

## INTRAVENOUS ANTIBACTERIAL USE IN AN UNIVERSITY MEDICAL CENTRE, CAMPO GRANDE, MATO GROSSO DO SUL, BRAZIL

Érica Freire de Vasconcelos-Pereira<sup>1\*</sup>, Vanessa Terezinha Gubert de Matos<sup>2</sup>, Mônica Cristina Toffoli-Kadri<sup>3</sup>

<sup>1</sup>Department of Pharmacy and Biochemistry, Federal University of Mato Grosso do Sul,

<sup>2</sup>Section of Hospital Pharmacy, University Medical Centre, Federal University of Mato Grosso do Sul,

<sup>3</sup>Department of Morphophysiology, Federal University of Mato Grosso do Sul, Brasil.

\*Corresponding author's E-mail: [ericafv@hotmail.com](mailto:ericafv@hotmail.com)

Accepted on: 15-02-2011; Finalized on: 28-04-2011.

### ABSTRACT

Many organizations have recommended that antibacterial drug use at national and local levels should be monitored to better understand the relationship between consumption and emerging bacterial resistance. The utilization of scientific methods to evaluate consumption, as Defined Daily Dose (DDD), assists in determining drug use pattern by unit of hospitalization and it has been used to establish the consumption of antibacterial agents. Whereas this therapeutic class is the most used in hospitals, this study aimed to identify the use of standardized and restricted intravenous antibacterial drugs at the University Medical Centre of Federal University of Mato Grosso do Sul during period of November 2007 to April 2008. Data collection was performed using antibacterial request forms and DDD per 100 bed-days. Ceftriaxone was the most requested drug during the study period and its consumption was 6.10 DDD/100 bed-days, followed by ciprofloxacin (4.55 DDD/100 bed-days) and vancomycin (2.15 DDD/100 bed-days). The use of DDD methodology enables to visualize the changes that occurred in the antibacterial use pattern, as well as monitoring the consumption of drugs recently included in the therapeutical arsenal.

**Keywords:** Antibacterials, evaluate consumption, Defined Daily Doses, Intravenous antibacterial use.

### INTRODUCTION

Antibacterial drugs represent a therapeutic group commonly prescribed at hospital environment for therapeutic and prophylactic situations<sup>1</sup>. When prescribed, dispensed or administered in inappropriate way, antibacterial drugs can cause problems as nosocomial infections, bacterial resistance and increased time of hospitalization<sup>2,3</sup>. These drugs are responsible for approximately 30% of drug costs in hospitals<sup>4</sup>.

Another problem is the availability of several antibacterial drugs that difficult professionals' update. At the same time, the easy access to pharmaceutical industries advertisements and the information quality of these materials is a worry to rational use<sup>5,6,7</sup>.

Trying to have a better antibacterial use, institutions are suggested to have infection control, guidelines, health staff continuing education as well as follow prescription habits and drug consumption<sup>8</sup>.

Drug utilization studies are defined as those focused on marketing, distribution, prescription and use of medicines in society. Furthermore, drug utilization studies give special emphasis to social, economic and medical consequences<sup>9</sup> and constitute a source of guidance for regulatory actions<sup>10</sup>. The Defined Daily Dose (DDD) is one of the used methodologies in quantitative drug utilization studies. DDD is a tool which allows the researcher to relate drug consumption at different periods of time and per unit of hospitalization as well as assess the prescribing habits<sup>11</sup>. It is still a technical unit of measure and

comparison defined as the average maintenance dose per day for a drug used for its main indication in adults<sup>9</sup>.

Thus, this study aimed to identify the use of standardized and restricted intravenous antibacterial drugs at the University Medical Centre of Federal University of Mato Grosso do Sul during period of November 2007 to April 2008.

### MATERIALS AND METHODS

This descriptive and transverse study was conducted at the University Medical Centre (NHU) of Federal University of Mato Grosso do Sul, Brazil. NHU is a general, public, third-care teaching hospital of 280-bed in the municipality of Campo Grande. It also composes the Brazilian Unified National Health System (SUS).

Data was collected between November 2007 and April 2008 from request forms of antibacterial drugs which had restrict use. The identified information were patient gender and age, clinic, diagnosis description, prescribed antibacterial, presence of justification for the use, culture request, nature of infection and opinion of the Hospital Infection Control Committee (HICC) and/or Pharmacy and Therapeutics Committee (PTC). Data regarding antibacterial dosage and length of treatment were collected from the Pharmacy spreadsheet.

