DOSE RELATED PROBLEMS IN PRESCRIBING ANTIBIOTICS IN KHARTOUM PEDIATRIC HOSPITALS

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ABSTRACT
Antibiotics are one of the most commonly used groups of drugs in pediatric patients. Prescribing correct doses for children is a problem worldwide. This work investigates prescribing in two public health pediatric hospitals. 385 medical records were reviewed, it was found that the majority of patients prescription contained an antibiotic (92%); higher than any rate in the region. When doses were calculated according to the body surface area 39% of the prescriptions were found with wrong doses, of these (57%) contained higher doses and (42%) were lesser than recommended. Most of antibiotics were administered intravenous either bolus or infusion. Third generation cephalosporins and benzyl penicillin were the commonly prescribed antibiotics. Moreover, gentamycin was prescribed in high dosing frequency.

KEYWORDS: incorrect doses, children, antibiotics.

INTRODUCTION
Children are particularly vulnerable to medication dosing errors. The most important aspect for selection of a drug and establishment of the proper pediatric dosage is the acknowledgment that the pediatric patient is not just a small adult. Newborns, children and adolescents have different physiological, pharmacokinetic and pharmacodynamic parameters compared to adults. Thus, guidelines of specific dosages and useful means for calculation of
pediatric dosages must be developed in order to enhance the effectiveness and therapeutic limit to prevent serious adverse effects.\textsuperscript{[1]}

Several published reports confirmed that irrational prescribing practices are common in pediatrics; the most commonly reported include the dispensing of inappropriate medication for the condition being treated, incorrect dosage or dosing interval, high prescribing of medications via the parenteral route, and inappropriate overprescribing of antibiotics that is not based on clinical criteria.\textsuperscript{[2, 3]} One study has shown that potentially harmful medication errors may be three times more common in the pediatric population than in adults.\textsuperscript{[4]}

Calculation of pediatric antibiotic doses using the Body Surface Area is better than those calculated according to age or weight.\textsuperscript{[5, 6]} Measurements of the volume of the fluid compartment and investigations on the blood concentrations of drugs have good correlation with the Body Surface Area.\textsuperscript{[7]}

Inappropriate antibiotic use is very common among pediatric patients\textsuperscript{[8]}, prescribing lower than the recommended dose was the most common form.\textsuperscript{[9]} Frequent intake of antibiotics in small doses constitutes a constant selective pressure on pathogens and results in antibiotic-resistant strains.\textsuperscript{[10,11]}

Bacterial antibiotic resistance is a serious problem worldwide, with implications for morbidity, mortality and health care in hospitals and in the community.\textsuperscript{[12,13]}

**Objectives**

To study the extent of dose-related off-label prescribing of antibiotics to children in pediatric hospitals in Khartoum state.

**Specific objectives**

- To calculate the percentage of incorrect doses administered to pediatric patients in Gaffer Ibn Auf and Ahmed Gasim pediatric hospitals.
- To identify the problem of antibiotics overuse in Gaffer Ibn Auf Children Hospital and Ahmed Gasim pediatric hospitals.
- To assess the correlation between incorrect dose calculation and different parameters related to prescribing.
Method
This was a descriptive, quantitative, cross-sectional, and hospital-based study. A sample of in-patients medical records that included antibiotic prescription for children aged less than 16 years in the time of data collection were recruited, and patients in stay at the hospital for more than 24 hours. The total number of in-patients (in January 2012) in Gaffer Ibn Auf hospital was 727, and that in Ahmed Gasim pediatric hospital was 594 patients, so the sample size was determined using this equation.

\[
n = \frac{N \times Z^2 \times p \times q}{(N-1)d^2 + z^2 \times p \times q} \]

\[
n = \frac{1321 \times (1.96)^2 \times 0.5 \times 0.5}{1320 \times (0.05)^2 + (1.96 \times 0.5 \times 0.5)} = 335
\]

N=population under study.
n=sample size.
Z=value of normal curve corresponding to level of confidence 95% (1.96).
P=proportion of the target group.
q=1-p.

The calculated sample was equal to 335 records, the study actually recruited 385 records.

