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Perioperative antibiotic prophylaxis in elective surgeries in Iran

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Abstract

Background: The use of antibiotic prior to surgery is widely accepted. The WHO has recommended the use of ATC/DDD (Anatomical Therapeutic Chemical / Defined Daily Dose) for the analysis of drug utilization. The aims of the present study are 1) to analyze the assessment of prophylactic antibiotic usage prior to surgery, 2) to assess the drug administration based on antibiograms and 3) to compare the results with the national and international standards.

Methods: The present study used ATC/DDD, in a retrospective manner. Cefazolin, ceftazidime, gentamicin, ciprofloxacin, metronidazole, vancomycin, imipenem and penicillin G from 21st March to 21st June 2011 were analyzed in a hospital. Out of 516 medical records, 384 patients had received prophylactic antibiotics.

Results: In comparison, the orthopaedic ward had used more antibiotics. The results showed that antibiotics were not selected based on the antibiogram antibiotic programs. Patients in the age range of 20-30 years were the most recipients of the antibiotics. Men had received more antibiotic in comparison with women. About 75% (384 out of 516) of patients in the study received antibiotics as prophylaxis. Cefazolin was the most frequently prescribed antibiotic.

Conclusion: Our findings showed differences in comparison with national and international studies, but insignificant differences. Data on in-hospital antibiotic usage are varying widely not only due to different antibiotic policies but also due to different methods of mesurement. These differences make the comparison difficult.

Keywords: Antibiotic prophylaxis, Elective surgery, Hospital.

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Introduction

The principles of antibiotic prophylaxis against postsurgical infection were established in laboratory studies in the early 1960s (1). Later this strategy has been applied to many areas of clinical surgery (2, 3). Prophylaxis is desirable and is based on a combination of perioperative preparation, surgical techniques, perioperative antibiotic prophylaxis and postoperative wound care. According to the Infectious Diseases Society of America, rational use of antibiotics requires the use of antibiotics with the appropriate medication that could influence the clinical needs of patients in certain geographic areas with the lowest side effects and cost of medications to the patient may be imposed (4). Despite the advances in surgical techniques there are still a significant number of postsurgical complications, the most common being, surgical wound infections, sepsis, respiratory and cardiovascular complications and thromboembolic events (5). Antibiotic prophylaxis has been routinely used to prevent such complications (6). The quantity of antibiotic use in hospitals and the community has been shown to correlate with antimicrobial resistance, resulting in increased morbidity, mortality, and cost of health care (6). Some evidences have shown that 30 – 60 % of cases of mismanagement and poor prescrip-

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tion or administration that cause these errors came by physicians, distributors or self-medication resulting inappropriate prescribing and unnecessary use of antibiotics raise antibiotic resistance as well as adverse drug events and expenditures (7).

The WHO recommended the Anatomical Therapeutic Chemical (ATC) methodology and Defined Daily Dose (DDD) as a measuring unit. This style facilitate to design and perform a standardized and repeatable drug consumption studies (8). The DDD is suitable as a statistical measure of drug consumption (9). It is used to standardize the comparison of drug usage between different drugs or different health care environments. The DDD is not to be confused with the therapeutic dose or with the dose actually prescribed by a physician for an individual patient. The system is used internationally and the number of users is increasing. Prescribed antibiotics were classified by generic names and according to the WHO/ATC .The purpose of the ATC/DDD system is to serve as a tool for drug utilization research in order to improve quality of drug use (10, 11). One component of this is the presentation and comparison of drug consumption statistics at international and other levels.

In the present study antibiotic prophylactic regimens used before elective surgeries procedures were evaluated in a university-affiliated multidisciplinary hospital in Iran.

Methods

Experimental Procedure

The ATC (Anatomical Therapeutic Chemical) classification: The Norwegian Medicinal Depot set off the ATC system in the 1970s. In 1982 the WHO Collaborating Centre for Drug Statisics Methodology in Oslo synchronized it. The center modified the ATC codes as necessary and maintained an online database and published index. Drugs were divided into special groups according to the organ or system on which they perform and/or their therapeutic and chemical characteristics. At least one ATC code was assigned for each drug. Afterward drugs classified into five different groups. See Table 1 for ATC antibiotics codes, J01 class, which was analyzed in the present study (Table 1).