The antibacterial drugs considered in the study were used for therapeutic treatment. They were cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, ciprofloxacin, imipenem + cilastatin, levofloxacin, linezolid, meropenem, piperacillin + tazobactam, polymyxin B, teicoplanin and vancomycin.



All NHU clinics that attended patients aged 18 years or over were included in this study. The clinics were Internal Medicine, Maternity, Intensive Care Unit, Coronary Care Unit, Infectious and Parasitic Diseases, Orthopedics, Urology, Surgical Clinic, Oncology and Emergency Medical Care. The Internal Medicine provided service of Cardiology, Rheumatology, Neurology and Pulmonary Medicine.

The antibacterials consumption was expressed in DDD per 100 beds-day and was calculated for each antibacterial included.

$$\text{DDD/100 beds-day} = \frac{\text{Drug consumption (milligram) during defined time (a)}}{\text{DDD (milligram) multiplied by number of days considered in defined time (a) multiplied by number of beds multiplied by Hospital Occupancy Rate}} \times 100$$

DDD in milligram was determined consulting data of WHO Collaborating Centre for Drug Statistics Methodology 2010. The number of available hospital beds and their occupancy rate were obtained from the NHU Medical Archives and Statistics. Data were analyzed and are presented as absolute and relative frequencies and DDD.

The study was submitted to the Institutional Review Board of Federal University of Mato Grosso do Sul and conducted after its approval and after Hospital Board permission.

## RESULTS AND DISCUSSION

It was analyzed 1717 request forms of intravenous antibacterial drugs during the study period and Table 1 shows the distribution of these forms. Only 0.1% of the request forms mentioned some non-standardized antibacterial.

Some changes were identified when comparing NHU current drug standardization and the list available during the period of 1995-1996. Aztreonam, cefepime, pefloxacin were withdrawn of the therapeutical arsenal and piperacillin + tazobactam, teicoplanin, levofloxacin, linezolid and polymyxin B were added.

Despite the availability of new therapeutic agents, the use of recently standardized antibacterial was not superior to the previously standardized agents. This suggests adequate knowledge of prescribers regarding the available therapeutic arsenal at the hospital.

Patients' average age was  $56.11 \pm 19.64$  years and elderly people were the group who most used antibacterial drugs. Population aging is a fact that has been observed over the years. In Brazil, it is estimated that by the year 2025 there will be 34 million of people aged 60 years or over<sup>12</sup>. The process of demographic transition at a fast pace increases the need of elderly people to use health service. In most cases, this need is due to physiological changes related to the increased age which may lead to the emergence of diseases, the need of polypharmacy with antibiotics and the need of hospitalization. The worry about inpatient situation, especially for long

periods, is because it subjects the patient to the risk of infection<sup>12,13,14</sup>.

The request forms of the three most dispensed antibacterial drugs represented 57.1% of the total and more than half of these were dispensed for male patients. This result may be related to men's habits such as sedentary lifestyle, smoking and alcohol in excess which contribute to increasing morbidity<sup>15</sup>.

The most requested antibacterial drugs in the study were also the most consumed ones (Table 2).

**Table 1:** Absolute and relative frequency of antibacterial request forms received by the hospital pharmacy of NHU/UFMS during the period of November 2007 to April 2008.

Prescribed Antibacterials	Absolute Frequency (n=1717)	Relative Frequency (%)
Ceftriaxone	441	25.7
Ciprofloxacin	323	18.8
Vancomycin	217	12.6
Levofloxacin	162	9.4
Meropenem	117	6.8
Cefepime	97	5.7
Cefotaxime	86	5.0
Imipenem + Cilastatin	71	4.1
Ceftazidime	58	3.4
Piperacillin + Tazobactam	55	3.2
Cefoxitin	28	1.6
Polymyxin B	26	1.5
Teicoplanin	21	1.3
Linezolid	13	0.8
Azithromycin	2	0.1
Total	1717	100.0

**Table 2:** Consumption of intravenous antibacterial drugs during the period of November 2007 to April 2008 at NHU/UFMS.

