

# EFFECTS OF PROLONGED SURGICAL ANTIBACTERIAL PROPHYLAXIS ON DRUG COST, NOSOCOMIAL INFECTIONS AND MORTALITY IN CASES PERFORMED CARDIOVASCULAR SURGERY

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## ABSTRACT

**Objective:** The aim of this study was to evaluate surgical antimicrobial prophylaxis (SAP), its cost and effects on nosocomial infections and mortality in Cardiovascular Surgery Intensive Care Unit.

**Material and Method:** This observational study was prospectively carried out between January-December 2002.

**Results:** Among 168 patients only three cases (1.7%)

received one day lasting SAP and 45 (26.7%) received SAP for two days. Cost of prolonged SAP was 19.933 EURO. Nosocomial infection incidence and overall mortality was not significantly different in patients who received longer SAP.

**Conclusion:** It is concluded that longer SAP does not mean less nosocomial infections or mortality but higher drug cost.

**Key Words:** Nosocomial infection, cardiac surgery, pharmacoeconomics. *Nobel Med 2012; 8(2): 55-58*

## UZUN SÜRELİ CERRAHİ ANTİBAKTERİYEL PROFİLAKSİNİN KARDİYOVASKÜLER CERRAHİ GEÇİREN OLGULARDAKİ İLAÇ MALİYETİ, HASTANE KÖKENLİ İNFEKSİYONLAR VE MORTALİTE ÜZERİNE ETKİSİ

### ÖZET

**Amaç:** Bu çalışmada cerrahi antimikrobiyal profilaksinin (CAP) kardiyovasküler cerrahi yoğun bakım hastalarında maliyete, hastane kökenli infeksiyon oranına ve mortaliteye etkisinin değerlendirilmesi amaçlanmıştır.

**Materyal ve Metod:** Bu prospektif gözleme dayalı ça-

alışma Ocak-Aralık 2002 arasında gerçekleştirilmiştir.

**Bulgular:** Yüz altmış sekiz hastadan yalnızca 3'ü (%1,7) bir gün süren, 45'i ise (%26,7) iki gün süren CAP almıştır. Bir günden uzun CAP'nin ilaç maliyeti 19.933 EURO olarak bulunmuştur. İki günden uzun süreli CAP alan hastalarda hastane kökenli infeksiyon oranı ve mortalite düşmemiştir.

**Sonuç:** Uzatılmış CAP'nin hastane infeksiyon oranı ve mortaliteyi düşürmediği fakat maliyeti artırdığı sonucuna varılmıştır.

**Anahtar Kelimeler:** Nasokomiyal infeksiyon, kalp cerrahisi, farmakoekonomi *Nobel Med 2012; 8(2): 55-58*

## INTRODUCTION

Antibiotics are among the most common inappropriately used drugs. Irrational and overuse of antibiotics lead not only to the emergence of resistant bacteria but also economical loss and adverse reactions.<sup>1,2</sup>

The goal of surgical antibiotic prophylaxis (SAP) is to prevent surgical site infections by the use of appropriate antibiotics for appropriate periods.<sup>3</sup> Longer duration of SAP is an important factor resulting in antibiotic resistance. Data about the effects of longer SAP is mainly from clinical trials, which show rarely →

less, usually similar or more nosocomial infections.<sup>2,4-6</sup>

The aim of this study was to evaluate SAP practice, its length, cost and effects on nosocomial infections and mortality in cardiovascular surgery intensive care unit (CSICU).

## MATERIAL and METHOD

This observational study was prospectively carried out between January and December 2002 in the CSICU of our setting which comprises 20 beds. Data were collected by daily visits on a standardized form.

In case of longer SAP, the cost of cephazolin (or in case of penicillin allergy cost of vancomycin) prophylaxis lasting one day was subtracted from total cost of SAP. Data were analyzed with Chi square and Student's t-tests by SPSS 11.0 software.

