6	4	21
Common cold	4	37	7	35	83
tonsillitis	18	7	17	6	48
Running nose	15	7	17	4	43
Total	110	75	110	75	370

Table III: Rate of antibiotic prescription before and after intervention

	group (A) total 110	Intervention group(A) Total 110	Significance*	Group(B) total 75	Control group (B) Total 75	Significance*
Acute pharyngitis	60.6%	51.42%	0.17	50%	64.7%	0.068
Non specific URTI	11.4%	3.4%	0.02	12.5%	33.3%	0.001
Otitis media	100%	100%	1	100%	75%	0.000
Common cold	0%	0%	1	0%	5.7%	0.128
Tonsillitis	100%	50%	0.000	100%	100%	1
Running nose	0%	0%	1	57.14%	100%	0.00
Overall prescriptions	42.72%	27.2%	0.016	30.66%	37.3%	0.388

*MC Nemar test with Yates' correction

Table IV: Comparing over all antibiotic prescription after intervention in control and intervention groups

Over all Antibiotics prescription	Intervention Total 110	Control Total 75	*p*-value
yes	30	28	*0.09
no	80	47	**CI :1.16 (0.94-1.43)

*Fisher exact one tail **CI: confidence interval

Table V: Risk models for prediction of antibiotic prescription considering some risk variables

Variables	B	S.E	Wald	Significance	Exp(B) RR CI 95%
Group	-2.117	.513	17.0 12	.000	.120 (.044 -.329)
Primary diagnosis	.307	.133	5.335	.021	1.359 (1.04-.329)
sputum	-3.041	.633	23.0 38	.000	.0489(.041-.165)
Pain	1.274	.389	10.694	.001	3.574 (1.66-7.66)
Discussion before prescribing with patient	2.244	.771	8.473	.004	9.432(2.081-42.73)

4. Discussion

Over-prescribing of antibiotics in health care settings has brought along the worldwide problem of resistant pathogens, [14] that the pharmaceutical industry is struggling to overcome by producing newer antibiotics. The existent recommendation that antibiotics are only indicated in bacterial infection is frequently not complied with. Physicians diagnose URTIs upon clinical findings but often disregard the fact that URTIs could be of viral origin and antibiotic treatment is not indicated [16]. It has been previously documented that clinicians pre-scribe antibiotics not only to relieve symptoms, but also to prevent disease transmission, prevent secondary infections and to satisfy patients demand for antibiotics[17, 18].Several research teams have attempted to reduce antibiotic prescribing for respiratory tract infections by an educational intervention[16] .

As shown in table I studied subjects were children whom were all had upper respiratory tract patients went to pediatric clinics shared in this study with mean age 4.58±2.83years, most of their parent were worked as employee 46.5% and 28.1 were professionals. In our study male children were 58.4%.

Most assessed overall antibiotic use for respiratory tract infections in general, and reported a drop in prescription rates.[19,20] however, only a few studies assessed the changes with regard to specific diagnoses[21]. As table II describes the most frequent diagnosed upper respiratory tract infection among study subject were acute pharyngitis, non specific upper respiratory tract, common cold, tonsillitis, running nose and otitis media respectively.

This study provided us with a picture of antibiotics description in four pediatric clinics in governmental sector of Qassim state KSA, after an educational intervention through establishment of standardized treatment guidelines for URTI in pediatric population and we convinced that assessing changes in antibiotic prescribing for specific diseases, make us better able to

pinpoint areas where further intervention might be needed.

There was a significant reduction in antibiotic prescription as showed In table III for the rate of antibiotic prescription for tonsillitis from 100% to 50% and non specific URTI from 11.4% to 3.4% in intervention group (A) while in control group which no intervention was done at all the rate of antibiotic prescription increased from 12.5% to 33.3% in cases diagnosed with non specific URTI and prescription rate remain 100% in cases diagnosed with tonsillitis. Yaron *et al.,* [14] studied effect of educational intervention on pattern of antibiotic prescription in children and experienced no change between pre and post intervention rate considering tonsillitis. In contrast to Melendar *et al.,* [22] which studied effect of medical audit on antibiotic prescription for children which experienced reduction of antibiotic prescription rate for tonsillitis from 94% to 77% and for non specific URTI from 13% to 8%. Acute pharyngitis showed decrease in prescription rate from 60.6%to 51.42% for intervention group (A) but in control group (B) the rate increased from 50% to 64.7%. In contrast to Yaron *et al.,*[14] otitis media showed reduction in prescription rate from 93% to 87.4%. In our study otitis media prescription rate in intervention group (A) showed no change and remained as high as 100% same as control group (B).

Cases diagnosed with common cold showed 0% prescription rate in both pre and post intervention periods in group 9 (A) but in control group (B) it increased from 57.14 to 100%.

Janothen *et al.,* [23] studied effect of outreach educational approach for physician and families on antibiotic prescription rate for pediatric upper respiratory tract infection founded that intervention group showed decrease in overall prescription rate by 15% in intervention group and 9.8% in control group which matched with our study result in which antibiotics prescription rate was decreased from 42.72 % pre intervention to 27.2% post intervention in intervention group (A) with high significant difference 0.016 while in control group (B) the rate increase from 30.66% pre intervention to 37.3% post intervention.

Table IV compare over all antibiotic prescriptions between intervention and control group after intervention by developing standardized treatment guidelines and its application on daily work in intervention clinic only group (A), group (B) or control group receive no intervention guidelines and we found that number of children receiving antibiotics in intervention group was 30 from 110 and in group (B) control group they were 28 from 75 with no significant difference, that findings didn't match with Finkelstein *et al.,* [24] who experienced decrease in overall antibiotics prescription in intervention group (18.6%) compared with (11.5%) in control practices, he related that to the study effect on both groups rather than intervention effect and our study result matched with Yaron *et al.,*[14] who found reduction in overall prescription for all URTI diagnosis after intervention but he couldn't relate all reduction to intervention effect because his study has no control group.

Using regression model on outcome variable which was antibiotic prescription as table V showed significance regarding comparisons groups as intervention and control group which enhance significant test result, also the type of primary diagnosis was significantly regress on antibiotic prescription which agreed with Janothen *et al*., [23] who found that rate of antibiotic prescription differ according to primary diagnosis. Fahima *et al.*, [25] found that patients experienced yellowish discharge and pain responded more to intervention method which were guidelines and patient pamphlet and showed reduction of antibiotic prescription but in our study presence of sputum, pain and discussion with patient father or mother before prescribing are factors which affected antibiotic prescription rate in our intervention group (A).

Conclusion & recommendation:

Using standardized guidelines for pediatric antibiotic prescription in upper respiratory tract infection as intervention method reduced prescribing rates of antibiotics for some respiratory tract diseases while maintaining a high level of prescription in others. Further research should focus on other intervention methods and comparing effectiveness, sustainability and cost effectiveness of different interventions.

Corresponding author
Ghada. M. Khalil
Department of Public Health Preventive and Social Medicine, Faculty of Medicine, Zagazig University, Egypt. [2]Department of Community Medicine,College of Medicine, Qassim University)
ghadamahmoud1@hotmail.com,
ghadamahmoud@qumed.edu.sa

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