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Pattern of Parenteral Antimicrobial Prescription among Pediatric Patients in Al-Watani Governmental Hospital in Palestine

نمط استخدام حقن المضادات الحيوية في قسم الأطفال في المستشفى الوطني الحكومي - فلسطين

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Abstract

Objective: No studies were carried out in Palestine to investigate the prescribed antimicrobial agents in hospitalized pediatric patients. The objective of this study was to evaluate and therapeutically analyze the pattern of parenteral antimicrobial prescriptions among pediatric patients in Al-Watani Government Hospital in Palestine. Such audit will be of great value to clinicians and health policy makers. **Material and Methods:** Data on antimicrobial prescribing were collected for 30 consecutive days for all pediatric patients admitted to Al-Watani government hospital. Data on antimicrobial prescribing were entered and analyzed using Statistical Package for Social Sciences (SPSS) program. Analysis was done for age, sex, diagnosis, site of infection, number of antimicrobial agents given, how many times the drug regimen has been changed and the frequency of individual drug use. **Results:** Three hundred and forty pediatric patients were admitted to Al-Watani government hospital during the study period. Gastroenteritis was the most common cause of hospitalization, while upper respiratory tract infection (URTI) was the most common cause of parenteral antimicrobial agent administration. Two hundred and ten (61.8%) patients received parenteral antimicrobial agents while 16 (4.7%) received both parenteral and oral antimicrobial agents. Single antimicrobial agent was prescribed for (50.6%) patients. Cefuroxime was the main single antimicrobial agent used; it was administered to 70/226 (31%) patients. **Conclusion:** Treatment patterns used for most patients were nearly according to current empiric therapeutic recommendations. However, improving the availability of rapid diagnostic methods to differentiate between viral and bacterial infections is suggested to reduce empiric therapy numbers by antimicrobial agents so as to decrease chance for drug resistance.

Key words: Antimicrobials, Pediatrics, Prescription, Palestine.

Short Running Title: Parenteral Antimicrobial in Pediatrics.

ملخص

الهدف: لم تجر أية دراسة لوصف المضادات الحيوية عند الأطفال المدخلين للمستشفى في فلسطين من قبل. الهدف من هذه الدراسة هو التدقيق والتحليل العلاجي لنمط الوصف الدوائي للمضادات الحيوية التي تعطى عن طريق الحقن الوريدي في قسم الأطفال في المستشفى الوطني الحكومي في فلسطين. وسيكون هذا التدقيق ذا قيمة كبيرة لواضعي السياسة الصحية والعملين في مجالها. **المادة ووسائل البحث:** تم تجميع البيانات عن المضادات الحيوية المستخدمة في علاج الأطفال الذين أدخلوا المستشفى الوطني الحكومي خلال ثلاثين يوما، و إدخال و تحليل البيانات عن طريق برنامج SPSS. اشتمل التحليل على عمر المريض وجنسه والتشخيص المرضي و موقع الالتهاب وعدد المضادات الحيوية المستخدمة وعدد المرات التي تم فيها تغيير برتوكول العلاج وعدد مرات استخدام الدواء وعدد جرعات الدواء المستخدمة. **النتائج:** في ذلك الشهر، أدخل المستشفى ٣٤٠ مريضا. وحقن ٢١٠ (٦١,٨%) من المرضى بمضادات حيوية، بينما عولج ١٦(٤,٧%) مريضا بمضادات حيوية عن طريق الفم و الحقن معا. تلقى (76.1%) 172 مريضا مضادا حيويا واحدا، وكان cefuroxime هو المضاد الحيوي الأكثر استخداما في هذه الحالات، و قد وصف ل ٢٢٦/٧٠ (٣١%) مريضاً. كانت التهابات الجهاز الهضمي هي السبب الرئيسي لدخول المرضى إلى المستشفى، بينما احتلت التهابات الجهاز ا لتنفسي العلوية المرتبة الأولى لانها كانت السبب الرئيسي لإعطاء المضادات الحيوية عن طريق الحقن. **الاستنتاج:** كانت الأنماط المتبعة في العلاج مقاربة لبروتوكولات العلاج الحديثة المتبعة عالميا. إن البحث عن طرق أفضل لتشخيص الالتهابات الفيروسية والبكتيرية والتمييز بينهما هو من التوصيات المقترحة لتقليل استخدام المضادات الحيوية في بداية العلاج، وتوجيه المضاد الحيوي المناسب - نتيجة لذلك - للكائن الدقيق المعزول من المريض و المسبب للمرض، و تقليل مقاومة الكائنات الدقيقة للمضادات الحيوية.