The effect of longer SAP on nosocomial infections was analyzed by dividing the patients into two groups. Since only three patients received SAP for one day, group 1 consisted of patients who received SAP  $\leq 2$  days. Group 2 consisted of patients who received SAP  $\geq 3$  days. Data were collected prospectively by daily visits. Nosocomial infections were diagnosed according to the criteria of Center for Diseases Control and Prevention (CDC).<sup>7</sup> Cost of the antimicrobial prophylaxis was calculated by using 2005 year prices in EURO (assuming that 1 EURO=1.8 TL).

## RESULTS

Total of 168 patients was included in this study. 118 were male and 50 were female (aged  $41.2 \pm 26.5$ ). Length of staying in CSICU was 689 days and length of staying in the hospital was 3184 days, respectively. Mean duration of SAP was  $4.65 \pm 3.2$  days (range 1-18) (Figure 1). Only three cases (1.8%) received SAP for one day two of them receiving combination therapy. Forty-five cases (26.7%) received SAP lasting for two days, where four of them received combination therapy. Total drug acquisition cost of SAP was 22.778 EURO, and cost of prolonged SAP was 19.933 EURO.

The number of the patients in group 1 was 48 and in group 2 was 120, respectively. Characteristics of patients in group 1 and 2 are summarized in Table 1. As expected average cost of SAP was higher in group 2 ( $21.5 \pm 21.6$  EURO for group 1 vs  $170.5 \pm 240.4$  EURO for group 2,  $p < 0.0001$ ). Twenty two nosocomial infection (NI) episodes were seen in 19 patients. Prolonged prophylaxis did not result in less nosocomial infection incidence and mortality but incidence density was lower ( $3.0$  vs  $6.7/1000$  patient days.) (Table 1 and 2).

## DISCUSSION

Inappropriate antibiotic usage is a global problem and prolonged SAP is an important contributor to antibiotic abuse.<sup>1-3</sup>

In spite of developments in surgery, postoperative infections still cause significant morbidity, mortality, longer hospital stay and costs. Controlled studies suggest a decrease in surgical site infections with SAP applied in appropriate durations but no preventive measure can replace the good surgical technique and asepsis.<sup>3-6</sup>

Data are simply not available to quantify the relative risk and benefits of prolonged SAP. Prolonged SAP may have non beneficial, beneficial or detrimental effects on the development of nosocomial infections in different operations.<sup>3-6</sup> There is no proven evidence for prolonged SAP for cardiac surgery.

Inappropriate SAP rate is reported as 15% in USA, 72% in Sweden, 80.6% in France and 47.7% in Turkey.<sup>8-11</sup> Surgical prophylaxis exceeded one day in 80% and three days in 68.2% of 3104 patients in a study from Taiwan.<sup>12</sup> Erdem et al. analyzed the SAP practice in 200 patients in a prospective study held in a Turkish State Hospital.<sup>13</sup> About 50% of 200 patients were reported to receive inappropriate antimicrobial prophylaxis and nosocomial infection rate was higher in the inappropriate SAP group ( $p < 0.05$ ). Cost of inappropriate SAP was 10.000 \$.

In our study only three cases (1.8%) received SAP for one day (two of them received combination therapy with amikacin) and 45 (26.8%) received SAP for two days. When appropriate prophylaxis was defined according to criteria of advisory statement of the American National Surgical Infection Prevention Project (cephazolin or cefuroxime or vancomycin in case of penicillin allergy for no more than 24 h), only one case received appropriate prophylaxis.<sup>3</sup>

To our knowledge 98.2% is unfortunately the highest reported prolonged SAP ratio. Prolonged SAP resulted in 19.933 EURO extra drug acquisition cost but not less nosocomial infection or mortality.

Although this is not a randomized controlled or case-control study, the results are interesting. A randomized study about the effects of inadequate prophylaxis is not possible because of the ethical issues.

Reported nosocomial infection rates in patients operated by cardiac surgeons range between 6.5-25.2%.<sup>14-16</sup> Li and Wang reported 4.5% nosocomial →

pneumonia rate in 1208 heart surgery patients.<sup>16</sup> Our findings are in concordance with these reported values. In our study all surgical site infections were in group 2 but the difference was not statistically significant ( $p>0.05$ ).

