ANTIBIOTIC USE IN SURGICAL PATIENTS AT CENTRAL AND PROVINCIAL HOSPITALS OF VIETNAM

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Abstract:
Background : The study aims to evaluate the use of antibiotics (AB) by surgical patients in 2 central hospitals and 7 provincial hospitals in Vietnam from June to December 2009. **Methods:** Descriptive, prospective study. **Results:** Of the total of 2072 patients admitted to the study, 29.9% had used AB before their operation. Over one third (34.7%) of patients were prescribed AB as a prophylaxis (during anesthesia), but only 5.4% stopped taking AB after their operation. About 94.6% of patients were prescribed AB long after their operation, with the mean (SD) period of AB use being 5.8 (2.8) days. Over half (55.8%) of patients were prescribed a combination of more than two kinds of AB, with the most common drug being cephalosporin 3rd generation (45.7%). Only 71.1% of patients who used AB were concordant with antibiogram. Percentage and amount of AB usage Defined Daily Doses (DDD) were high and not different among hospitals, however the length of therapy (evaluated by Days of Therapy (DOT)) at provincial hospitals was higher than at central hospitals. **Conclusions:** The study has proven that AB use by surgical patients in Vietnamese hospitals was mostly inappropriate. AB were used during hospitalization, even in clean wounds and without sign of infections. It is important that hospital leaders consider applying an antibiotic stewardship program to control AB usage.
Key words: Antibiotic use, surgical patients

1. BACKGROUND

One of the important causes of a large increase in AB resistance in Vietnam is inappropriate AB usage. AB resistance is severe in Vietnam. For example, the rate of E.coli and Klebsiella resistant to Ampiciline is 88% and 97% respectively, and resistance to Amoxiciline is 38.9% and 42% respectively. A study investigating AB use in a tertiary hospital in Vietnam in 2009 found that 100% of surgical patients were prescribed AB after operations, with a combination of Cephalosporins 3rd generation and Aminoglycosides. A study that evaluated the knowledge, attitudes and practices of surgeons in terms of AB use at 10 hospitals in Vietnam found that although 86.5% of surgeon responded appropriately about AB prophylaxis in surgical patients., Only 7.9% and 23.8% of surgeons respectively answered that they always and often used AB prophylaxis in clean wounds. In addition, 79.8% and 89.3% of surgeons indicated that they always and usually used AB more than 7 days after operations in clean wounds.

There are many unanswered questions regarding AB use among surgical patients in central hospitals as well as provincial hospitals in Vietnam. What percent of surgical patients are given antibiotics as prophylaxis without continuing their use after surgery for clean wounds and clean-contaminated wounds? How many days were ABs used before and after surgery on average and by wound class? Were AB given for patients developing

surgical site infections appropriately? What are the definitions of daily dose of AB used for surgical patients?

Thus, there is a need to investigate AB use in the surgical population in order to provide recommendations for surgeons and policy makers in the hospitals for control of AB use and AB resistance. To evaluate the AB use of surgical patients, the study mainly aims to determine: the percentage of surgical patients who were given antibiotics as prophylaxis without continuing their use after their operation for clean wounds and clean-contaminated wounds; the duration of AB use before and after operations in surgical patients; the rate of appropriate AB use in surgical patients and the dose of AB used by surgical patients.

2. METHODS

This is a descriptive, prospective study to evaluate:

- AB use stratified by disease and stratified by ward.
- Defined daily doses (DDD) per 1000 patient-days (DDD/1000 pt-days).
- Type of AB, amount of AB used, the indications of AB.

The AB use was measured using the DDDs and the days of therapy (DOT) of AB use. DDDs are WHO statistical measures of drug consumption. In this study, DDDs were used to standardize the comparative usage of various drugs compared to one another or between different health care environments. According to WHO's definition, DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. A common problem when comparing drugs is that different medication can be of different strengths and different potency. Simply comparing 1g of one, with 1mg of another can be confusing, particularly if different countries use different doses. DDDs aim to solve this by relating all drug use to a standardized unit which is analogous to one day's worth.

The formula for calculating DDDs is as follows.

$$Drug\ Usage(DDDs) = \left(\frac{Items\ issued \times Amount\ of\ Drug\ per\ item}{WHO\ DDD\ Measure} \right)$$

The days of therapy (DOT) of AB use was also evaluated. The DOT is the sum of the number of days that each individual AB was administered to a patient.. For example, if on the first day, a patient was prescribed Vancomycin plus Piperazine-Tobactam plus Levofloxacine, thenthe DOT will be 3.If on the second day, the patient took Piperazine-Tobactam plus Levofloxacine: The DOT will be 5, but the length of treatment only 2 days.

