Tendency of the consumption and weighted average price in regard to the cost of anti-infective drugs in a pediatric hospital

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Abstract

Background. We undertook this study to evaluate the tendency of the consumption (defined daily doses/100 bed-days), weighted average price (WAP) and total cost of antibacterials, antimycotics, antimycobacterials and antiviral subgroups from 2005 to 2007, as well as the influence of the consumption and the WAP on the total costs. Methods. We used the database of the hospital pharmacy in order to calculate consumption, WAP and total cost of each drug for therapeutic subgroups. Multiple linear regression and Spearman correlation coefficient were used for statistical analyses.

Results. The antibacterial subgroup showed the highest consumption and the total cost. The antiviral subgroup showed the highest WAP. Consumption and WAP had a significant influence on the total costs. The change by each unit of consumption and WAP produced an increase of $190,893.80 (USD) (95% CI 118,196.1–263,591.6) and $3,050.40 (USD) (95% CI 1,912.5–4,188.3), respectively.

Conclusion. The progressive percentage increase of the total cost of anti-infective drugs in comparison with the total cost of hospital’s therapeutic subgroups was due to the consumption and WAP. Statistical analysis and percentage of variations can identify the effect of consumption and WAP on total costs according to therapeutic subgroups. The analysis of high-cost drugs allows interpretation of some behaviors. Therefore, it is recommended to carry out these types of evaluations so as to identify the different variables that can influence costs.

Key words: anti-infective drugs, systemic use, cost, defined daily doses, weighted average price, pediatric hospital.

Introduction

The current world economic crisis, which also involves Mexico, requires governments and organizations that deal with health issues to carry out studies for the purpose of reducing costs without affecting the health of patients. This is the case with pharmacoeconomic studies at health institutions or medical units.1

The annual costs of drugs have, in general, increased progressively as a result, among other causes, of a greater number of prescriptions in patients with chronic degenerative diseases, as well as the appearance of new medications. Along with these are the high costs of biotechnologies and the inflationary process itself.2,3 Of the total health expenditures in different countries, medications represent a high proportion of between 8 and 20%,4 and in the case of Mexico it is 21%.5 Of

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these, systemic anti-infectives are those that have higher costs in hospitals\(^6\) and may account for up to 30% of total drug expenditures.\(^7\)

In Mexico, although anti-infective drugs have been investigated, the information remains insufficient.\(^8,9\) They are among the most widely sold and consumed medications with an annual market of $960 million (USD)\(^8\) without ignoring the impact of their overuse on bacterial resistance.\(^10,11\) The prescription rates of antibiotics in children is high,\(^12\) and in the Hospital Infantil de Mexico “Federico Gomez” (HIMFG) it was found that the therapeutic group of infectious and parasitic diseases ranked first in total costs of prescription drugs.\(^13\) Using a simple approach, one might think that the increase in recent years in the total costs of these drugs is directly related to the increase in price, consumption, or both. However, in Mexico there are no data on which of the two most influencing factors impact on the total cost and whether these factors have had a trend to increase and, therefore, have resulted in increased total costs.

Although there are some publications related to the consumption of anti-infective drugs for systemic use (Group J) in pediatric hospitals, using the defined daily dose (DDD)/100 hospital-days,\(^14,15\) there were no studies that evaluate, in addition to consumption, cost and weighted average price (WAP) of Group J medications. For this reason, it was decided to analyze the interaction of consumption and WAP in the total cost of a pediatric hospital in four of the six subgroups that make up Group J from 2005-2007 in the HIMFG with the following objectives to evaluate:

- The total cost represented by the four subgroups per year with respect to the total cost of the other therapeutic groups different from Group J:
  - Antibacterials for systemic use (J01)
  - Antimycotics for systemic use (J02)
  - Antimycobacterials (J04)
  - Antivirals for systemic use (J05)

- The tendency in the consumption (DDD/100 hospital-days), WAP and cost of medications of the four subgroups
- The tendency of the most representative medications by their consumption, total cost, or both
- The influence of consumption, WAP, or both on the total cost of the subgroups