Drug	DDD/100 beds-day
Ceftriaxone	6.10
Ciprofloxacin	4.55
Vancomycin	2.15
Cefepime	1.65
Levofloxacin	1.24
Imipenem + Cilastatin	1.18
Piperacillin+Tazobactam	0.74
Meropenem	0.65
Polymyxin B	0.43
Ceftazidime	0.21
Teicoplanin	0.18
Cefotaxime	0.08
Linezolid	0.02
Cefoxitin	0.01
<b>TOTAL</b>	<b>19.20</b>

A study performed at the same hospital from 1994 until 1996 also identified ceftriaxone as the most requested antibacterial drug. By that time, the utilization ranged from 2.25 DDD/100 beds-days to 4.50 DDD/100 beds-days<sup>16</sup>.



In Porto Alegre, a study in the 1990s at the University Medical Centre reported 5.49 DDD/100 bed-days as the consumption of 3rd-generation cephalosporins<sup>17</sup>. A recent survey conducted in a teaching hospital of a similar size to NHU described ceftriaxone consumption as 6.8 DDD/100 beds-days in 2003 and 6.4 DDD/100 bed-days in 2004<sup>2</sup>. Both studies had found values higher than the described at NHU but it has to be observed that analyzed period was also longer.

The preferential use of third generation cephalosporins can be explained by its therapeutic flexibility, excellent safety profile and inclusion in different clinical treatment protocols<sup>18</sup>. However, overuse has led to development of bacterial resistance<sup>19</sup> which affects the patient in treatment and the population in contact with this patient<sup>20,21</sup>.

The request profile of ciprofloxacin was not described as significant by Toledo *et al.* (2000)<sup>16</sup>. Even though, the authors make reference to the solicitation of pefloxacin (0.8 DDD/100 beds-days to 1.5 days DDD/100-beds) which is not in the current therapeutic arsenal. A study conducted in 58 hospitals in France during the period of 1995 to 2001 described the fluoroquinolones as the second therapeutic class of largest DDD<sup>22</sup>. Rocha, Carneiro and Castilho (2009)<sup>2</sup> described ciprofloxacin values of use ranging from 6.3 DDD/100 bed-days in 2003 and 7.3 DDD/100 bed-days in 2004.

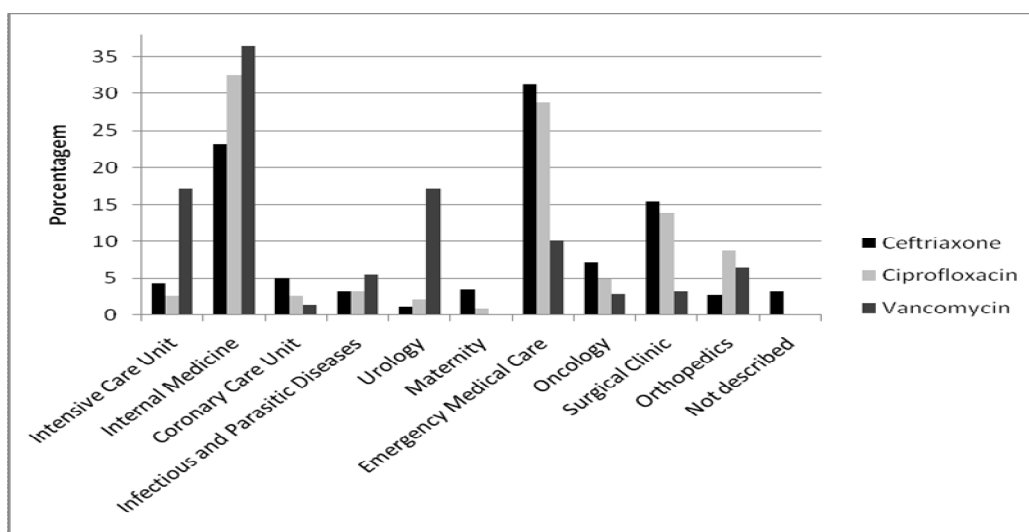
Analyzing vancomycin consumption, Castro *et al.* (2002)<sup>17</sup> observed gradual increase in the use of this antibacterial during the seven years of their study. When comparing vancomycin use at NHU (2.15 DDD/100 bed-days) with a tertiary hospital in Rio de Janeiro (0.8 DDD/100 bed-days in 2003 and 0.9 DDD/100 beds- days in 2004), it is observed a very different profile of use<sup>2</sup>. It is important to notice that NHU study time was smaller than the other studies.