Introduction

According to the 2003 annual report issued by the Palestinian Ministry of Health, 437 deaths among infants and children less than five years were caused by infectious diseases (1). This suggests that more attention is needed for the investigation of the protocols used in the diagnosis and management of infectious diseases among infants and children who are the most vulnerable population groups to contract illnesses. Although the antimicrobial agents are effective and play an important role in the management of infectious diseases, they have serious consequences. The worldwide multi-drug resistant microorganisms were identified and were associated with the widespread use of antimicrobial agents in both inpatients and outpatients (2-3). For example, many studies have shown that there is an emergence of resistant strains of *Streptococcus pneumoniae* to antimicrobial agents and these strains are rapidly increasing (4). The emergence of multi-drug resistant microorganisms is expected to lead to more serious infections than what we have initially encountered. Another serious problem associated with the irrational use of antimicrobials, especially among pediatrics, is the ability of strong antibiotics to disturb the colonization of gastro-intestinal microflora which may induce serious clinical symptoms like pseudomembranous colitis and toxic megacolon (5). An effective method to prevent the transmission of multi-drug resistant pathogens and other complications of antimicrobial use can be achieved by strict antibiotic policy and rational use of antimicrobial agents which also have shown to be cost saving and to prolong antibiotic usefulness (6-8).

Little is known about the antimicrobial utilization in Palestine specially among pediatrics in particular. Such knowledge is important for health policy-makers to identify targets for improving antimicrobial utilization and thus optimizing costs, therapy and disease management. The objective of this study was to investigate the use of antimicrobial agents in the pediatric department of Al-Watani Governmental Hospital in Nablus, which is a referral center for pediatrics from northern West Bank, and to determine if the current utilization was according to recommended guidelines.

Material and Methods

This study was carried out in the pediatric department of Al-Watani Governmental Hospital in Nablus, Palestine. This department is supervised by board certified pediatricians and pediatric-board-eligible physicians. The study was conducted by evaluating the treatment charts of all admitted pediatric patients and was carried out for thirty days starting from October 10 and ending on November 9, 2004. All prescriptions for all admitted patients within the 30 days were reviewed. Access to patient medical files was made possible based on an educational agreement between An-Najah National University and the Palestinian Ministry of Health. Data collection was done using a pre-designed form that included patient's file number, age, sex, diagnosis, site of infection, and the drug given. The site of infection was defined as the tissue or organ affected by the microorganism. For example, CNS infections are those infections in which the microorganism is affecting the meningies or any part of the CNS. Data analysis was done using Statistical Package for Social Sciences (SPSS version 11) program in terms of age, sex, diagnosis, site of infection, number of anti-microbial agents given, how many times the drug regimen has been changed, and frequency of individual drug use. Diagnosis was classified as being either single, mixed, unidentified or no infection. The term “single” was used when one infection is diagnosed; “mixed” is used when two infections were diagnosed and “unidentified” infection was used when the patient was given antimicrobial agents but no specific infection was diagnosed.

Results

Data analysis showed that 266/340 (78%) of the admitted patients were less than five years of age. One third of those patients were less than one year of age. The number of admitted males were 203 representing 60% of the total patients. Patients with no infection who were admitted to the hospital were 55 (16.2%). Among the admitted patients, 214 (63%) were diagnosed with single infection while mixed infections were diagnosed in 28 patients (8.3%). Further investigation of infections showed that gastrointestinal and respiratory tract infections accounted for most of the diagnosed single infections as shown in Table1.

Table (1): Data distribution based on site of infection.