Setting and study period

A hospital-based study was conducted in Imam Hossein Hospital, Shahrood, Iran. The hospital is a university-affiliated multidisciplinary with 313 beds. Now the center of ear, nose and throat, surgery, ophthalmology, internal medicine, general surgery, neurology, cardiology, obstetrics and gynecology, pediatrics, urology, orthopedics, neurology, psychiatry, infectious disease, infants, dialysis, ICU, CCU, NICU and is part of the Clinical and Laboratory medicine. This study was carried out for a period of ninety following days from 21st March to 21st June 2011 in the orthopedic and general surgery wards (Tables 2 and 3).

Study population and operation characteristics

From a total of 516 patients, 384 cases (men = 265 and women = 119) were prescribed prophylactic antibiotics before their surgical operations. The median age of the patients was 26 years. Most of them were residents of Shahrood, however, some of them came from near cities and villages. The median operation duration was 58 minutes (interquartile range 42 to 83).

Data gathering procedure

Data was collected from elective surgeries from general surgery and orthopedic wards. The general surgery had 37 and orthopedic ward had 26 beds. The other wards of the hospital were excluded to prevent data accumulation. This would help the research to focus on the wards which were used more antibiotics.

Orthopedic and general surgery bed occupancy for the first six months were 82.7% and 83.4% respectively. Therefore, the occupancy indexes for the orthopedic and general surgery were 0.827 and 0.834 respectively. The average occupancy index

Table 1. Cumulative overview of some DDD (Defined Daily Dose) performed in the period 1982-2011(Last updated: 2011-12-19, WHO). Table shows only some of the J01 class of ATC drugs classification.

ATC Code	ATC Drug Name	DDD	U	Administration Rote
J01DB04	Cefazolin	3	g	P
J01DD02	Ceftazidime	4	g	P
J01DD04	Cefrtiaxone	2	g	P
J01MA02	Ciprofloxacin	0.5	g	P
J01XD01	Metronidazol	1.5	g	P
J01GB03	Gentamycin	0.24	g	P
J01GB06	Amikacin	1	g	P
J01XA01	Vancomycin	2	g	P
J01FF01	Clindamycin	1.8	g	P
J01DH51	Imipenem & enzyme inhibitor (refer to Imipenem)	2	g	P
J01CE01	Penicillin G Na 5000000u (is equivalent to 312 mg)	3.6	g	P

for both wards was 0.83.

A data collection form was designed by the authors. The pre-designed form included items regarding patient demographics, type of surgical procedure, drug history and allergy, choice of antibiotic regimen, time of administration, dose and repeated doses and duration of operation. To assess whether the data collection form was filled correctly and accurately, the author checked the items that must be measured. If it was comprehensive enough to collect all the information needed to address the purpose and goals of the study then a pilot test for 30 patients was set up. The form was filled out by 5 paramedic students. The contribution of students was just filling the forms based on patients' medical profiles and records.

Retrospective follow-up was performed to the day of discharge, using patients' profiles and records. Data collection was made based on the officially authorized agreement between research committee of the university and the hospital to access to the patients' profiles and records.

On completion, the data was reviewed, organized, tabulated and analyzed. To perform a standardized and reproducible study, the ATC/DDD methodology was used. The quantity of systemic antibiotics prescribed for in-patients over a period of 90 days was converted to DDDs which is then calculated as DDD per 100 bed-days. The following equation is used to calculate and compare antibiotic usage in hospitals.

Definition of DDD

In the present study, DDD was used as a unit to calculate the total antibiotics prescribed. The DDD is the assumed average preservation dose per day for a drug used for its main indication in adults. A DDD will only be assigned for drugs that already have an ATC code. The defined daily dose is a unit of measurement and does not necessarily reflect the recommended or Prescribed Daily Dose. Doses for individual patients and patient groups will often differ from the DDD and will necessarily have to be based on individual characteristics (e.g. age and weight) and pharmacokinetic concerns. The DDDs per 100 bed-days is a useful aspect when in-hospital drug consumption is considered. For example 100 DDD per 100 bed days specifies that for instance 20 indivuals get a certain treatment for 5 days.

DDD/ 100 bed-days

To calculate the DDD per 100 bed days the number of units administrated in a given period was multiplied by 100 and the divided by: the multiplication of "DDD", "number of days in the period", "number of beds" and the "occupancy index". In the present study the occupancy index was 0.83 for the wards. The number of days in the study was 90 and the total numbers of beds in the general surgery and orthopedic wards were 63. The DDD value for each antibiotic is given by the DDD/ATC WHO system.