### Methods

**Characteristics of the HIMFG**

HIMFG is one of hospitals belonging to the National Institutes of Health in Mexico that serves children with complex diseases such as cancer, immunodeficiencies, HIV-AIDS, cardiac, gastrointestinal tract and central nervous system malformations. Kidney, liver, bone marrow and heart transplants are carried out.\(^16\) HIMFG has 202 medical beds and 114 surgical beds, which include neonatal intensive therapies, surgical and medical. On average, 7000 children per year are admitted and 5600 surgeries are performed. Mortality rate is 2.5%, and 10 nosocomial infections are reported per 100 discharges.

The average hospital stay is 8 days and the hospital occupancy rate is 87.1%. The population served by the HIMFG, in general, is characterized by children from low-income families without access to social security services.

Basic chart and catalog of drugs for the health sector in Mexico

Unlike the case with other international classifications, the basic chart and list of medications of the Health Sector in Mexico (CBCMSSM) is characterized by and includes 23 therapeutic groups. In its latest edition it contains 808 active substances and 1287 pharmaceutical forms.\(^17\) It is manda-
tory for the procurement of drugs by the health sector but does not apply to the private sector. The therapeutic group of the CBCMSSM (labeled with the number six) corresponds to “Infectious and Parasitic Diseases”, which does not conform to the Anatomic Therapeutic Chemical classification (ATC/DDD), which is recommended by the World Health Organization (WHO/ATC) and widely used in countries belonging to the European Community. Therefore, to assess consumption in DDD/100 hospital-days of anti-infectives for systemic use, a conversion to this methodology was done without inclusion of antiparasitic drugs, which according to the ATC/DDD classification corresponds to groups different from the J group. From this, we used the second (pharmacological/therapeutic subgroup) and the fifth level (chemical substance). From the second level only those drugs that make up the subgroups mentioned in the objectives were included.

The database of drugs administered to hospitalized children was obtained from the Department of Pharmacy at the HIMFG, which was used for calculations of consumption of each drug expressed in DDD/100 hospital-days based on the following equation:

$$\text{DDD/100 bed-days} = \frac{[a \times b \times c]}{\text{DDD active principle} \times 100} \times \text{Hospital bed-days}$$

where “a” is the number of grams per unit dose, “b” is the number of unit doses per package and “c” is the number of packets consumed during the study year. If the same chemical was administered orally, parenteral, or both, the respective summaries were made in DDD/100 hospital-days.

Cost of medications
The total annual cost of drugs was obtained with the sum of the costs of each of the drugs used, which took into account only those that were administered during hospitalization of children. In this analysis, within the group of antivirals for systemic use, those corresponding to the subgroups J05AF, J05AG, and J05AR were not included because they are directly funded by the federal government.

Instead of using the arithmetic average of the prices of medicines consumed in the HIMFG, we used the WAP, which adjusts prices based on the quantity purchased, based on the following formula:

$$\text{WAP} = \frac{a_1 b_1 + a_2 b_2 + a_3 b_3 + \ldots}{a_1 + a_2 + a_3 + \ldots}$$

where “a” is the quantity acquired of each drug in the presentation authorized in the CBCMSSM during each year and “b” is the cost of acquiring the same drug for that year. To analyze the evolution over time of drugs of the fifth level (chemical substances), the higher costs were selected as representative of level 2 subgroups.

Statistical analysis
We performed a retrospective and descriptive study that statistically evaluated the interior of the J01 subgroup with the ANOVA test and by the sample size of the three remaining subgroups using Spearman correlation coefficient.

To evaluate the effect of consumption and the WAP over the total cost, multiple linear regression for subgroup J01 was used. Due to sample size of subgroups J02, J04 and J05, this methodology was not able to be used. We used SPSS v. 16.0 software. A p value <0.05 was considered statistically significant.

