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Major article

Economic evaluation of appropriate duration of antibiotic prophylaxis for prevention of neurosurgical infections in a middle-income country

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Background: Preoperative antibiotic prophylaxis is one of the preventive measures for surgical site infections (SSIs). Very little data about the cost effectiveness of the appropriate duration of antibiotic prophylaxis in low- and middle-income countries are available. We aim to assess the cost effectiveness of the use of antibiotic prophylaxis for <24 hours to prevent neurosurgical infections in a middle-income country, Turkey.

Methods: A 1-year prospective study was performed between June 2012 and June 2013. During this study period patients were followed-up on for the development of SSI by means of hospital and post-discharge surveillance. Patients included in the study group received appropriate duration of antibiotic prophylaxis (<24 hours), and the duration of prophylaxis was longer in the control group. The antibiotic costs per patient, including prophylaxis and treatment, were calculated.

Results: A total of 822 operations consisting of craniotomy (n = 558), spinal fusion (n = 220), and ventricular shunt (n = 44) were included in the study. The study group included 488 (59.4%) patients who underwent operations with appropriate duration (<24 hours) of antibiotic prophylaxis. Prophylactic antibiotic cost per patient was significantly lower in the study group ($3.35 and $20.41, respectively). The SSI rates did not differ between the 2 groups: 3.5% (17/488) in the study group and 3.6 (12/822) in the control group ($P > .05$).

Conclusion: This cost-analysis study demonstrates that prolonged antibiotic prophylaxis correlates with increased burden of cost, but it is not preventive for SSI.

Surgical site infections (SSIs) remain a significant proportion of health care– associated infections, accounting for 31% of all infections among hospitalized patients.[1] These infections are often associated with significant morbidity, mortality, increased length of hospital stay, and costs. Preoperative antibiotic prophylaxis (PAP) is one of the preventive measures for SSIs recommended by current guidelines.[2] However, the important elements of PAP, such as the selection of an antibiotic regimen, timing of administration, and duration of prophylaxis, are still not well established, and hospital compliance to these preventive recommendations is not routinely followed in most institutions of low- and middle-income countries.[3-6]

In developing countries, the size of the problem is more remarkable; nevertheless, data on the financial burden of SSIs and the cost effectiveness of appropriate PAP are inadequate. Several limitations in health care facilities, including infrastructure, patient load, and staff shortage, in these countries may lead clinicians to overuse antibiotics. Surgeons continue to give additional doses of antibiotics after surgery, if the patient is believed to be at a high risk of SSI. On the other hand, the prolonged use of antibiotics increases the likelihood of developing antibiotic-resistant infections, exposes patients to more adverse drug reactions, and increases overall health care costs.

Many studies from developed and developing countries have reported increased hospital expenditures caused by the prolonged

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use of antibiotic prophylaxis. Very little data about the cost effectiveness of the appropriate duration of antibiotic prophylaxis in low- and middle-income countries are available.[4-7] The objective of this prospective study is to assess the risk for SSI and economical evaluation of the use of antibiotic prophylaxis for <24 hours to prevent neurosurgical infections in a middle-income country, Turkey.

MATERIALS AND METHODS

Setting

This study was conducted in the neurosurgery unit of Erciyes University Hospital, which is a tertiary care hospital with 1,300 beds. The division of neurosurgery consists of a 49-bed unit and a separate 13-bed intensive care unit, with a total of 17 surgeons (6 professors, 3 specialists, 8 assistant doctors) employed.

Definitions

SSI was defined as an infection related to an operative procedure that occurred at or near the surgical incision within 30 days of the procedure or within 90 days if prosthetic material was implanted during the surgery.[2] SSI was classified as superficial incisional, deep incisional, and organ or space SSIs according to revised Centers for Disease Control and Prevention criteria.[2] The wound class system used by the American College of Surgeons wound classification schema is divided into 4 classes: clean, clean-contaminated, contaminate, and dirty.[8] The National Nosocomial Infection Surveillance Risk Index (composed of the American Society of Anesthesiologists score, surgical wound contamination potential, and surgery duration) is applied for all surgeries, on a scale from 0-3 points.[2]