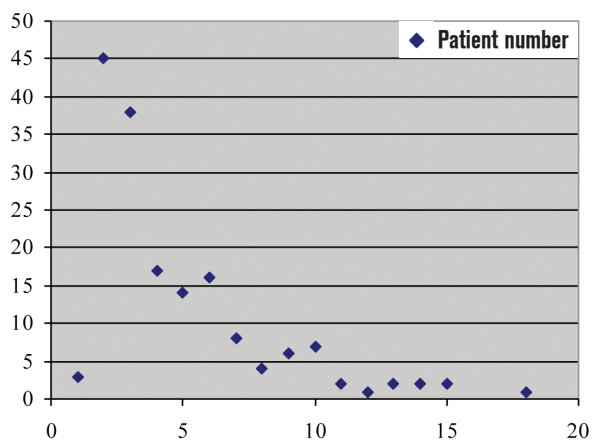
Knowledge and attitudes on SAP is relatively poor in Turkish surgeons. In a study performed on 95 surgeons in a tertiary-care educational hospital, 44% stated that they implemented  $>3$  days SAP, and 33% stated that they implemented SAP with combined regimens.<sup>17</sup> In a multicenter national survey of SAP in Turkey, 88% of 439 surgeons stated that they applied more than one dose prophylaxis and 46% stated that they used  $>48$  h SAP.<sup>18</sup> Only 112 surgeons (26%) were using definitely appropriate prophylaxis in all aspects. The study-group comprised of 46 heart surgeons and the mean declared duration of SAP in CABG was 5 days. Guidelines and educational programs may result in limited improvements in the SAP practice.<sup>19-20</sup> Gorecki et al. analyzed the effect of Surgical Infection Society Guidelines on SAP practice, mortality and morbidity.<sup>19</sup> Although prophylaxis duration was lower in the group supported the guidelines, mortality and morbidity was similar. In another educational interventional study performed in Turkey, improvements were achieved in indications, choice, and dosing of surgical antimicrobial prophylaxis. However, it failed to improve prolonged use and total compliance rate, and to lower the costs sufficiently.<sup>20</sup> Currently there is no national or local guideline used in our setting.

## CONCLUSION

In this study we observed a very high rate of prolonged use of antibiotics for surgical prophylaxis. Total cost of SAP was high. Although it is not a randomized study, it is seen that SAP longer than known criteria does not mean less nosocomial infections, surgical site infections and mortality. It is concluded that improved education of surgeons and residents regarding surgical antimicrobial chemoprophylaxis can be one of the important ways to change to the evidence-based practice habits. Strategies are needed to improve the

	Group 1 (n:48)	Group 2 (n:120)	p
Age	38.3±25.5	42.1±26.9	$>0.05$
Male	19	31	$>0.05$
Female	29	89	$>0.05$
Mortality	1/48	14/120	$<0.05$
Nosocomial surgical site infection	0/48	3/120	$>0.05$
Nosocomial infection incidence	4.1% (2/48)	14.1% (17/120)	$>0.05$

Nosocomial Infections	n	Organisms
Pneumonia	12	Cultures did not reveal any specific pathogen (9) Klebsiella pneumoniae (1) Acinetobacter baumannii (1) Enterobacter cloacea (1)
Catheter Related Bloodstream Infection	6	Staphylococcus aureus (3) Coagulase negative Staphylococci (2) Enterobacter cloacea (1)
Surgical Site Infection	3	Klebsiella pneumoniae (1) Pseudomonas aeruginosa (1) Acinetobacter baumannii (1)
Urinary Tract Infection	1	Klebsiella pneumoniae (1)



**Figure 1.** Distribution of length of surgical antimicrobial prophylaxis regimens observed during the study period\* (Apsis-length of SAP, ordinat: patient number.)

appropriate use of SAP not only to reduce costs but more importantly to decrease antibiotic-related side effects and to delay the emergence of nosocomial infections due to resistant of microorganisms.<sup>21</sup>

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