In Chile, a survey that included 29 hospitals showed 0.23 DDD/100 bed-days as minimum consumption of vancomycin, 4.86 DDD/100 bed-days as maximum and 1.97 DDD/100 bed-days as the average. The regular control over dispensation and use of this antibacterial is indispensable to avoid vancomycin overuse. The overuse has been associated to high prevalence of resistant strains of *Staphylococcus aureus*<sup>22,23</sup>. In Brasilia, a study at the Intensive Care Unit during the years 2001 to 2004 demonstrated the utilization of penicillins with beta-lactamase inhibitors, such as ampicillin + sulbactam, and carbapenems in the presence of *S. aureus* as an option to reduce vancomycin consumption<sup>24</sup>.

The pattern of filling in the request forms of the most used antibacterial at NHU during the study period is shown in Table 3.

**Table 3:** Pattern of filling in the request forms of the most used intravenous antibacterial during the period of November 2007 to April 2008 at NHU/UFMS.

Items filled in request form	Antibacterials		
	Ceftriaxone	Ciprofloxacin	Vancomycin
Diagnosis description	97.7	99.7	99.7
Justification for the request	92.3	85.0	86.0
Culture request	54.8	46.5	57.1
Description of infection	50.3	39.9	57.4
HICC/PTC opinion	47.1	44.0	48.2



**Figure 1:** Relative request frequency of the three most prescribed antibacterials according to the clinic, during the period of November 2007 to April 2008 at NHU/UFMS.

The description of patients' diagnosis was present on average in 99.0% of the forms while the justification for the antibacterial request was in 87.8% of these. This difference may indicate lack of knowledge of the reason for choosing a specific therapeutic agent, once the request is filled in by the resident doctor under preceptor indication. It is noteworthy that the study was conducted in a teaching hospital and that further studies are needed to confirm this hypothesis.

Despite the result of Microbial Sensitivity Tests establishes the most appropriate drug for patient treatment, this test was requested in only 53% of the forms. Choosing the treatment based on the result of Microbial Sensitivity Test prevents the rise of resistant strains as well as contributes to the knowledge of hospital pattern of bacterial resistance and the knowledge of clinics with a higher risk of infection. All these information still collaborate to the establishment of effective actions by Hospital Infection Control Committee<sup>25</sup>.

The description of the type of infection was found in 49.2% of request forms. The lack of this information may hinder the analysis performed by the Hospital Pharmacy and the actions of Hospital Infection Control Committee.

Regarding the opinion of Hospital Infection Control Committee and/or Pharmacy and Therapeutics Committee, approximately 46% of the request forms contained such information. Besides the existence of nosocomial antibacterial rationalization policy, the effective participation of the multidisciplinary team is necessary to obtain satisfactory results. Rational use depends on a number of actions that include request forms correctly filled in, forms evaluation and health staff training<sup>24,26</sup>. Monitoring the antimicrobial use contributes to the reduction of nosocomial infection, bacterial resistance and costs of hospital care<sup>27</sup>.

Figure 1 shows the request frequency of the three antibacterials of highest consumption in all clinics included in the study. The Internal Medicine was the clinic with the greatest number of ciprofloxacin and vancomycin requests. The large amount of antibacterial use in this clinic can be justified by the services provided, besides the existence and occupancy of some beds equipped similarly to the intensive care unit. According to Castro *et al.* (2002)<sup>17</sup>, inappropriate prescribing habits, low adherence to the drug use protocols and complexity of hospital procedures may be related to the high consumption of drugs.

The pattern of ceftriaxone use was slightly different from the other two most used drugs with higher consumption at the Emergency Medical Care. Martinez *et al.* (2005)<sup>4</sup> considered that urgency and emergency unit should be excluded from this kind of study because DDD is calculated as the number of available beds what should not exist at the Emergency Medical Care. However, due to unavailability of beds in some clinics, the Emergency Medical Care has been used for patient admission into the study hospital.

Antimicrobials utilization studies have demonstrated the importance of epidemiological problems identification and interventions. In this sense, the use of DDD methodology allows to visualize the changes that occurred in the pattern of antibiotics use as well as monitoring the consumption of drugs recently included in the therapeutic arsenal.

The results also showed the need to strengthen measures of drug use control. It should be done especially in relation to the opinion of Hospital Infection Control Committee and/or Pharmacy and Therapeutics Committee regarding restricted drug dispensation but should include antibacterial action and indication training to resident doctors.

Studies conducted over a longer period including all antimicrobials, examining justification quality for the antimicrobial use and the outcome of interventions could contribute to the proper knowledge of this drug class use as well as monitoring compliance with current standards.