Site of Infection	Frequency	Percent
GI Infection	84	24.7
URTI	59	17.4
No Infection	55	16.2
LRTI	41	12.1
Unidentified Infection	32	9.4
GI+URTI	18	5.3
CNS Infection	11	3.2
Prophylactic	11	3.2
UTI	9	2.6
Kidney Infection	5	1.5
Skin Infection	4	1.2
URTI+UTI	3	0.9
GI+LRTI	3	0.9
GI+UTI	2	0.6
Liver Infection	1	0.3
CNS+ Kidney Infection	1	0.3
Kidney Infection+ URTI	1	0.3
Total	340	100

GI: Gastrointestinal Infection, URTI: Upper Respiratory Tract **Infection, LRTI:** Lower Respiratory Tract Infection, CNS: Central **Nervous System, UTI:** Urinary Tract Infection

Concerning therapy of the 340 patients admitted, 210 (61.8%) received parenteral anti-microbial therapy, 16 (4.7%) received both parenteral and oral treatment, 7 (2.1%) received oral therapy alone, and 107 (31.5%) didn't receive any anti-microbial therapy. Beta-lactams, metronidazole and aminoglycosides constituted the majority of administered anti-microbial agents. Among the 226 patient whom received parenteral antimicrobial agents, cephalosporins were the most commonly used group of B-lactams. Cefuroxime, a second generation cephalosporin, was used in 70 (31%) patients. It was repeatedly used for chest infection, unidentified infections and pneumonia. Ceftriaxone, a third generation cephalosporin, was used among a total of 56 (24.8%) patients. It was used for meningitis, unidentified infections and upper respiratory tract infections (URTI). Cefazolin, a first generation cephalosporin, was mainly used for gastroenteritis. Crystalline penicillin, a parenteral penicillin, was used in 21 (9.3%) patients. Half of them were having tonsillitis. In contrast, ampicillin was used in 39 (17.2%) patients mainly for URTI. Metronidazole, a chemotherapeutic agent effective against anaerobic bacteria and certain parasites, was used in 21 (9.3%) patients for treatment of amebiasis and gastroenteritis. Aminoglycosides were used in 15 (6.6%) patients with amikacin and gentamycin being used in equal extents.

The number of antimicrobial agents administered to patients was also assessed. Single antimicrobial therapy was used in 50.6% (172/340) of cases. Cefuroxime was the predominant single antimicrobial therapy used (15%), followed by cefazolin (9.4%), ampicillin (7.4%), ceftriaxone (7.1%), crystalline penicillin (4.7%) and metronidazole (2.4%). Combinational antimicrobial therapy was given to approximately 18% of the admitted patients. The combination consisted of ceftriaxone + aminoglycoside in 2.2%, followed by cefazolin + metronidazole in 1.5% and cefotaxime + ampicillin in 1.2% of the treated patients.

In the treatment of single infections, no fixed therapeutic regimen was employed as shown in Table 2. For most of the admitted patients, the therapeutic regimens were never changed during their stay in the hospital. However, in 8.2% of the cases, the regimen was changed at least once. The change was not done based on microbiological culture; rather, it was based on patient's clinical response, as Antibiotic susceptibility test was done only for 5.6% of the admitted patients.

Table (2): The most common drug regimen used

Diagnosis	Total no.	Most Common Drug/s Used	No. of Cases / Percentage
Amebiasis	12	Metronidazole	9 (75%)
		Cefazolin+Metronidazole	3 (25%)
Bronchiolitis	8	Cefotaxime+Ampicillin	1 (12.5%)
		Cefuroxime	4 (50%)
Cellulites	3	Ceftriaxone+Cloxacillin	2 (67%)
		Cloxacillin	1 (33%)
Gastroenteritis	64	Cefazolin	9 (14%)
		Cefazolin+Metronidazole	3 (5%)
		Ampicillin	4 (6%)
		Ceftriaxone	2 (3%)
		Ceftriaxone+Metronidazole+ TMP/SMX	2 (3%)
Laryngitis	3	Ampicillin	1(33%)
		Cefazolin	1 (33%)
Meningitis	10	Ceftriaxone	8 (80%)
		Ceftriaxone+Vancomycin	1 (10%)
		acyclovir+ceftriaxone+vancomycin-amikacin+cefotaxime	1 (10%)
Otitis Media	4	Ceftriaxone	3 (75%)
		Gentamycin+Ceftriaxone	1 (25%)
Pneumonia	14	Aminoglycoside+Ceftriaxone	3 (21%)

