A pilot study on the rational use of medicines in four tertiary care hospitals through validated World Health Organization prescribing drugs indicators

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Key words: World Health Organization, Drug Utilization, Antibiotics, Outpatients, Hospitals, Pakistan

Parole chiave: Organizzazione Mondiale di Sanità, Utilizzazione dei farmaci, Antibiotici, Ambulatori, Pazienti ambulatoriali, Ospedali, Pakistan

Abstract

Background. Appropriate utilization of therapeutic agents is a basic component of the quality of health outcomes for the patients and the community. A pilot study was conducted to evaluate the rational use of medicines and antibiotics, based on World Health Organization (WHO) prescribing indicators.

Study design. We performed a retrospective, descriptive, cross-sectional pilot study in the medical outpatient departments in four tertiary care hospitals of Islamabad, Pakistan, in order to verify the correct prescribing of medicines according to the validated indicators prepared by the World Health Organization (WHO).

Methods. The Registries of all the prescriptions formulated during the period April 02 2017 – April 01 2018 by the outpatient departments of four tertiary care hospitals (two government funded hospitals (GH-A and GH-B) and two private funded hospitals (PH-C and PH-D) were considered. According to the World Health Organization recommendations, during the following month (April 02 2018 to May 1 2018), 600 prescriptions (150 per hospital) were collected by a random sampling method, verified and analyzed through a statistical tool (SPSS version 22.0).

Results. Mean number of medicines per prescription were 4.6 (Optimal value ≤ 2), with the highest value observed in GH-B hospital. Out of these, 350 (58.3%) (Optimal value < 30%) prescriptions consisted of antibiotics and 340 (56.6%) (Optimal value < 25%) prescriptions consisted of injectable medicines, with marked differences between hospitals. About 550 (19.6%) medicines were prescribed by generic name in all selected prescriptions with the lowest value observed in PH-D (9.9%) (Optimal value = 100%). Overall, 88% medicines were prescribed from National essential medicine list/formulary (Optimal value = 100%). All the prescribing core indicators showed significant difference between hospitals (P = 0.001). The most commonly prescribed antibiotic was ceftriaxone (37.4%), followed by ciprofloxacin (15.1%).

Conclusions. Poor adherence to WHO prescribing indicators were observed in all medical outpatient departments in selected hospitals. WHO recommended core interventions should be implemented on trial basis to develop strategies to achieve long-lasting benefits.
Introduction

Rational use of medicines includes appropriate prescribing, dispensing and utilization of medications for diagnosis, treating, mitigation and prevention of diseases (1, 2). Self-medication, polypharmacy, inappropriate use of antibiotics, injectables misuse, and lack of interest in following standard treatment guidelines for prescribing practice are the most common causes of irrational use of therapeutic agents (3-5). It was reported that pharmaceutical expenditures are more than 70% of the budget in countries with low and middle economic status (1). According to the World Health Organization (WHO), more than 50% of all medicines are irrationally prescribed or dispensed and also more than 50% of the patients have adherence problems with the prescribed regimens (1, 6). As a result, irrational use of medicines adversely affects the total costs of healthcare, the pharmaceutical quality and adds to antibiotics resistance development. Additional possible adverse effects include a rise in adverse drug reaction, drug-drug interaction and patient non-adherence to medication therapy (1, 4, 6, 7).

Investigation about the types, extent, and reasons behind medication usage are the limiting steps to irrational use. Therefore, some core and complementary drug use indicators were established by WHO for the evaluation of medicines utilization in healthcare settings. WHO validated and considered core drug use indicators as a first line indicator for assessment of medicines use. These indicators are highly informative, easily achievable and less likely to vary over time and place (6, 7). Considering these problems and the importance of WHO prescribing indicators, the present pilot research aimed to evaluate the rational use of medicines, based on WHO prescribing indicators, in the medical outpatient departments of four tertiary care hospitals in Islamabad, Pakistan. The antibiotic utilization pattern was also investigated in the same context.