Results
Of the total budget in the medications used in the HIMFG, subgroups evaluated (J01, J02, J04 and J05) reported 23.4%, 25.8% and 33.1% of expenditures for the years 2005, 2006 and 2007,
respectively. As the years passed, it was established that this percentage increase was the result of the total of the remaining therapeutic groups other than anti-infectives for systemic use, where there would have been lower consumption, lower WAP or both.

Table 1 shows that antibiotics had the highest consumption whereas evaluation by WAP showed that antiviral drugs represented the highest cost. It is also demonstrated that the total individual cost of each subgroup showed a progressive increase during the years studied, with the exception of subgroup J05. Despite this, statistical analysis for years within each subgroup of drugs did not reveal significant statistical differences ($p<0.05$) in terms of consumption, WAP, and total cost.

The percentage change in consumption (percentage increase or decrease) between the years 2005 and 2007 is shown in Table 2 and revealed a decrease in the subgroup of antibacterial and antifungal agents, whereas there was an increase in consumption for the subgroup of antivirals.

### Table 1. Tendencies in consumption, WAP and total cost of subgroups J01, J02, J04 and J05 pertaining to systemic use of anti-infective drugs

<table>
<thead>
<tr>
<th>Variables</th>
<th>Años</th>
<th>J01 (n=30)</th>
<th>J02 (n=5)</th>
<th>J04 (n=3)</th>
<th>J05 (n=4)</th>
<th>Totales (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consumption (DDD/100 bed-days)</td>
<td>2005</td>
<td>68.9</td>
<td>7.7</td>
<td>1.3</td>
<td>0.02</td>
<td>77.8</td>
</tr>
<tr>
<td></td>
<td>2006</td>
<td>70.4</td>
<td>9.3</td>
<td>3.5</td>
<td>0.3</td>
<td>83.5</td>
</tr>
<tr>
<td></td>
<td>2007</td>
<td>60.7</td>
<td>7.0</td>
<td>1.8</td>
<td>0.3</td>
<td>69.7</td>
</tr>
<tr>
<td>$p$</td>
<td>2005</td>
<td>0.876</td>
<td>0.881</td>
<td>0.745</td>
<td>0.560</td>
<td>0.902</td>
</tr>
<tr>
<td></td>
<td>2006</td>
<td>10.8</td>
<td>77.6</td>
<td>564.0</td>
<td>12.5</td>
<td>166.2</td>
</tr>
<tr>
<td></td>
<td>2007</td>
<td>12.3</td>
<td>89.5</td>
<td>562.8</td>
<td>72.3</td>
<td>184.2</td>
</tr>
<tr>
<td>WAP (USD$)</td>
<td>2005</td>
<td>9.7</td>
<td>88.1</td>
<td>565.6</td>
<td>8.8</td>
<td>168.1</td>
</tr>
<tr>
<td></td>
<td>2006</td>
<td>12.3</td>
<td>89.5</td>
<td>562.8</td>
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<td>184.2</td>
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<td>89.5</td>
<td>562.8</td>
<td>72.3</td>
<td>184.2</td>
</tr>
<tr>
<td>$p$</td>
<td>2005</td>
<td>0.983</td>
<td>0.982</td>
<td>0.999</td>
<td>0.359</td>
<td>0.991</td>
</tr>
<tr>
<td></td>
<td>2006</td>
<td>0.982</td>
<td>0.998</td>
<td>0.999</td>
<td>0.359</td>
<td>0.991</td>
</tr>
<tr>
<td>Total cost (USD$)</td>
<td>2005</td>
<td>753,274.8</td>
<td>225,039.3</td>
<td>66,787.8</td>
<td>25.1</td>
<td>1,045,127.1</td>
</tr>
<tr>
<td></td>
<td>2006</td>
<td>907,509.3</td>
<td>328,108.8</td>
<td>139,448.2</td>
<td>58.9</td>
<td>1,375,125.3</td>
</tr>
<tr>
<td></td>
<td>2007</td>
<td>1,006,387.1</td>
<td>346,489.0</td>
<td>82,963.0</td>
<td>330.1</td>
<td>1,436,169.2</td>
</tr>
<tr>
<td>$p$</td>
<td>2005</td>
<td>0.996</td>
<td>0.330</td>
<td>0.770</td>
<td>0.5</td>
<td>0.978</td>
</tr>
<tr>
<td></td>
<td>2006</td>
<td>0.983</td>
<td>0.982</td>
<td>0.999</td>
<td>0.359</td>
<td>0.991</td>
</tr>
</tbody>
</table>

$J_01=$ systemic use of antibacterials, $J_02=$ systemic use of antymycotics, $J_04=$ systemic use of antimycobacterials, $J_05=$ systemic use of antivirals, WAP= weighted average price, DDD= defined daily dose.