Age, weight, height of the patient, medical diagnosis, the prescribed antibiotic and its dose, the route of drug administration, and the duration of treatment were extracted from the medical records, and listed in a data sheet. Data was analyzed using SPSS version 16 and Microsoft Excel 2007. Descriptive analysis was conducted. A value of p < 0.05 was considered statistically significant.

RESULTS
From the 385 records studied, 356 (92.47%) of them included an antibiotic. The majority of patients were males 225 (63.2%), and females were 131 (36.8%).

Table (1) Patients’ age groups.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Percentage(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 mon</td>
<td>5.1</td>
</tr>
<tr>
<td>1-6 mon</td>
<td>25.6</td>
</tr>
<tr>
<td>7-12 mon</td>
<td>17.1</td>
</tr>
<tr>
<td>1-5 yrs</td>
<td>38.8</td>
</tr>
</tbody>
</table>
Table 1 specified the age groups of the study population 47.8% were aged less than one year, 38.8% were aged 1-5 years and 13.5 more than 5 years.

The correct dose for each case was calculated according to Body Surface Area using this formula.

\[ \text{BSA} = \sqrt{\text{weight} \times \text{height}/3600}, \]

Pediatric dose = \((\text{BSA}/1.8) \times \text{adult dose}\).

Only 174 medical records included height and weight of children, this was used to calculate the correct dose. It was found that 39.1% of the prescribed antibiotics were calculated incorrectly. Looking into the deviations from correct dose: (57.35%) were higher than the upper limit, and (42.65%) were less than the lower limit.

Table (2) frequencies of the medical diagnosis for the indication of an antibiotic

<table>
<thead>
<tr>
<th>The medical diagnosis</th>
<th>Frequency</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory tract infections</td>
<td>172</td>
<td>48.3</td>
</tr>
<tr>
<td>GIT infections</td>
<td>40</td>
<td>11.2</td>
</tr>
<tr>
<td>Neonatal sepsis</td>
<td>15</td>
<td>4.2</td>
</tr>
<tr>
<td>Meningitis</td>
<td>15</td>
<td>4.2</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>22</td>
<td>6.2</td>
</tr>
<tr>
<td>Anaemias</td>
<td>17</td>
<td>4.8</td>
</tr>
<tr>
<td>T.B</td>
<td>5</td>
<td>1.4</td>
</tr>
<tr>
<td>febrile convulsions</td>
<td>12</td>
<td>3.4</td>
</tr>
<tr>
<td>malaria + anaemia</td>
<td>14</td>
<td>3.9</td>
</tr>
<tr>
<td>others</td>
<td>40</td>
<td>11.2</td>
</tr>
</tbody>
</table>

Table (2) listed the medical diagnosis of the studied population for the indication of an antibiotic. It was observed that respiratory tract infections (RTIs) and Gastro-intestinal tract infections (GITIs) constituted 59.5% of all medical conditions treated at the hospitals.

The mean number of drugs prescribed per prescription was 1.4, it was found that almost two thirds (63.2%) of the prescriptions were for 1 drug, 34.5% were for 2 drugs, and 2.25% were 3 drugs or antibiotics.
Figure (1) shows the routes of antibiotic administration prescribed for the study population. The percentage of prescriptions that included an I.V injection was (82.58%).

**Table (3): Prescribed antibiotics.**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriazone</td>
<td>41.9</td>
</tr>
<tr>
<td>Benzyl penicillin</td>
<td>35.4</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>29.2</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>11.8</td>
</tr>
<tr>
<td>Ampiclox</td>
<td>11.8</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>4.2</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1.4</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>0.8</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>0.8</td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td>0.8</td>
</tr>
<tr>
<td>Penicillin V</td>
<td>0.6</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Table 3 shows the whole list of the prescribed agents. Third generation cephalosporins and benzyl penicillin were the most frequently prescribed antibiotics.
No association was found between patients’ age, gender or diagnosis and the prescribed antibiotics. However, there was significant relation between incorrect dose calculation and the oral route, and oral & I.V infusion being associated with high percentage of incorrect calculation (p-value 0.011) as in figure 2.