Methods

A retrospective, descriptive, cross-sectional study was conducted to assess the rational use of medicines by applying WHO core drug use indicators. The study was conducted according to the respect of ethics in research and accepted by the Ethical/Institutional review Boards of the concerned hospitals. Medical outpatient departments of two government funded hospitals (GH-A and GH-B) and of two private funded hospitals (PH-C and PH-D) were selected in Islamabad, the capital city of Pakistan with a population of 2,001,579 (8), for data collection. These hospitals are the main referral tertiary care teaching hospitals with similar specialities and provide health facilities to the different areas (Rawalpindi, Azad Jammu Kashmir, Khyber Pakhtunkhwa and areas of Punjab) of Pakistan. Therefore, they are approached by a population of different regions of Pakistan, and this fact may offer an indication of the country’s health status.

According to the recommendations of WHO, all the prescriptions corresponding to a full year activity (from April 02 2017 to April 01 2018) were harvested from all the Medical Outpatient Departments of the above four hospitals. During the following month (April 2 2018 to May 01 2018), 600 prescriptions (150 from each hospital) were retrospectively selected through a random systematic sampling from all the above prescriptions. The selection was irrespective of age, gender and diagnosis. However, prescriptions with illegible hand writing, missing information, providing administration limited to topical preparations (such as creams/ointments for skin and ophthalmic drops/ointments),
or providing no drugs but only medical supplies (like bandages, glove and syringe), were excluded, and substituted by other prescriptions randomly sampled.

The ideal standards for prescribing care indicators were assumed from former studies (1, 4, 7). The prescribing indicators cover: the average number of medicines prescribed per single prescription (optimal value 1.6–1.8), the percentage of prescriptions containing antibiotics (optimal value 20.0–26.8%), the percentage of prescriptions of injectables (optimal value 13.4–24.1%), the percentage of medicines prescribed by generic name (optimal value 100%), and the percentage of medicines prescribed from the National Essential Medicine List (NEML) (9) (optimal value 100%). The pattern and utilization of antibiotics were also determined according to the WHO/Anatomical Therapeutic Classification System (WHO/ATC) (10).

Different statistical tools were applied for the data analysis. Descriptive statistics (like mean, frequency, and percentages) and inferential statistics (like one-way ANOVA) were used to analyze and present data. The analysis was performed using statistical tool SPSS version 22 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, New York, USA: IBM Corporation). The statistically significant p value was considered as less than 0.05.

Results

All the collected prescriptions were evaluated by using WHO prescribing indicators. About 2,802 medicines were prescribed overall in the specified period for the 600 patients. Mean medicines per prescription were 4.7 (Optimal value ≤ 2), with the highest value observed in GH-B hospital. 350 out of 600 prescriptions (58.3%) (Optimal value < 30%) included antibiotics and 340 (56.6%) included injectable medicines, with appreciable variation among all hospitals. About 550 (19.6%) medicines (Optimal value =100%) were prescribed by generic name, with the lowest value observed in PH-D (9.9%). Overall, 88% of medicines were prescribed from the NEML/formulary (Optimal value =100%). All the prescribing core indicators show statistically significant deviation from the WHO optimal values (P = 0.001) (Table 1).

Table 1 - Overall analysis of WHO prescribing indicators in selected settings (total prescriptions = 600)

<table>
<thead>
<tr>
<th>Prescribing indicators</th>
<th>Total</th>
<th>P-value</th>
<th>WHO-Optimal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of medicines</td>
<td>2,802</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Average number of medicines/Rx</td>
<td>4.7</td>
<td>0.001</td>
<td>≤ 2</td>
</tr>
<tr>
<td>Total number of prescriptions containing antibiotics</td>
<td>350</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>% of prescription with antibiotics</td>
<td>58.3%</td>
<td>0.001</td>
<td>(20–26.8%)</td>
</tr>
<tr>
<td>Total number of prescriptions containing injections</td>
<td>340</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>% of prescription with injections</td>
<td>56.6%</td>
<td>0.001</td>
<td>13.4–24.1%</td>
</tr>
<tr>
<td>Total number of medicines with generic name prescribing</td>
<td>550</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>% of generic name prescribing out of 2,802 medicines</td>
<td>19.6%</td>
<td>0.001</td>
<td>100%</td>
</tr>
<tr>
<td>Total number of medicines prescribed from NEML/Drug formulary list</td>
<td>2,467</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>% of medicines prescribed from NEML/Drug formulary list</td>
<td>88%</td>
<td>0.001</td>
<td>100%</td>
</tr>
</tbody>
</table>

Legends: Rx Prescription, n Number, % percentage, NEML National Essential Medicines List, p value less than 0.05 was considered statistically significant.
Differences of prescription behaviour among hospitals were observed. Further, significant differences were observed between hospitals and WHO optimal values (P<0.05) (Table 2).