### Table 2. Percent of variation of 2005 vs 2007 according to consumption (DDD/100 bed-days), according to WAP and cost (USD 2007) of subgroups J01, J02, J04 and J05

<table>
<thead>
<tr>
<th></th>
<th>J01 (n=30)</th>
<th>J02 (n=5)</th>
<th>J04 (n=3)</th>
<th>J05 (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDD/100 bed-days 2005</td>
<td>68.9</td>
<td>7.7</td>
<td>0.02</td>
<td>1.3</td>
</tr>
<tr>
<td>DDD/100 bed-days 2007</td>
<td>60.7</td>
<td>7.0</td>
<td>0.3</td>
<td>1.8</td>
</tr>
<tr>
<td>$\Delta %$ 2007/2005 DDD/100 bed-days</td>
<td>-11.9</td>
<td>-9.0</td>
<td>1,451.3</td>
<td>40.8</td>
</tr>
<tr>
<td>WAP 2005 (USD$)</td>
<td>10.8</td>
<td>77.6</td>
<td>12.5</td>
<td>564.0</td>
</tr>
<tr>
<td>WAP 2007(USD$)</td>
<td>12.2</td>
<td>89.5</td>
<td>72.3</td>
<td>562.7</td>
</tr>
<tr>
<td>$\Delta %$ 2007/2005WAP</td>
<td>13.5</td>
<td>15.3</td>
<td>476.3</td>
<td>-0.2</td>
</tr>
<tr>
<td>Total cost 2005 (USD$)</td>
<td>753,274.8</td>
<td>225,039.3</td>
<td>25.1</td>
<td>66,787.8</td>
</tr>
<tr>
<td>Total cost 2007(USD$)</td>
<td>1,006,387.1</td>
<td>346,489.0</td>
<td>330.0</td>
<td>82,963.0</td>
</tr>
<tr>
<td>$\Delta %$ 2007/2005 Total cost</td>
<td>33.6</td>
<td>53.9</td>
<td>1,215.1</td>
<td>24.2</td>
</tr>
</tbody>
</table>

$J_01=$ systemic use of antibacterials, $J_02=$ systemic use of antymycotics, $J_04=$ systemic use of antimycobacterials, $J_05=$ systemic use of antivirals, WAP= weighted average price.
of antimycobacterial and antiviral drugs. Regarding WAP, antibacterials, antifungals and antimycobacterials had a positive percentage change and antivirals had a minimal negative change. Finally, the total cost was positive in the four subgroups between 2005 and 2007.

Table 3 shows that between 2005 and 2007, the first five drugs had a positive percentage variation in consumption and in the remainder of the drugs the change was negative. Seven out of ten drugs experienced a negative change in the WAP. However, when the three variables were analyzed horizontally, one can see that the total cost of each was affected directly by the consumption or the WAP, except for meropenem, piperacillin-tazobactam and amphotericin B.

In multiple linear regression analysis on the effect that consumption and WAP may have on the total cost (Table 4), it was found that in the J01 subgroup, both in consumption and WAP, the effect was very important because the price explained up to 39% of the variation in total cost and consumption up to 38%. The change for each unit of consumption resulted in an increase of $190,893.80 (USD) and the change in unit price resulted in an increase of $3050.40 (USD).