The Numbers of antibiotics per prescription was significantly associated with incorrect dose calculation, the higher the number the more incidence of incorrect doses being prescribed (p-value 0.043), as shown in figure 3.

**DISCUSSION**

A substantial overuse of antibiotics (92.47%) was identified in this study, which is far higher than the accepted value of <30% as recommended by WHO. Prescribing of antibiotics
observed in our study was the highest compared with all local previous studies, which had a range between 59% in the Revolving Drug Fund Health Facilities study\textsuperscript{[15]} and 73% in the Health Care Centers study.\textsuperscript{[16]}

This injudicious use of antibiotics may contribute to the risk of antibiotic resistance, as observational and interventional studies from several countries support the link between the rate of antibiotic use and the emergence of resistance. Factors leading to antibiotic overuse are complex, involving physician beliefs, lack of knowledge about the accurate use of antibiotics, diagnostic uncertainty, and meeting patients’ demands.\textsuperscript{[17, 18]}

In our study 39.1% of the prescribed antibiotics were calculated incorrectly, 57.4% of these were higher than the recommended dose (22.4% of all prescribed antibiotics). While 43.6% were lower than the recommended dose (16.7% of all prescribed antibiotics).

The results of the study shows that respiratory tract infections and GIT infections constituted (59.5\%) of all medical diagnosis for the indication of antibiotics which is similar to a study conducted by McCaig and Hughes who reported that upper respiratory tract infections (URIs) and bronchitis ranked second and third among conditions associated with antibiotic prescriptions by US ambulatory physicians 1992.\textsuperscript{[19]}

Essential elements in the management of children with diarrhea are the provision of oral rehydration therapy; provide children with zinc supplementation and continuing feeding.\textsuperscript{[20]} Inappropriate use of antibiotics in treatment of diarrhea in children diverts attention and resources away from these simple measures.

The average number of drugs prescribed per prescription in this study was 1.4, which was lower than the number observed in previous local studies in patients of all ages.\textsuperscript{[14,15]} Our findings indicate absence of polypharmacy, however; it has been proposed that the average number of drugs per prescription should be about 2.\textsuperscript{[21]} The small number of drugs prescribed per prescription in this study may be attributed to the fact that the prescribers considered the economic status of the patients and may not necessarily be due to good prescribing practice. Bearing in mind that the majority of patients in public health facilities are usually of low incomes.

The overall percentage of prescriptions for injections in our study was almost 85%. There are many problems associated with frequent use of injections. The use of injections compared to
oral drug therapy is more expensive and less convenient, unsafe use could be associated with transmission of infectious diseases such as AIDS, hepatitis B and C viruses, and other complications such as abscesses and septicemia.\textsuperscript{[22]}

Severe nausea and severity of illness may necessitate initial parenteral antibiotic administration. When nausea abates and the patient is clinically stable, the patient may be switched to oral chemotherapy. Such an adjustment of therapy reduces the length of hospital stay while providing effective and safe treatment.

In our study 71.1\% of the prescribed antibiotics were broad spectrum third generation cephalosporins (ceftriaxone and cefotaxime) this pattern of prescribing deviates from the systemic approach for selection of antimicrobial regimen, since choosing an antimicrobial agent to treat an infection is far more complicated than matching a drug to a known or suspected pathogen.\textsuperscript{[23]}

Moreover; we found that all children prescribed the aminoglycoside gentamycin were given the drug three times per day. This may subject the patients to toxicity or renal damage, especially after the approval of the extended-interval amino glycoside dosing (EIAD) concept.\textsuperscript{[24, 25]}

CONCLUSION

Our findings revealed problem areas in prescribing and dose calculation of antibiotics in the pediatric hospitals in Khartoum State. Substantial overuse of antibiotics, high percentage of incorrect dose calculation with most doses calculated as higher than the correct dose, was among the most apparent problems.

The study highlighted significant high prescribing of injections, high use of broad spectrum antibiotics, and significant relation between incorrect dose calculations and the oral route of drug administration and multiple drugs per prescription.

REFERENCES