… Continue table 2

Diagnosis	Total no.	Most Common Drug/s Used	No. of Cases / Percentage
		Amikacin+Ceftriaxone+Vanocomycin	2 (14%)
		Erythromycin+Cefuroxime	1 (7%)
		Ceftriaxone	1 (7%)
		Cefuroxime	5 (36%)
		Cefuroxime+Vancomycin	1 (7%)
		Erythromycin+Cefuroxime+Vancomycin	1 (7%)
Tonsillitis	16	Crystalline Penicillin	11 (69%)
		Ampicillin	3 (19%)
		Cefuroxime	1 (6%)
		Ceftraixone	1 (6%)
URTI	31	Ampicillin	8 (26%)
		Cefuroxime	8 (26%)
		Ceftriaxone	7 (23%)
		Cefazolin	2 (6.5%)
		Crystalline Penicillin	2 (6.5%)
		Cefazolin+Gentamycin	1 (3%)
UTI	9	Cefuroxime	4 (44%)
		Cefazolin	2 (22%)
		Ceftriaxone	1 (11%)
		Cefuroxime+Gentamycin	1 (11%)
		Metronidazole+Amoxy/Clavul.	1 (11%)

Discussion

Inappropriate utilization of antimicrobial agents forced many researchers to evaluate the antimicrobial drugs consumption in order to restrict and control the risk of antibiotic misuse. Several studies were published worldwide to assess this problem. A study done in a tertiary hospital in Spain showed extensive inappropriate third generation cephalosporine utilization, although guidelines for rational antibiotic use were developed, but they haven't been implemented or encouraged (9). A survey of drug use practice and antibiotic prescribing pattern at a general hospital in Nigeria revealed that appreciable gap in knowledge with respect to rational drug use still existed among healthcare professionals (10). Prescription audit reveals that it's possible to achieve a change in the utilization of antibiotic in treatment of RTIs (11). Getting audit and feed back information about clinical records has been shown to decrease inappropriate utilization of antibiotics. For continuous benefit, these records should be continuously updated (12). Pharmacists should have a role in promoting optimal antimicrobial use. They can play a major role through clinician education and focused clinical services (13).

Studying the antimicrobial prescribing pattern in an Indian tertiary hospital has showed that two antimicrobials per prescription was maximum in pediatrics, while one antimicrobial was maximum in surgery, urology and internal medicine departments. Amikacin, ciprofloxacin, cefotaxime and cloxacillin were the most preferred drug(14).

Recent estimates indicate that 1.9 million children worldwide die each year from acute respiratory illnesses, many of which are lower respiratory infections (LRIs) (15). Pneumonia is one of the serious LRTI. It is known that viruses are the most common cause of pneumonia in preschool children while *Streptococcus pneumoniae* are the most common bacterial pathogens among pre- and school-aged children and adolescents with community acquired pneumonia (16). *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* can also cause pneumonia in older children (16). The recommended inpatient drug regimen for the treatment of bacterial pneumonia is cefotaxime or cefuroxime for the preschool aged children and cefuroxime or cefotaxime plus erythromycin for 5 years and older [17]. For severe pneumonia infection, ceftriaxone or cefotaxime ± macrolide ± vancomycin is suggested as initial empirical treatment for pediatric community acquired pneuomonia [18]. The drug regimens used in the treatment of pneumonia in this study were according to current recommendation mentioned above. Three cases of pneumonia were treated with the addition of either amikacin or gentamycin. This treatment regimen could be used in children younger than 2 months of age [19] or in hospital acquired pneumonia [20-21].

Upper respiratory tract infections (URTIs) are among the most frequent reasons for physician office visits in pediatrics. Despite their predominant viral etiology, URTIs continue to be treated with antimicrobials [22]. Tonsilitis, pharyngitis and laryngitis constitute the majority of cases of URTI. The most important causative pathogen in tonsillitis is *group A Streptococcus* and is successfully treated with penicillins [23]. Better results were obtained with cefadroxil and cefuroxime axetil (orally) than with penicillin V [24-26]. Clindamycin, cephalosporins, and erythromycin can also be used and they are associated with lower recurrence rates than penicillin [24]. In this study, it was noted that most cases of tonsillitis (11/16) were treated with penicillin which is in general harmony with the recommended guidelines.