Table 2. Type of surgeries performed during the 90 days of the study (n = 516, 357 male plus 159 female). It would be mentioned that 129 patients had surgeries without antibiotics prophylaxis in the period of the study.

Type of Surgery	Total Number of patients in month 1	Total Number of patients in month 2	Total Number of patients in month 3
General	79	56	58
Orthopedic	159	80	84

Table 3. Patients' age (years) in each month with and without antibiotic prophylaxis.

Range of Age/ Period of Study	< 10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	> 80	Patients with antibiotic prophylaxis	Patients without antibiotic prophylaxis	Total
Month 1	33	51	65	32	24	16	10	5	2	147	91	238
Month 2	16	26	46	17	15	10	3	1	2	120	16	136
Month 3	19	25	45	16	22	9	4	1	1	117	25	142

$$\text{DDD/100 bed day} = \frac{(\text{Antibiotic consumption in grams}) \times 100}{\text{DDD} \times \text{number of days} \times \text{number of beds} \times \text{occupancy index}}$$

The occupancy index was calculated every month and was derived by dividing the number of occupied beds by the total number of beds in the wards.

Statistical analysis

All data were analyzed using SPSS, version 21. Frequencies and percentages were calculated.

Results

The results revealed that cephalosporins are used in highly variable dosages for different indications, which should be reflected in the assigned DDDs. Indications for cephalosporins prescription (i.e. the severity of the infections) vary rather extensive from one country to another. The assigned DDDs are placed in the upper area of the dose range for moderate to severe infections. J01DB First-generation cephalosporins have relatively narrow spectrum of activity focused primarily on the gram-positive cocci.

The percentage of patients receiving perioperative antibiotic was 74.41% (Table 4).

There was not any evidence in patients' files related to selecting the antibiotics by antibiograms. Host factors such as immunity contribute to the selective process. Antibiotics themselves may support bacterial diversity, either mediated by the random drift effect or triggering the increase of mutational proceedings under bacterial stress. Analysis of selective environment-related antibiotic-host-bacteria interactions is essential to reach better outcomes.

Discussion

Based on the main goal of the present study which was the usage pattern of prophylactic antibiotics in elective surger-

Table 4. Type of parenteral administrated antibiotic prior to surgery (n = 384). The numbers in brackets show the number of patients. The numbers aside brackets show the total dosage form which were applied.

Period of Study/ Antibiotics Used	Month 1	Month 2	Month 3	Total	WHO/ DDD	DDD/ 100 bed days
Cephazoline 500mg	98 (29)	15 (3)	17 (3)	130	3	26.43
Cephazoline 1g	1267 (76)	1237 (73)	1003 (68)	3667		
Ceftazidime 500mg	1 (1)	4 (1)	5 (2)	10	4	0.02
Cefrtiaxone 1g	70 (5)	72 (6)	18 (2)	160	2	1.7
Ciprofluxacin 200mg	62 (5)	40 (1)	57 (4)	159	0.5	1.73
Ciprofluxacin 500mg	4 (1)	14 (3)	- (-)	18		
Metronidazol 500mg	12 (2)	- (-)	- (-)	12	1.5	0.08
Gentamycin 80mg	136 (21)	96 (15)	122 (17)	354	0.24	2.5
Amikacin 500mg	16 (3)	94 (11)	66 (7)	176	1	1.87
Vancomycin 500mg	45 (3)	-(-)	65 (5)	110	2	0.58
Clindamycin 300mg	3 (1)	237 (5)	88 (6)	328	1.8	1.36
Clindamycin 600mg	- (-)	(-)	28 (2)	28		
Imipenem 500mg	- (-)	33 (1)	- (-)	33	2	0.17
Penicillin G Na 5000000u	- (-)	12 (1)	4 (1)	16	3.6	0