The utilization pattern was also variable between hospitals. Most commonly prescribed antibiotic was ceftriaxone (n = 131, 37.4%), followed by ciprofloxacin (n = 53, 15.1%). Prescribing behaviour with respect to antibiotic utilization was different among hospitals. Details are listed in Table 3.

### Discussion

Inappropriate prescribing practices are a worldwide problem, responsible for adverse effects in patients (3, 11). In this pilot study, WHO prescribing indicators were utilized to assess existing prescribing practice. This study is helpful to analyze the health system of Pakistan, namely whether the main hospitals are applying or not the guidelines to verify the quality of medical practice. This pilot scale study provides information on how the therapy is managed nationally and can help to put the basis to improve our healthcare system.

The average number of medicines per prescription revealed by the present study was higher than the standard WHO value of 1.6–1.8 (7) (Table 1). The mean number of medicines per prescription shows significant difference between the medical departments of the involved hospitals (P = 0.001) (Table 2). Similar findings were reported by other studies outside Pakistan, for example, 4.8 in Ghana (12) and 3.9 in Afghanistan (13). Lower values were reported by studies conducted in Ethiopia (2.3) (1) and Sudan (1.4) (14). Whereas, a higher number of medicines per prescription were reported in India (5.6) (15). However, the data of this study are not sufficient for determining the ultimate cause of poly-pharmacy, which...
might be due to inadequate professional competency, poor or no availability of clinical pharmacists, incentives to the prescribers, inadequate system for delivering healthcare, or a therapeutic approach based on symptoms or even the habit of empirical prescribing, variations in socioeconomic status, insufficiently known morbidity and mortality, and lack of resources for providing precise medications (1, 4, 16). Polypharmacy has a negative impact on treatment outcomes, e.g. it can cause drug-drug interactions, increase chances of adverse drug reactions, wastage of medicines and augmented expenses for patients and national healthcare systems (7, 11).

Antibiotics percentage per prescription was 58.3%, which is more than twice the WHO/INRUD standard (20–26.8%) (7) (Table 1). The variation between hospitals was statistically significant (P=0.001) (Table 2). This result was much higher than in similar studies conducted in other developing countries like India (39.6%) (17), Brazil (28.8%) (18), Nigeria (28.1%) (19) and Bangladesh (25%) (20). These results indicate that in our Country antibiotics prescription is not under control. The reasons behind antibiotics irrational prescribing may be cultural, or patient’s belief in antibiotic prescription or prescriber’s belief that antibiotics are less efficacious (4). Evaluation studies on medicines use can be performed to confirm antibiotics prescription as rational or irrational.

This study showed that 56.6% of prescriptions included at least one injectable product (optimal value 13.4–24.1%) (7) (Table 1). The variation between selected hospitals was also statistically significant (P<0.05) (Table 2). This value was too high compared to the studies conducted in Kuwait (9.1%) (21), Egypt (9.9%) (11), Afghanistan (17%) (13) and China (22.9%) (22). Possible causes for the over utilization of injections could be (i) physician and patient confidence on injections and their faith for their effectiveness; (ii) preference for the use of injections in seriously ill patients, hoping for prompt action. Injections are very costly formulations, that need qualified and practically proficient personnel for administration. Additionally, contaminated injections can potentially endanger the health of patients because they are responsible for the increase accident of pathogens transmission, like hepatitis, HIV/AIDS, and blood-borne diseases (4, 11).