Study population:

Two central hospitals (Cho Ray and Hue Central Hospital) and 7 provincial hospitals (4 from the South and 3 from the central of Vietnam) were included in the study. The 3 hospitals from the South include: Long An, Dong Nai, Ben Tre, Khanh Hoa. The 3 hospitals from the Central region include: Quang Nam, Binh Dinh, Phu Yen.

3. RESULTS

The total number of patients included in the study were 2072, distributed by hospitals as follows: Cho ray 429 (20.7%), Hue 413 (19.9%), Ben Tre 300 (14.5%), Long An 160 (7.7%), Dong Nai 170 (8.2%), Khanh Hoa 150 (7.2%), Binh Dinh 150 (7.2%), Phu yen 150 (7.2%), Quang Nam 150 (7.2%).

3.1. Patient characteristics: The mean (SD) age of patients was 37.6 years (19.8) and there were no differences in patients characteristics between hospitals. 45.6% were male; 6.5% had underlying diseasesand 88.5% required operations. The mean (SD) duration of surgery was 99.8 minutes (64.5). 56.2% of operations took place in emergency departments. 35.5% were clean operations, while 52.8% were clean-contaminated operations. 8.0% involved contaminated wounds, and 4.2% involved dirty wounds. The characteristics of patients by hospitals are presented in Table 1:

Table 1. Patients' characteristics by hospitals

	Cho Ray	Hue	Ben Tre	Long An	Dong Nai	Khanh Hoa	Binh Dinh	Phu Yen	Quang Nam
Mean (SD) Age	43.6 (21.1)	38.4 (21.3)	36.9 (18.4)	38.5 (19.6)	30.0 (11.7)	36.5 (20.9)	35.9 (23.2)	30.7 (13.7)	36.7 (17.1)
% Male	59.0	58.4	27.3	50.6	17.7	68.7	40.0	32.7	30.0
% underline diseases	21.1	2.7	3	0.7	2.9	9.3	0	0.7	2.7
% operation	53.9	100	100	98.1	95.3	99.3	88.7	100	98.7
% Clean	45.3	32.5	24.3	31.9	19.8	30.9	26.2	4.0	30.2
Clean – contaminated	36.7	58.1	64.3	47.1	71.0	31.5	66.7	88.0	52.4
Contaminated	12.3	5.8	6.7	4.5	6.2	26.2	2.8	4.0	13.4
Dirty	5.7	3.6	4.7	16.6	3.1	11.4	4.3	4.0	4.0
Mean (SD) duration of operation	99.7 (84.5)	80.3 (57.8)	37.5 (18.4)	38.7 (16.9)	43.0 (18.4)	60.3 (27.1)	47.3 (23.7)	41.7 (15.3)	73.7 (31.6)
Emergency operation (%)	24.4	31.5	71.1	65.6	89.5	58.8	62.4	88.7	55.0

Types of infections: The incidence of HAIs overall was 1.2% , while SSI incidence was 0,8%. Nosocomial infections comprised 0.2%, urinary tract infections were 0,2 %, other types of infections were0,1%, and there were no BSI . The incidence of HAIs by hospitals is presented in Table 2.

Table 2. Incidence of HAIs by hospitals

	Cho Ray N=429	Hue N=412	Ben Tre N=298	Long An N=160	Dong Nai N=170	Khanh Hoa N=150	Binh Dinh N=150	Phu Yen N=150	Quang Nam N=150
HAIs *	7 (1.6)	8 (1.9)	4 (1.3)	0.0	0.0	1 (0.7)	3(2.0)	0.0	1 (0.7)
SSI**	5 (2.3)	3 (0.7)	3 (1.0)	0.0	0.0	1 (0.7)	3(2.3)	0.0	1 (0.7)
NP	0.0	3 (0.7)	1 (0.3)	0.0	0.0	0.0	0.0	0.0	0.0
UTI	0.0	2 (0.5)	0.0	0.0	0.0	1 (0.7)	0.0	0.0	1 (0.7)
BSI	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Others	4 (0.9)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

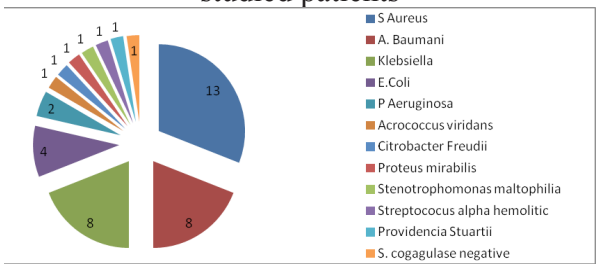
* Some patients have two different HAIs

Denomination for patients with SSI was patients with operations. Number of operations were: Cho Ray **221, Hue 413, Ben Tre 298, Long An 157, Khanh Hoa 149, Binh Dinh 133, Phu Yen 150, Quang Nam 148.