Discussion
Analysis of drugs according to therapeutic groups or subgroups is an international strategy that allows comparisons among or within hospitals as well as among countries and regions in order to evaluate, among other things, drug use, increases in the cost of the purchase prices of the drugs, and the impact of the total cost over time on the budgets of the medical units, which are relevant aspects for decision-making in health care organizations. There is an international recommendation not to use the DDD/100 hospital-days for cost analysis, and that their use in children is not recommended because the defined daily dose is calculated for adults.

In this study, whose perspective corresponds to the Health System, DDD/100 hospital-days were not used to evaluate the costs. Being aware of their limitations in children, it is also true that there are pediatric publications in this regard. However, because the objectives of the study were to evaluate the different interactions of consumption, WAP and cost, it was considered appropriate to use them.
In the few international experiences in pediatric hospitals it was found that the cost of anti-infectives for systemic use among the total drugs administered or prescribed varies from hospital to hospital (21-50%)\(^{14,15}\) and varies in Mexico (32.1-37.8%).\(^{22,23}\) In this study it was demonstrated that the progressive percentage increases of the costs of anti-infectives for systemic use from 2005 to 2007 was due to the effect of increased consumption and WAP and not as consequence that it would have reduced the total cost at the expense of consumption and WAP of the different therapeutic groups of anti-infectives for systemic use.

Therefore, it is recommended that when conducting analyses of the percentage of costs of a therapeutic group in relation to others, one should always determine that the percentage increase or decrease is not the result of an increase or decrease in the total cost of the remaining treatment groups.

As shown in Table 1, subgroup J01 had the highest consumption during the 3 years followed by subgroups J02, J05 and J04, which for the year 2007, for example, accounted for 87.0%, 10.0%, 2.5% and 0.43%, respectively. It should be noted that there was no research conducted in hospitalized children found in the literature; therefore, we decided to use the results of a study done in Spain.\(^{24}\) In this study, despite having been performed on an outpatient basis and not being specific to children, it was reported that the J01 subgroup occupied the highest percentage (95.6%) followed by subgroups J04 (2.2%), J02 (1.6%) and J05 (0.49%), expressed in dose per hospital-days.

The percentage variations in consumption of the subgroups over time may be positive or negative, as has been demonstrated in some publications, either in ambulatory patients\(^{25-26}\) or in hospitalized children.\(^{14}\) However, as shown in Table 2, percentage variations in 2005 vs. 2007 were negative for subgroups J01 and J02, which apparently translates as lower consumption of these drugs and, consequently, an increase in the total costs of these subgroups would be attributed solely to the increase in WAP.

For such assessments it will be necessary to perform multiple linear correlations to demonstrate if there is only the WAP effect, consumption or both. This is important because, as shown, total costs can be influenced by demographics,\(^{27}\) prescribing habits according to the introduction of new medications and increase or decrease in demand for some diseases.\(^{28}\) Regarding the latter, the profile of risk factors for the disease involved and the stability of the diagnostic categories must be considered. For example, an increase in the prevalence of hospital infectious diseases would not indicate that costs will increase proportionately. There is also the possibility that treatment methods could be modified.\(^{29}\)

Any variable used in economic evaluations is subject to uncertainties that may cause methodological disagreements, inaccurate data, failure to extrapolate results over time and the variation in outcomes among institutions or among other countries. Therefore, these can be seen as weaknesses in the present study on failing to carry out sensitivity analysis to determine the direction and extent to which the economic evaluation results vary, with a change in the variables or having examined the external validity of results, including also not having assessed the rate of discount and direct and indirect costs.\(^{30-31}\)

The percentage variation of the WAP for different subgroups and their total in 2007 compared to 2005 was above the inflation and the consumer price index, a situation already identified in Mexico.\(^{32}\) The largest WAP of antivirals compared with other subgroups during the 3 years evaluated (in which antiretrovirals were not included, which are also expensive) make it necessary to implant measures in our hospital that lead to a more rational use of them, a situation similar to that being applied to the antibacterials for systemic use.
Finally, it should be noted that in the present study, analysis of consumption and the WAP using only percentage changes, as has been published, do not fully identify the impact of each of them on the total costs per unit of variation, as demonstrated here using the statistical tool of linear regression.

References

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