ABSTRACT

Background: The appropriate choice of antibiotics is a complex procedure that requires clinical judgment and detailed knowledge of pharmacological and microbiological factors. The irrational prescribing of antibacterial drugs will lead to the emergence of bacterial resistance which in turn led to the development of adverse effects; in addition to that, the irrational use of antibiotics is cost effective. The principles of appropriate and effective antibiotic prescribing are widely and simply outlined but practically they are difficult to implement, thus the treatment with antibiotics should be reviewed to lower the irrational use of those drugs.

Aim: To determine the extent and the rationale of antibiotic prescriptions for pediatric patients admitted with different respiratory tract infections in Mosul pediatric hospitals and to discuss the pressure on physicians and health staff to overuse of antibiotics.

Patients and Methods: A prospective observational study was conducted on 232 hospitalized pediatric patients with respiratory tract infections, those patients selected randomly from Ibn-alatheer and al-Khansaa pediatric hospitals, their age range from (0-11 years). The antibiotic prescriptions of patients were collected over a period of 6 months and then analyzed to determine the antibiotic prescription habits of medical staff in Mosul.

Results: two hundred thirty two pediatric patients were under study ,admitted with pneumonia(20%),bronchitis(18%),lower respiratory tract infection and asthmatic patient with chest infection (15%)and (16%)respectively. About (11 %) of patients under study received antibiotics without documented reason. (74%) of children receive prescription of one antibiotic and the remaining (26%) prescribed a combinations of two antibiotics. Total of (304) antibiotic drugs were prescribed, with high prescription rate for Ampiclox (50%) and Cefotaxime (29%). The off- label status of antibiotic prescription is determined for diagnosis, age, route and dose with most frequently off- label antibiotic prescription for diagnosis (different indication) which is (64%).

Conclusion: The study demonstrated that, high percentage of antibiotic prescriptions for pediatric patients with respiratory infections is inappropriate and this mainly due to prescribing of antibiotics for conditions caused by viral infection, thus an education strategies are required for both physicians and pharmacists to diminish the effect of the problem.
INTRODUCTION

While medicines prescribed for adults undergo formal evaluation of efficacy, safety and optimal dose, children still remain therapeutic orphans since most of the drugs used to treat them are based on extrapolation of adult data (1,2,3) therefore many studies are conducted to evaluate the drug prescribing habits of health care staff in children (4,5). In 1969 95% of physicians surveyed gave patients one or more prescription drugs for the common cold: about 60% were antibiotics (6). Antibiotics are the most frequently prescribed therapeutic agents, accounting for 20-30% of drug prescription (7) and there irrational use therefore, it can not only lead to overall rise in healthcare costs but also the emergence of bacterial resistance (7). Misuse of antibiotics is found in both developing and developed nations but the problem is more acute in the former because of limited finance (8). In general practice antibiotic drug use is highest among children and approximately 70% of all antibiotics in children are prescribed for respiratory tract infections. The antimicrobial resistance among respiratory pathogens has become a common clinical problem and its management a part of routine office practice (9, 10). Guidelines have been propagated for decades and yet they frequently are not followed (11) thus it is very important to study the use of antibiotics and introduce interventions depending upon the local requirements and this process should involve the physicians/prescribes and the pharmacists in order to achieve judicious use of antibiotic drugs. There is no previous study that evaluate the antibiotic drug prescriptions for pediatric patients with respiratory tract infections in Mosul, thus in this study we obtained an insight into the antibiotics prescription pattern in pediatric wards in Mosul and evaluating these prescription patterns by determining the proportion of appropriate and inappropriate antibiotic prescriptions through the determination of the off-label drug use (use of drugs outside the term of the summary of product characteristics) (12).

PATIENT & METHODS

This study was prospectively conducted on two hundred thirty two (232) pediatric patients hospitalized with different respiratory tract infections such as pneumonia, acute bronchitis, bronchiolitis, etc... , their age range from (0-11 y) (mean ± S.E. 16.96 ± 1.54 months). The patients under study are randomly selected from Ibn-Alatheer and Al-khansaa hospitals over a period of 6 months between October 1 2008 and March 30 2009. The antibiotic prescriptions of those pediatric patients were collected and all information including the patient name, age, weight, diagnosis, antibiotic drug used, dose and route are recorded. The data collected is then analyzed according to the cause of admission, type of antibiotic drug used and the antibiotic prescription is then further analyzed to determine the extent of off-label drug use according to indication, age, dose, and route to evaluate the antibiotic drug prescriptions and the reference source that is used was the British National Formulary for children 2007 (23) and the NELSON textbook of pediatrics (28).