The distribution of pathogens is presented in Figure 1. Forty nine (2.4%) of microbiology cultures were done in 42 patients, 63.9% from pus, 16.3% from sputum, 8.2 % from urine, 6.1% from blood, and 6.1 % from drainage. The distribution of pathogens was presented in Figure 1. Most of the microbiology cultures were done in central hospitals (Cho Ray 18,

Hue: 14, Binh Dinh 5, Ben Tre: 3, Khanh Hoa 2, Long An: 0, Phu Yen: 0, Dong Nai 0, Quang Nam: 9). All (6/6) were MRSA. All (8/8) *Acinetobacter Baumanii* were resistant to imipenem. The rate of ESBL was 16.7% (7/42).

Figure 1. Pathogen causing HAIs in studied patients



3.2. Antibiotic use

Pre-operative antibiotic use

Nearly thirty percent (29.9%) of patients were prescribed AB before operations. ABs prescription was recorded beforeall kinds of operations: Clean operations: 23.1% Clean – contaminated: 29.5%, contaminated: 43.5%, dirty: 50.5%. Pre-operative antibiotic use stratified by the wound classification and hospitals is presented in Table 3. Type of AB and dosing is presented in Table 4. The rate of using AB before operation was highest in Cho Ray hospital and lowest in Dong Nai hospital. The most common AB use was 3rd generation (38.8%) and Fluoro-quinolone (11.4%). There were only 13 cases that were cultured before surgery, of which 10/13 cases were prescribed AB concordant with the culture results.

Prophylactic antibiotic use

One third (34.7%) of patients who had clean or clean–contaminated operations were prescribed AB as a prophylaxis (during anesthesia). The most common AB chosen for prophylaxis was 3rd generation (55.1%), 2nd generation (10.1%), and PNC with enzyme inhibitors (Amox/clav; ampi/sulbactam) (13.3%).

Post-operative antibiotic use

Among 1843 patients who received an operation, 94.6% of patients were prescribed AB post-operatively, with the mean (SD) duration of the first AB found to be 5.8 days (2.8). Only 815 patients (44.2%) used just one kind of AB. The majority of patients were prescribed a combination of more than 2 types of AB: 1 (0.05%) patient was provided with 9 types of AB, 1 patient (0.05%) with 6 types, 10 patients (0.5%) with 5 types, and 46 patients (1.8%) with 4 types of AB. 143 patients (7.8%) were prescribed with 3 types of AB, while 840 (45.6%) patients prescribed a combination of two AB during hospitalization. Post-operative antibiotic use stratified by the wound classification and hospital is presented in Table 5. The rate of using AB before operations was highest in Phu Yen and Quang nam hospitals (100%), and lowest in Long An hospital. The most common AB chosen for prophylaxis was 3rd generation (45.7%), 2nd generation (11.3%), and Fluoroquinolone (7.3%) and PNC with enzyme inhibitors (Amox/clav; ampi/sulbactam) (7.0%).

AB was prescribed post-operatively in the case of all kinds of operations: clean operation: 91.8 % clean –contaminated: 96.3%, contaminated: 96.7%, and dirty: 98.3 %. In patients for which a microbiological culture was conducted, only 71.1% were prescribed AB concordant with the culture results. Forty five cases had a culture taken after their operations, of which 32 cases (71.1%) were prescribed AB concordant with the culture results.

The percentage and DDD of each type of AB used post operatively is presented in Table 4. The mean (SD) of DOT post operatively was 8.2 (7.8), ranging from 1 to 104 DOT, while the mean (SD) of length of stay was 9.3 days(7.4), ranging from 1 to 78 days. The DOT and Length of Stay (LOS) in each hospital is presented in Figure 2.