Table 3 - Utilization pattern of antibiotics in outpatient departments of hospitals (n = 350)

<table>
<thead>
<tr>
<th>Antibiotic class with ATC code</th>
<th>GH-A n (%)</th>
<th>GH-B n (%)</th>
<th>PH-C n (%)</th>
<th>PH-D n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone (J01DD04)</td>
<td>42 (33.6)</td>
<td>34 (42)</td>
<td>22 (31.4)</td>
<td>33 (44.6)</td>
<td>131 (37.4)</td>
</tr>
<tr>
<td>Ciprofloxacin J01MA02</td>
<td>23 (18.4)</td>
<td>18 (22.2)</td>
<td>9 (12.8)</td>
<td>3 (4)</td>
<td>53 (15.1)</td>
</tr>
<tr>
<td>Amoxicillin and enzyme inhibitor (J01CR02)</td>
<td>15 (12)</td>
<td>10 (12.3)</td>
<td>16 (22.8)</td>
<td>10 (13.5)</td>
<td>51 (14.6)</td>
</tr>
<tr>
<td>Cefuroxime (J01DC02)</td>
<td>12 (9.6)</td>
<td>4 (4.9)</td>
<td>9 (12.8)</td>
<td>12 (16.2)</td>
<td>37 (10.6)</td>
</tr>
<tr>
<td>Cefazolin (J01DB04)</td>
<td>10 (8)</td>
<td>9 (11)</td>
<td>7 (10)</td>
<td>1 (1.3)</td>
<td>27 (7.7)</td>
</tr>
<tr>
<td>Azithromycin (J01FA10)</td>
<td>9 (7.2)</td>
<td>0 (0)</td>
<td>3 (4.3)</td>
<td>7 (9.5)</td>
<td>19 (5.4)</td>
</tr>
<tr>
<td>Cefradine (J01DB09)</td>
<td>6 (4.8)</td>
<td>3 (3.7)</td>
<td>1 (1.4)</td>
<td>2 (2.7)</td>
<td>12 (3.4)</td>
</tr>
<tr>
<td>Cefoperazone+ Sulbactam (J01DD62)</td>
<td>5 (4)</td>
<td>3 (3.7)</td>
<td>1 (1.4)</td>
<td>0 (0)</td>
<td>9 (2.6)</td>
</tr>
<tr>
<td>Erythromycin (J01FA01)</td>
<td>3 (2.4)</td>
<td>0 (0)</td>
<td>2 (2.8)</td>
<td>6 (8.1)</td>
<td>11 (3.1)</td>
</tr>
<tr>
<td>Total n (%)</td>
<td>125 (100)</td>
<td>81 (100)</td>
<td>70 (100)</td>
<td>74 (100)</td>
<td>350 (100)</td>
</tr>
</tbody>
</table>

Generics prescribing percentage was at a level of 19.6% (optimal value being 100%), with the lowest value recorded in PH-D (9.9%) (Table 1 and Table 2). The difference between all the four hospitals was statistically significant (P = 0.001) (Table 2). Similar findings were reported by an Indian study (25%) (23), however, a lower value of generics prescribing was reported in Andorra (6%) (24). Furthermore, higher values were observed in the studies carried out in Ethiopia (98.7%) (4), Timor-Leste (92%) (25), Punjab Pakistan (83.1%) (3), China (64.1%) (22) and Nigeria (49.3%) (19). We found that generics prescribing in selected settings was very low. These findings are alarming for several reasons. Brand prescribing results in additional unjustified cost, in added complexity of recalling medications and accessibility (1, 7). WHO approved some logical recommendations to promote generics prescribing pattern for enhancing patient safety (3, 7, 11).

About 88% of medicines were prescribed from NEML/formulary with statistically significant p-value difference between hospitals (P = 0.001) (Table 1 and Table 2). Similar finding was reported in Lao People’s Republic (86.2%) (18). Higher values were reported by research studies conducted in Ethiopia (96.6%) (4) and Egypt (95.4%) (11). However, lower values were reported by studies conducted in others countries like Serbia (in Kragujevac: 70%) (26), China (67.7%) (22) and India (66%) (23). WHO issued Essential Medicine List (EML) to ensure rational prescribing, like using an optimal medicine. These medicines are cost-effective, established, easily available and accessible as compared to brands of medicine (3, 11).

Ceftriaxone shared the maximum percentage amongst all the antibiotics in this study (Table 3). Similar findings were also reported in others studies (3, 6). It is obvious from the literature that the pattern of prescription of antimicrobials is peaking up, with variation in type and quantity. The growing trend of multi-drug therapies is explained by the high possibility of antimicrobial resistance and lack of development of sophisticated, targeted antimicrobials (3, 15).