## REFERENCES

1. WORLD HEALTH ORGANIZATION. WHO global strategy for containment of antimicrobial resistance [Internet]. Switzerland: WHO; 2001. [cited 2010 May 29]. Available from: <[www.who.int/csr/resources/publications/drugresist/WHO\\_CDS\\_CSR\\_DRS\\_2001\\_2\\_EN/esp](http://www.who.int/csr/resources/publications/drugresist/WHO_CDS_CSR_DRS_2001_2_EN/esp)>
2. ROCHA, M.A.; CARNEIRO, P.M.; CASTILHO, S.R. Estudo da utilização de medicamentos antimicrobianos de 2003 à 2004 em pacientes adultos em hospital terciário no Rio de Janeiro. *Rev. Bras. Farm.*, v.90, n.1, p.50-53, 2009.
3. SILVA, A.B.; FONTANA, M.; ALMEIDA, A.S.; WANNMACHER, L. Utilização de ceftriaxona no hospital universitário de Passo Fundo. *Rev. Méd. Hosp. São Vicente de Paulo*, v.11, n.26, p.26-30, 2000.
4. MARTÍNEZ, A.R.; SANTOS, I.C.; GARCIA, R.M.; CORBELLA, E.C. Calidad de la prescripción de antibióticos en un servicio de urgencia hospitalario. *An. Med. Interna*, v.22, n.6, p. 266-270, 2005.
5. BARROS, J.A.C.; JOANY, S. Anúncios de medicamentos em revistas médicas: Ajudando a promover a boa prescrição. *Ciênc. Saúde Colet.*, v.7, n.4, p.891-898, 2002.
6. VIDOTTI, C.C.F.; HOEFLER, R.; SILVA, E.V.; BERGSTEN-MENDES, G. Sistema Brasileiro de Informação sobre Medicamentos – SISMED. *Cad. Saúde Pública*, v.16, n.4, p.1121-1126, 2000.
7. HEINECK, I.; GALLINA, S.M.; SILVA, T.; DAL PIZZOL, F.; SCHENKEL, E.P. Análise da publicidade de medicamentos veiculada em emissoras de rádio do Rio Grande do Sul, Brasil. *Cad. Saúde Pública*, v.14, n.1, p.193-198, 1998.
8. BERQUÓ, L.S.; BARROS, A.J.D.; LIMA, R.C.; BERTOLDI, A.D. Utilização de antimicrobianos em uma população urbana. *Rev. Saúde Pública*, v.38, n.2, p.239-246, 2004.
9. WORLD HEALTH ORGANIZATION. Collaborating Centre for Drug Statistics Methodology. Available at: <<http://www.whocc.no/>>. Accessed on: 14 jul. 2010.