RESULT

Two hundred thirty two pediatric patients were studied, hospitalized with different respiratory tract infections. (Figure 1) shows the recorded diagnoses of respiratory tract infections for which the antibiotic drugs were prescribed with the most commonly was for Pneumonia (20%) , acute bronchitis (18%) , and (11%) of
antibiotic drugs were prescribed without documented diagnosis. During their admission period those patients receive (304) antibiotic drug prescriptions with total of (7) types of antibiotic medications and the higher rate of prescribing are for Ampiclox (50%) and cefotaxime (29%). (Figure 2) shows the types of antibiotics prescribed for pediatric patients under the study. About (74%) of pediatrics patients receive prescriptions of one Antibiotic drug and the other (26%) receive prescriptions of combination of two antibiotic drugs. (Figure 3) shows the Antibiotic drug combinations that prescribed for children with respiratory tract infections and the most frequently prescribed combination was Ampiclox + Cefotaxime (60%). The off-label status of Antibiotic drug prescriptions is shown in (Table 1) indicating that higher proportion of the off-label Antibiotic drug use was for different indication (64.1%) and different dose (32.5%), the Off – label use of Antibiotic drugs with low dose comprises higher rate of drug use. From the (232) Children under study, only six (2.6%) patients for whom a culture sensitivity test were made before the prescribing of antibiotic drugs and their antibiotic drugs changed after culture test. (91%) of patients receive antibiotic drugs through I.V. route, (7%) I.M. route and (2%) oral route.

**DISCUSSION**

The use of inappropriate antibiotic therapy has gained considerable attention in the medical literature during the last five years. This prospective study of children with respiratory tract infections is similar to other studies conducted in many areas around the world to evaluate the appropriateness of antibiotics prescribed for pediatric patients (13, 14). A study by the World Health Organization Program for appropriate health care technology has shown a correlation between the occurrence of multi resistant bacteria and antibiotic consumption pattern (15). In our study the most frequent diagnoses for which antibiotic drugs were prescribed, are pneumonia and acute bronchitis (Fig. 1) this may be due to that the study is conducted in winter months, our result is supported by another study done by Esposito S et al which found that 92% of children received antimicrobial drugs were hospitalized for acute bronchitis or pneumonia (16). A significant proportion of children under study are treated with antibiotics in the absence of documented bacterial infection and this can be explained by the opinion of the use of empirical antibiotic therapy (17, 18). It is important for an empirical broad spectrum antibiotic therapy to be reserved for high risk situation such as immunocompromised patients (18, 19). And to avoid the use of antibiotics as antipyretics (20) because the presence of fever not always means that there is bacterial infection (8). In this study the antibiotic drugs are prescribed for bronchiolitis, acute bronchitis, croup, and influenza which are mainly caused by viral pathogens rather than bacterial and the antibiotics did not decrease the incidence of complications or hasten recovery (21). A significant proportion of children diagnosed as having chest infection, upper respiratory tract infection, and cough which require further investigations and culture test to confirm the bacterial infection. A recent study by Leila ES et al demonstrated that pediatric asthmatic patients received significantly more antibiotic prescriptions than non asthmatics for conditions caused by bacteria as well as for conditions more likely to be viral in origin (22). In our study all asthmatic patients receive
antibiotic prescriptions regardless of the culture and sensitivity test result and according to guidelines for the diagnosis and management of asthma reported by the National Asthma Education and Prevention Program, the antibiotics are not recommended for the treatment of asthma exacerbations except as needed for co morbid conditions such as fever and purulent sputum, evidence of pneumonia or suspected bacterial sinusitis (22). So, it is irrational to use antibiotics for respiratory tract infections without culture and sensitivity test to determine the type of antibiotic drug to be used to reduce the adverse effects because only (2.6 %) of patients admitted to hospital having culture and sensitivity test and their antibiotic drugs were changed according to the result of the test ,this may be due to the short time of residence of patient in the hospital and to the difficulty in the collection of specimen (swab) in small aged children. We found that I.V. route of administration constitute for higher percentage (91%). In spite of that I.V. route should be reserved for severe infections in order to avoid adverse effects, whenever possible painful I.M. injection should be avoided in small children (23).

Off-label drug use and prescription represent a very common phenomenon documented in several countries and in different settings (24). We found that the extent of off–label antibiotic use is high in Mosul city, and the categories most frequently perceived as off-label are different indication and low dose.

To our knowledge, our study is the first to describe the off-label use of antibiotic drugs in children hospitalized with respiratory tract infections in Mosul. Similar study conducted by Vladimir G et al illustrated that higher percentage of off-label prescriptions of antibiotics is for different dose followed by age and different indication (25). It is obvious from our study that, the proportion of inappropriate antibiotic drug use is significantly high in Mosul pediatric wards which may lead to the emergence of bacterial resistance and increase the risk of the development of adverse drug reactions. This antibiotic misuse is mainly due to the pressures on physicians to prescribe antibiotics for conditions caused by viral infection. The two most important pressures on physicians are: 1) low educational status of parents and parental expectations and 2) the physicians desire to have a feeling of doing something (26, 27). So, it is important to outline a Guidelines that standardize medical treatment of infectious diseases such as respiratory tract infections and improve the physicians/clinical pharmacist educational strategies that stress the minimization of antibiotic use in viral infections and encourage the performing of culture and sensitivity test in all patients receive antibiotic drugs , by this way we can reduce the possibility of adverse effects occurrence and bacterial resistance and as a result make the antibiotic utilization in hospitals less cost effective.
Fig. 1  The diagnoses of respiratory tract infections for which antibiotic drugs are prescribed.