Study

A 1-year prospective study was performed between June 2012 and June 2013. During this study period, patients were observed with regard to the appropriateness of PAP and the development of SSI. Appropriate use of antibiotic prophylaxis is determined by current guidelines.[2] The agent, timing, and duration of antibiotic prophylaxis in patients were recorded. Patients included in the study group received a weight-based dose (cefazolin 1-2 g intravenously, 3 g for patients ≥80 kg), with appropriate time (at induction), frequency (every 4 hours during surgery), and duration (<24 hours) of PAP. If the patients received an appropriate dose, time, and frequency of the antibiotic prophylaxis, but the duration of prophylaxis was >24 hours (without the indication of excessive blood loss), they were included in the control group. Finally, the cost analysis per patient was calculated for the groups (in constant 2013 US $). The purchase price of cefazolin 1 g (Mustafa Nevzat, Istanbul, Turkey) was $2.04. Data on the costs were obtained using the hospital's accounting system. Patients who already had an infection during the surgery and those with contaminated and dirty wound infections and <15 years of age were excluded.

Operations for spinal fusion, craniotomy, and ventricular shunt were included in the study. Patients were followed-up prospectively for the development of SSI by means of hospital and postdischarge surveillance. Hospital surveillance was performed by daily visits by the infection control team during the patients' hospitalization. The demographic data, associated risk factors, and laboratory data, including gram stain and culture results, were collected. Postdischarge surveillance was performed by calling all patients; an interview was conducted over the phone. Patients were questioned about the symptoms of any SSI within the first 30 days after discharge or within 90 days if any prosthetic material was implanted during surgery.

Two of the surgeons were informed about the course of the study and were knowledgeable about the PAP protocol (antibiotic selection, timing, and alternatives in case of allergy were determined according to guidelines). Infection control nurses were authorized to discontinue the antibiotics in case of inappropriate use for >24 hours in this group. No intervention was performed for the routine PAP practice by other surgeons.

The demographic data, details of operations, and infection control measures of the 2 groups of patients were compared. The antibiotic costs per patient, including antibiotics for PAP and treatment, were calculated. Statistical analysis was performed using SPSS software version 15.0 (IBM, Armonk, NY). The χ^2 test was used for categorical variables. The Mann-Whitney U test was used to compare the differences between two groups. The level of significance was set at $P < 0.05$ for all tests.

This study was approved by the Research Ethics Committee of Erciyes University.

RESULTS

A total of 822 operations consisting of craniotomy (n = 558), spinal fusion (n = 220), and ventricular shunt (n = 44) were included in the study. Of these operations, 60 (7.3%) were emergency surgeries, and 753 (91.6%) were clean operations. The study group included 488 (59.4%) patients who underwent operations with appropriate duration (<24 hours) of antibiotic prophylaxis. The control group consisted of 334 (40.6%) patients who received the correct antibiotics but with inappropriate duration (>24 hours).

The demographic characteristics, underlying diseases, and invasive procedures of the groups did not differ. The study group was found to be hospitalized longer during the preoperative period ($P < .001$) (Table 1). Craniotomy operations were significantly more frequent in the study group. SSI rates were also calculated for each type of operation, and there was no significant difference between the study and control groups ($P > .05$). Emergent operations were performed slightly more in the control group. However, the difference was not statistically significant ($P = .145$). Based on the Risk Index Category (RIC) scores, patients in the study group were more likely to be included in the RIC = 0 category, whereas patients in the control group were in the RIC = 1 category (Table 2).

There was no difference between the groups in terms of infection control measures presented in Table 3.

Prophylactic antibiotic cost per patient was significantly lower in the study group ($3.35 and $20.41, respectively). Also, the total cost of antibiotics for prophylaxis and treatment of infections per patient was significantly higher in the control group ($P = .001$) (Table 4). The SSI rates did not differ between the 2 groups: 3.5% (17/488) in the study group and 3.6% (12/822) in the control group ($P > .05$).

The 12 microorganisms isolated in the sample of 29 patients with SSIs were as follows: *Acinetobacter baumannii* in 5 (17.2%), *Staphylococcus aureus* in 4 (13.7%), *Pseudomonas aeruginosa* in 2 (6%), and *Enterobacter cloacae* in 1 (3.4%). The rate of imipenem resistance was 100% for *A baumanni* and *P aeruginosa*. *S aureus* strains were all methicillin sensitive.

DISCUSSION

The most crucial outcome of irrational use of antibiotics in various settings is the contribution to the global antibiotic resistance threat. A significant proportion of inappropriate antibiotic usage is for surgical prophylaxis. The frequency of antibiotic prescriptions for surgical prophylaxis is substantially high and inappropriate in Turkey, as previously reported in a multicenter study.[9] Also, Turkey was found to have the highest antibiotic use in Europe when compared with the other eastern countries in the European