10. OSORIO-DE-CASTRO, C. G. S. (Coord.). *Estudos de utilização de medicamentos - noções básicas*. Rio de Janeiro: Editora Fiocruz, 2000. 92 p.
11. CAPELLÀ, D.; LAPORTE, J.R. Métodos aplicados en estudios descriptivos de utilización de medicamentos. In: LAPORTE, J.R., TOGNONI, G. (Orgs.). *Principios da epidemiologia del medicamento*. 2008. Available at: <<http://www.icf.uab.es/pem/llibre.htm>>. Accessed on: 14 mar. 2008.
12. GALATO, D.; ZAMPARETTI, F.O.; LUCIANO, L.T.R. Utilização de medicamentos em uma instituição de longa permanência para idosos do sul de Santa Catarina-Brasil. *Lat. Am. J. Pharm.*, v.27, n.4, p. 553-559, 2008.
13. COLET, C.F.; MAYORGA, P.; AMADOR, T.A. Utilização de medicamentos por idosos inseridos em grupos de convivência do município de Porto Alegre/RS/Brasil. *Lat. Am. J. Pharm.*, v.27, n.3, p. 460-467, 2008.
14. RIBEIRO, A.Q.; ARAÚJO, C.M.C.; ACURCIO, F.A.; MAGALHÃES, S.M.S.; CHAIMOWICZ, F. Qualidade do uso de medicamentos por idosos: uma revisão dos métodos de avaliação disponíveis. *Ciênc. Saúde Coletiva*, v.10, n.4, p. 1037-1045, 2005.
15. MAZZOLA, D.; POLESE, J.C.; SCHUSTER, R.C.; OLIVEIRA, S.G. Perfil dos pacientes acometidos por acidente vascular encefálico assistidos na Clínica de Fisioterapia Neurológica da Universidade de Passo Fundo. *Rev. Bras. Promoç. Saúde*, v.20, n.1, p.22-27, 2007.
16. TOLEDO, M.I.; MARCONCINI, S.M.; RODRIGUES, M.A.; CORRÊA, T.F.; CASTRO, L.L.C. Utilização de antimicrobianos de uso restrito no núcleo do Hospital Universitário da Universidade Federal do Mato Grosso do Sul: Análise da solicitação de uso. *Rev. Ciênc. Farm.*, v.21, n.1, p.57-68, 2000.
17. CASTRO, M.S.; PILGER, D.; FERREIRA, M.B.; KOPITKE, L. Tendências na utilização de antimicrobianos em um hospital universitário. 1990-1996. *Rev. Saúde Públ.*, v.36, n.5, p.553-558, 2002.
18. FICA, C.A.; CABELLO, M.A.; JULIET, L.C.; PRADO, D.P.; BAVESTRELLO, F.L. Consumo de antimicrobianos parenterales en diferentes hospitales de Chile durante el año 2005. *Rev. Chil. Infect.*, v.25, n.6, p.419-427, 2008.
19. VANDER STICHELE, R.H.; ELSEVIERS, M.M.; FERRECH, M.; BLOT, S.; GOOSSENS, H. Hospital consumption of antibiotics in 15 European countries: results of the ESAC retrospective data collection (1997-2002). *J. Antimicrob. Chemother.*, v.58, n.4, p.159-167, 2006.
20. WANNMACHER, L. Uso indiscriminado de antibióticos e resistência microbiana: uma guerra perdida? *Uso Racion. Medicam., Temas Sel.* v.1, n.4, 2004. Available at: <[http://www.opas.org.br/medicamentos/docs/HSE\\_UR\\_M\\_ATB\\_0304.pdf](http://www.opas.org.br/medicamentos/docs/HSE_UR_M_ATB_0304.pdf)>. Accessed on: 14 jul. 2010.
21. WEINSTEIN, R.A. Controlling antimicrobial resistance in hospitals: infection control and use of antibiotics. *Emerg. Infect. Dis.*, v.7, n.2, p.188-192, 2001.
22. ALFANDARI, S.; BONENFANT, C.; DEPRETERE, L.; BEAUCAIRE, G. Use of 27 parenteral antimicrobial agents in north of France hospitals. *Med. Mal. Infect.*, v.37, n.2, p. 103-107, 2007.
23. OLIVEIRA, G.A.; OKADA, S.S.; GUENTA, R.S.; MAMIZUKA, E.M. Avaliação da tolerância à vancomicina em 395 cepas hospitalares de *Staphylococcus aureus* resistentes a oxacilina. *J. Bras. Patol. Med. Lab.*, v.37, n.4, p.239-246, 2001.
24. SANTOS, E.F.; LAURIA-PIRES, L.; PEREIRA, M.G.; SILVA, A.E.; RODRIGUES, I.P.; MAIA, M.O. Use of antibacterial agents in an intensive care unit in a hospital in Brazil. *Braz. J. Infect. Dis.*, v. 11, n.3, p.355-358, 2007.
25. LIMA, M.E.; ANDRADE, D.; HAAS, V.J. Avaliação prospectiva da ocorrência de infecção em pacientes críticos da unidade de terapia intensiva. *Rev. Bras. Ter. Intensiva*, v.19, n.3, p.342-347, 2007.
26. QUEIROZ, R.; GRINBAUM, R.S.; GALVÃO, L.L.; TAVARES, F.G.; BERGSTEN-MENDES, G. Antibiotic prophylaxis in orthopedic surgeries: the results of an implemented protocol. *Braz. J. Infect. Dis.*, v.9, n.4, p.283-287, 2005.
27. ARDA, B.; SIPAHI, O.R.; YAMEZHAN, T.; TASBAKAN, M.; PULLUKCU, H.; TUNGER, A.; BUKE, C.; ULUSOY, S. Short-term effect of antibiotic control policy on the usage patterns and cost of antimicrobials, mortality, nosocomial infection rates and antibacterial resistance. *J. Infect.*, v.55, n.1, p.41-48, 2007.

\*\*\*\*\*