Fig. 2  The antibiotic drugs prescribed for children with respiratory tract infections
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Fig. 3  Antibiotic drugs combinations that prescribed for children with respiratory tract infections

(Table 1) the off-label Antibiotic drug use in children with respiratory tract infections

<table>
<thead>
<tr>
<th>Off – label status</th>
<th>No.</th>
<th>( % )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Different indication</td>
<td>205</td>
<td>(64% )</td>
</tr>
<tr>
<td>Dose</td>
<td>104</td>
<td>(32.5 %)</td>
</tr>
<tr>
<td>- High dose</td>
<td>12</td>
<td>(3.75 %)</td>
</tr>
<tr>
<td>- Low Dose</td>
<td>92</td>
<td>(28.75 %)</td>
</tr>
<tr>
<td>Age</td>
<td>6</td>
<td>(1.9 %)</td>
</tr>
<tr>
<td>Route</td>
<td>5</td>
<td>(1.6 %)</td>
</tr>
<tr>
<td>Total off- label</td>
<td>320</td>
<td>(100)</td>
</tr>
</tbody>
</table>
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الخلاصة

التوصيات: إن الاختيار المناسب للمضادات الحيوية هو إجراء متعقد يطلب معرفة مفصلة عن العوامل الدوائية والبيولوجية لهذه المضادات الحيوية. والاستخدام الغير منصوص قد يؤدي إلى ظهور الآثار الجانبية الضارة، بالإضافة إلى ذلك، فإن الاستخدام الغير المنظم للمضادات الحيوية يساهم في زيادة تكلفة استهلاك المضادات الحيوية في المستشفيات.

الهدف: تحديد مدى والاستخدام المنطقي لوصفات المضادات الحيوية لعلاج الأطفال الذين دخلوا مع التهابات الجهاز التنفسي المختلفة للأطفال في مستشفيات الموصل لبحث الضغط على الأطباء والعاملين الصحيين في استخدام المضادات الحيوية.

المريضي وطرق العمل: أجريت دراسة على 237 من الأطفال المرضى الواردين في المستشفى مع التهابات الجهاز التنفسي، والمرضى الذين تم اختيارهم عشوائيا من مستشفيات الأطفال ابن الأثير، وينتمون أعمارهم من (0-11 سنة) جميعهم تلقيوا وصفات طبية للمضادات الحيوية. جمع المرضى خلال فترة 6 أشهر وتم تحليطها في تحديد الاستعمال الطبي خارج التوصية للمضادات الحيوية في ردات الأطفال في اثنان من مستشفيات مدينة الموصل.

المصطلحات: مريض واثنان وثلاثون مريض من الأطفال كانوا قد سبق الدراسة، كانت نسبة المنوية للمصابين بالإعتداء الرئوي (20%) والتهاب الشعب الهوائية (18%)، تم اعتداء نحو (11%) من المرضى في الدراسة المضادات الحيوية دون سبب موثق. أن نسبة الأطفال الذين أعطوا ممضات حبيبية واحدة (41%) و الذين أعطوا أكثر من مضادات حبيبي واحد (24%) أن نسبة الادوية التي تم إعطاؤها خارج التوصية كانت بصورة أساسية لدواعي الاستعمال المختلفة والجرعة التي هي أقل من المقررات والتي تؤدي بانتظار الأبعادات الكبيرة المباشرة.

النتائج: أظهرت الدراسة أن نسبة عالية من وصفات المضادات الحيوية للأطفال المرضى المصابة بالالتهابات الجهاز التنفسي غير مناسبة وهذا يرجع أساسا إلى وصف المضادات الحيوية لظروف ت牥مة عن الأمراض الفيروسية، وبالتالي هناك حاجة لاستراتيجيات علمية تعليمية وتقنية لكلاً من الأطباء والصيدلانيين للحد من تأثير المشكلة.

الاستنتاج: أظهرت الدراسة أن نسبة عالية من وصفات المضادات الحيوية للأطفال المرضى المصابة بالالتهابات الجهاز التنفسي غير مناسبة وهذا يرجع أساسا إلى وصف المضادات الحيوية لظروف تflammatory عن الأمراض الفيروسية، وبالتالي هناك حاجة لاستراتيجيات علمية تعليمية وتقنية لكلاً من الأطباء والصيدلانيين للحد من تأثير المشكلة.