ies the utilization of antibacterial agents, J01 class, was evaluated and compared between the surgical wards of the hospital using the WHO ATC/DDD procedure. Most commonly used agent in the wards, according to the DDD was cefazoline followed by gentamicin and amikacin. Perioperative antimicrobial prophylaxis was used in 384 elective surgeries (74.4%). The DDD/100 bed-days for the perioperative antimicrobial prophylaxis for the most frequently used antimicrobials, cefazolin, in the period of the study was 26.43 (Table 4). No statistically significant difference in antibiotic utilization was found between the wards when measured by DDD/100 bed days. However, the total DDD of antibacterial agents utilized was less than 100 DDD/100 bed days in both units indicating reasonably acceptable use of antibiotics as prophylaxis. Typically, prophylactic antimicrobials are not indicated for clean surgeries (12). They are particularly beneficial in surgical procedures associated with a high rate of infection and the agent chosen should have activity against the most common surgical wound pathogens. Cephalosporins are appropriate first-line antimicrobials for most surgical procedures, targeting the most likely organisms (12, 13). It is advisable to avoid broad-spectrum antimicrobial therapy that may lead to the development of antimicrobial resistance (14). In addition the results of the present study showed lesser than those reported from surgical departments in hospitals in Spain, Estonia and Sweden (15).

It should be mentioned that our results is not in parallel with other studies which have been previousy published such as Mahdaviazad et al, 2011 (16) and Hatam et al, 2011 (17) because our results did not indicate that over- and misuse of prophylactic antibiotics in Imam Hossein Hospital. Therefore, the novelty of the present research communication was that antibiotics consumption in the surgical wards was acceptable in Imam Hossein hospital. This would mark this hospital as a clean health care environment with research, education and treatment missions.

A study at Al-Watani governmental hospital in Nablus, Palestine revealed that the use of antibacterial agents was less than optimal and reached a total of 39 DDD/ 100 bed-days (18). In contrast in a study carried out at Emam hospital in Sari, Iran, the total DDD/100 bed-days in general surgery was 121 in 2000 and this declined to 107 in 2005 (19).

The difference between the results of our study and those published from the other countries may be attributed to the infection control and prevention programs, as well as special guidelines for antibiotic use in surgical wards. Antimicrobial administration is not recommended for all surgical procedures. The present study revealed that antibiotics' consumption in the orthopedic and general surgery wards was acceptable. However it is difficult to compare the results with the other studies. For example a study done by Akalin et al revealed that the most frequently used antimicrobials were cefazolin with 117.9 DDD/100-operation (20). Thus reports on antibiotic use, often lack complete definitions of the units of measurement, hampering the comparison of data between hospitals around the world (21-23).

It is generally accepted that the use of perioperative antibiotics prophylaxis reduces the risk of postoperative infection sites (24-28); yet few studies have described the association between perioperative antibiotics usages and the risk of surgical complication (29). In addition there are a few published descriptions or comparisons of antibiotic consumption. This lack of information has hindered rational discussions about desirable levels of consumption (5, 15).

Another noticeable concern is this fact that the use of perioperative antibiotics might be standard practice in hospitals that provide generally better care, so perhaps this better care, not antibiotics, caused the better outcomes of patients receiving antibiotics prophylaxis (14, 30-34). There is a possibility that physicians who do not use prophylactic antibiotics have higher complications rates because the care they deliver is inadequate in other ways (35). Since we might expect patients operated between 6 PM to 6 AM to be at increased risk either because inadequate staffing or urgent conditions (36). These are the concerns that would influence the patients' outcomes without any relations with antibiotics as prophylaxis (37).

As well as antibiotic prophylaxis being a generally effective intervention for preventing postoperative site infection, the level of this effectiveness would appear to be reasonably independent of what type of surgery is being considered. Therefore, the general prevailing attitude that antibiotic prophylaxis should be assumed to be ineffective unless its effectiveness has been experimentally proven beyond doubt for the specific type of surgery being considered, perhaps should be revised. In particular, a sensible philosophy would be to assume that antibiotic prophylaxis is effective in reducing the risk of wound infection for all types of surgery, even ones where no clinical trial data exists and make exceptions to this rule if, for certain types of surgery, it can be proved to the contrary.

Conclusion

The findings showed differences when compared with national and international studies although the difference was not dramatic. Data on in-hospital antibiotic usage are varying widely not only due to different antibiotic policies but also due to different methods of measurement. These differences make the comparison difficult.

Limitation

Our study had some limitations, including the retrospective design and lack of randomizationd. Moreover, a small number of patients were analyzed from a single center. Furthermore, we could not judge the appropriateness of the empirical antibiotic treatment in this study. Thus further studies will need to assess this valuable and important issue.

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