Gastroenteritis is very common in pediatrics and is mostly caused by rotavirus infection [27]. The cornerstone for treatment of gastroenteritis is fluid and electrolyte replacement [28-29]. Antibiotic therapy use in gastroenteritis treatment depends on the causative microorganism. It is recommended in cases of *Shigella* infection (Trimethoprim-Sulfamethoxasole) or *Campylobacter* (Macrolides), while no antibiotic treatment is recommended in *Salmonella* or *Escherichia coli* infections [30]. In this study, antibiotics, mostly cefazolin, were administered to one third of the admitted patients having gastroenteritis, although it's not indicated in any of gastroenteritis treatment regimens. The lack of stool cultures makes it difficult to judge the rationale of antibiotic use in these cases.

Escherichia coli are responsible for most cases of community-acquired urinary tract infections (31). Other micro-organisms that may be involved include *Enterococcus faecalis, Proteus mirabilis, Klebsiella oxytoca, Pseudomonas aeruginosa* (32). In the Gaza Strip, it was found that a large proportion of isolated pathogens, causing community-acquired urinary tract infections, were resistant to amoxicillin, doxycycline and trimethoprim-sulfamethoxasole (TMP-SMX) suggesting that a susceptibility test is a must before prescribing these agents (33). In this study, all urinary tract infected patients received antibiotics either as monotherapy or as part of multiple therapy regimens. The most commonly used regimen was the second generation cephalosporin, cefuroxime. In general, the regimens prescribed for the patients were appropriate.

Meningitis is a major cause of mortality and morbidity among infants and children especially among countries where effective vaccines are not available. *Streptococcus agalactiae*, *E.coli* and *Listeria monocytogenes* are the causes of bacterial meningitis in children younger than 3 months old while *Nisseria meningitidis*, *Streptococcus pneumoniae* or *Hemophilus influenza* are the active agents in older children (34-35). For the management of bacterial meningitis in patients less than 3 months old, ampicillin plus a broad spectrum cephalosporine (cefotaxime or ceftriaxone) is indicated while a broad spectrum cephalosprine alone is used in age group of 3 months -18 years old. (35). Acyclovir should be added to the treatment regimen if Herpes Simplex Virus (HSV) infection is suspected (36) but in our country HSV is not among the causative agents of meningitis, so there is no need for acyclovir. Instead, enterovirus is the common cause of viral meningitis in the region (37) for which no specific therapy is available (30). In our study, there were 10 cases of meningitis. Based on Lumber Puncture (LP), 7 cases were suspected to be viral and 3 cases were suspected to be bacterial. Lumber Puncture (LP) was done to confirm the diagnosis of meningitis but not as a guide for treatment. All the meningitis cases were treated as if they were bacterial. Antibacterial therapy was initiated in all cases of meningitis as a protective strategy since viral meningitis could lead to bacterial meningitis. Culture and sensitivity tests were not always carried out because of economic reasons or that the therapy must be initiated as soon as possible while results for culture and sensitivity take time.

Conclusion

Based on what we have found, the treatment regimens implemented in the management of infectious diseases among hospitalized pediatrics were somewhat according to literature. Management protocols did not fully abide to the current guidelines since culture and sensitivity tests were not carried out for most cases. The most common problem we have faced was the non-specific terms used in diagnosis as chest infection and upper respiratory tract infection. Chest infection could be pneumonia or bronchiolitis, while upper respiratory tract could be otitis media, tonsillitis, pharyngitis or laryngitis. Physicians need to be more specific in their diagnostic terminology, and culture and sensitivity tests must be done despite the financial burden or time constraints.

We have provided an overview about utilization of parenteral antimicrobial agents among pediatrics in a pediatric ward, studies on which are relatively lacking. This study might be the basis for more specific research in the future. Antimicrobial agents were used for both bacterial and viral infection. Improving the availability of rapid diagnostic methods to differentiate between viral and bacterial infections is suggested to reduce empiric therapy numbers by antimicrobial agents so as to decrease chance for drug resistance.

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