Table 3. Pre-operative antibiotic use stratified by the wound classification and hospitals

	Cho Ray	Hue	Ben Tre	Long An	Dong Nai	Khanh Hoa	Binh Dinh	Phu Yen	Quang Nam
Total	43.8	26.6	28.8	18.8	17.4	27.3	36.1	52.7	20.7
Clean	26.0	18.7	39.7	22.0	13.3	10.9	37.1	50.0	11.1
Clean-contaminated	54.2	27.9	20.8	10.8	9.7	44.7	30.3	50.8	23.1
Contaminated	59.8	37.5	42.8	28.6	90.0	23.1	75.0	83.3	30.0
Dirty	61.5	60.0	55.0	34.6	100.0	35.3	100.0	66.7	33.3

Table 4. Pre-operative Antibiotic usage

Antibiotic (specified-agents)	Total % N=544	Number of DDDs Mean (SD)
Aminoglycosides (Gentamicin, Tobramycin, netilmicin, amikacin)	3.3	7.7(14.4)
Cephalosporins		
1st generation (cephalexin, cephadroxil, cefazolin)	3.7	2.3 (2.5)
2nd generation (cefuroxim,cephalexin)	11.4	5.5 (5.9)
3rd generation (cefotaxime,ceftriaxone, cefoperazone,ceftazidime)	38.8	1.6 (2.2)
3rd generation combination (cefoperazone-sulbatam)	2.9	3.7 (3.3)
3rd generation oral (cefixim, cefpodoxime))	3.7	6.6 (8.7)
4th generation (cefepime)	2.4	6.3 (4.4)
Chloramphenicol	0.2	6
Cotrimoxazole	0.6	N/A
Fosfomycin	0.4	4.4 (3.2)
Sulbactam	3.9	5.6 (3.2)
Metronidazol	3.9	3.6 (3.2)
Fluoroquinolones (Levofloxacine,Ciprofloxacin, Pefloxacin, Ofloxacin)	11.4	8.5 (4.6)
Macrolides (clarithromycine, azithromycine..)	1.5	9 (4.3)
Lincosamides (Clindamycin or Lincomycin)	2.4	1.4 (1.1)
Penicillins		
Aminopenicillins (ampicillin, amoxycillin)	3.3	5.1 (6.9)
PNC with enzyme inhibitors (Amox/clav; ampi/sulbactam)	5.7	1.2 (5.2)
Antistaphylococcal (Oxacillin)	0.2	3
Vancomycin	0.6	6.5 (4.9)

* Since patients received ≥ 1 agent, total percentages are >100%

DDD and DOT were calculated for the most common AB in each group (see underlined)

Table 5. Post-operative antibiotic use stratified by the wound classification and hospitals

	Cho Ray	Hue	Ben Tre	Long An	Dong Nai	Khanh Hoa	Binh Dinh	Phu Yen	Quang Nam
Total	89.2	99.8	99.0	72.6	96.3	91.3	93.2	100.0	100.0
Clean	87.8	100	98.6	62.0	90.6	90.6	90.6	100.0	100.0
Clean-contaminated	95.6	99.6	98.9	72.9	99.1	87.2	93.5	100.0	100.0
Contaminated	95.9	100	100	71.4	100.0	94.9	100	100.0	100.0
Dirty	100.0	100	100	92.3	100.0	100.0	100	100.0	100.0

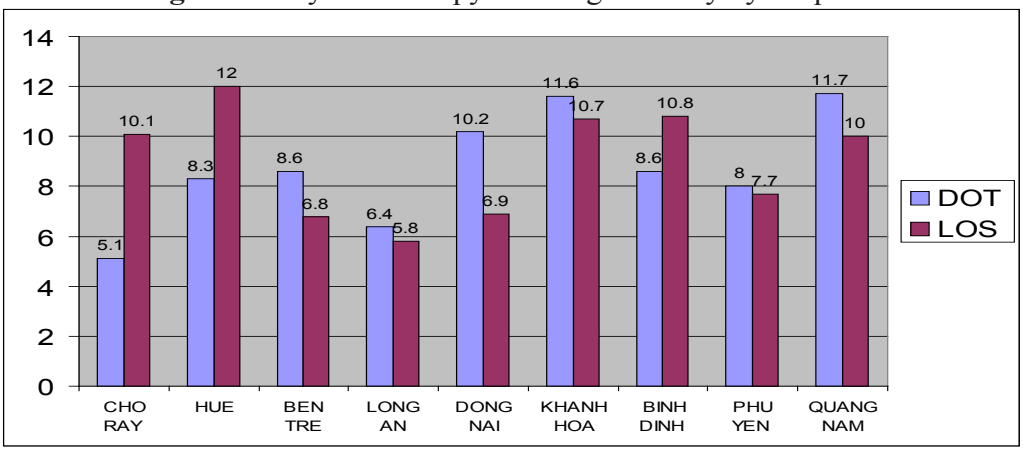
Table 6. Post-operative Antibiotic usage