Data collection from four outpatient medical departments in four tertiary care teaching hospitals, and their elaboration during one-month pilot study was a challenging task. A sample size of 600 prescriptions and their analysis according to WHO methodology confirms the authenticity of the findings and indicates the steps as the best to strengthen the study. Additionally, all the core drug use indicators approved by WHO were implemented in the mentioned department of hospitals. According to the areas associated with the medicines used, the problems were identified and the degree of problems also measured. Results of this study are fruitful for the policy makers to implement and improve the rational prescribing process according to WHO indicators, and suggest the adoption of periodic audit sessions devoted to medicines utilization in healthcare settings. These steps are crucial for an effective distribution of services for the patients and the community. The limitations of this study should be stated. First, it should be noted that results of this study might not be globalized nationally and internationally. However, these results add to the growing literature on medicines use in the health systems of developing countries. Further, the multiple causes of irrational use of medicines can’t be fully understood from our findings.

Conclusions

In conclusions, the major problems identified that require special attention by healthcare authorities were polypharmacy, over-prescribing of antibiotics and injections and the insufficient generics prescriptions. The results of the recommended WHO core
indicators were poor, in all the four hospitals. To identify the fundamental causes of the problem in these settings, a comprehensive research is needed, to be realized starting from this study as a baseline. WHO recommended core interventions should be implemented on trial basis to develop strategies to achieve long-lasting benefits. Interventional and cohort longitudinal studies will be adopted for further in-depth investigations.

The departments and institutions in which the work was conducted
GH-A: Outpatient Department of Pakistan Institute of Medical Sciences, Islamabad, Pakistan.
GH-B: Outpatient Department of Holy Family Hospital, Islamabad, Pakistan.
PH-C: Outpatient Department of Shifa International Hospital, Islamabad, Pakistan.
PH-D: Outpatient Department of Kulsum International Hospital, Islamabad, Pakistan.

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Riassunto

Studio pilota sull’uso razionale di farmaci mediante indicatori di prescrizione validati dell’OMS in quattro ospedali di cure terziarie

Introduzione. L’utilizzo appropriato di agenti terapeutici è una componente basilare della qualità degli esiti sanitari per i pazienti e per la comunità.


Metodi. Sono stati considerati i registri di tutte le prescrizioni formulate nel periodo compreso tra il 2 aprile 2017 ed il 1 aprile 2018 dagli ambulatori di quattro ospedali di assistenza terziaria (due ospedali finanziati dal governo (GH-A e GH-B) e due ospedali finanziati da privati (PH-C e PH-D). Sulla base delle raccomandazioni dell’OMS, durante il mese successivo (dal 02 aprile 2018 al 01 maggio 2018), 600 prescrizioni (150 per ospedale) sono state raccolte con un metodo di campionamento casuale, verificate e analizzate attraverso il programma SPSS Statistics 22 Software.

Risultati. Il numero medio di farmaci per prescrizione è risultato pari a 4,6 (valore ottimale ≤ 2), con il valore più alto osservato nell’ospedale GH-B. Di questi, 350 (58,3%) (valore ottimale < 30%) erano antibiotici e 340 (56,6%) (valore ottimale <25%) erano medicinali iniettabili, con marcate differenze tra gli ospedali. Circa 550 (19,6%) farmaci sono stati prescritti con il nome generico in tutte le prescrizioni selezionate con il valore più basso osservato nell’ospedale PH-D (9,9%) (valore ottimale = 100%). Complessivamente, l’88% dei medicinali è stato prescritto dall’elenco/formulario Nazionale di medicina essenziale (valore ottimale = 100%). Tutti gli indicatori chiave di prescrizione hanno mostrato differenze significative tra gli ospedali (P = 0,001). L’antibiotico più comunemente prescritto era il ceftriaxone (37,4%), seguito dalla ciprofloxacina (15,1%).

Conclusioni. La scarsa adesione agli indicatori di prescrizione dell’OMS è stata osservata in tutti gli ambulatori medici degli ospedali selezionati. Gli interventi di base raccomandati dall’OMS dovrebbero essere implementati su base sperimentale al fine di sviluppare strategie per ottenere benefici a lungo termine.

References


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