Antibiotic (specified-agents)	Total % N=1723	Number of DDDs Mean (SD)
Aminoglycosides (Gentamicin, Tobramycin, netilmicin, amikacin)	1.2	4.7(5.9)
Cephalosporins 1st generation (cephalexin, cefazolin) 2nd generation (cefuroxim,cephalexin) 3rd generation (cefotaxime,ceftriaxone, cefoperazone,ceftazidime) 3rd generation combination 3rd generation oral (cefixim, cefpodoxime) 4th generation (cefepim)	 1.5 11.3 45.7 4.2 0.7 3.0	 2.4 (1.6) 12.5 (8.1) 3.9 (1.7) 3.9 (2.7) 3.7 (2.9) 6.7 (3.7)
Imipenem	0.1	7.8 (6.9)
Chloramphenicol	0.5	1.5
Fosfomycin	0.1	4.3 (0.5)
Cotrimoxazole	0.7	N/A
Sulbactam	3.5	5.6 (3.2)
Metronidazol	6.6	3.2 (1.3)
Fluoroquinolones (Levofloxacine, Ciprofloxacin, Pefloxacin, Ofloxacin)	7.3	11.6 (7.1)
Macrolides (clarithromycine, azithromycine)	1.1	26.5 (13.9)
Lincosamides (Clindamycin or Lincomycin)	3.6	4.7 (2.4)
Aminopenicillins (ampicillin, amoxycillin) PNC with enzyme inhibitors (Amox/clav; ampi/sulbactam) Antistaphylococcal (Oxacillin)	0.5 7.0 0.6	12.7 (18.9) 8.6 (3.0) 3.6 (1.3)
Vancomycin	0.9	9.5 (7.1)

* Since patients received ≥ 1 agent, total percent was >100%

DDD was calculated for the most common AB in each group (name was underlined)

Figure 2. Days of Therapy and length of stay by hospitals



4. DISCUSSION

The study has shown inappropriate AB use in surgical patients in all studied hospital. Although the incidence of HAIs and SSI in all studied hospitals was not high (1.2% and 0.8% respectively), the patients were prescribed a large amount of AB.

ABs was prescribed for the entire duration of patients' stay in hospital and beyond: before, in and after hospital. Even with clean or **c**lean–contaminated wounds, doctors prescribed AB for patients before surgery (23.1% & 29.5% respectively). Only one third (34.7%) of patients with clean or clean–contaminated wounds were prescribed AB as prophylaxis (during anesthesia). After operations, almost all patients were given AB (94.6%) for at least 5.8 (2.8) days. Combinations of drugs (2 or more) were common. The AB used were mostly those which common pathogens have developed resistance to.

The number of DDDs was rather different among the types of AB. In this study we could not analyze the reasons for these differences. A high number of DDD could reflect a high level of AB prescription to a patient, but a low number of DDD did not mean that patients were prescribed a low level of AB, because this may have been caused by the change of one type of AB to another…The very high number of DDDs in the Macrolids group should be further analyzed to check if the prescription following the recommended dose.

We also calculated the DOT to add information about the use of combinations of drugs. If the DOT is higher than the LOS, this meant a high use of AB combinations. In this study, interestingly, DOT of AB in central hospitals was lower than in provincial hospitals. This reflected that AB were prescribed for longer durations and more frequently in combinations of two or more typesin provincial hospitals.

The microbiology cultures were performed in rather few hospitals (2.4%), and mostly in central hospitals (Cho Ray and Hue accounted for two thirds of all cultures). This suggested that improvements in the microbiology capacity of provincial hospitals are also required. The high level of resistance of pathogens showed that there is an urgent need for methods for reducing AB resistance and of controlling AB use.

5. CONCLUSIONS

The study provides useful data for hospital policy makers in regard to antibiotic use. Inappropriate AB use for surgical patients was found throughout all hospitals. Despite the low incidence of HAIs and SSIs (1.2% and 0.8%), there were high levels of prescription of antibiotics. The amount of AB use was high, as reflected through high DDD, the prescription of combinations of AB for long

periods was common, as reflected by high DOT. Microbiology cultures were conducted mostly in central hospitals.

The findings from this study should be used to influence policy makers to address AB usage urgently. It is very important to perform intervention programs, such as an antibiotic stewardship program, across Vietnam to reduce inappropriate AB use in this population. Improvements in the microbiology capacity of provincial hospitals is required to guide AB use.

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