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Evaluation of Antibiotic Prophylaxis Regimens in Gynecological Surgeries in a Referral Teaching Hospital: A Cross Sectional Study

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ABSTRACT

Background: Drug utilization Evaluation is the main tool to assess the clinical and economic effects of drug on health-care system. The aim of the current study is to evaluate the regimens of antibiotic prophylaxis in common gynecological surgeries in a referral teaching hospital

Methods: This cross-sectional study was done in Alzahra hospital, Tabriz, Iran, from July 2017 to December 2017. Patients who received antibiotics as surgical site infection prophylaxis were enrolled. Data were collected from patients' medical records and adherence rate to the American Society of Health-System Pharmacists (ASHP) guideline was studied as the primary endpoint.

Results: A total of 210 patients who undergoes common gynecological surgeries were evaluated. Cesarean section (58.6%) and total abdominal hysterectomy (28.1%) were the majority of surgeries. The type of administered antibiotic was adherent to guideline in 71.4%. Doses and duration of prescribed antibiotic (Cefazolin, the most prescribed antibiotic) were not in accordance with the guideline in 100%. Only in 58%, the time of antibiotic administration was corrected.

Conclusion: In this study, the misuse of antibiotics in most cases was documented in terms of type, dose and duration of drug administration in Al-Zahra Hospital. It seems necessary to publish evidence-based guidelines and monitor their proper implementation, not only to reduce costs but also to combat antibiotic resistance.

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Introduction

Preoperative antimicrobial prophylaxis is characterized as the administration of antibiotics before surgery to diminish the postoperative infections (1). Thirty percent of in-hospital antibiotic utilization is for surgical prophylaxis (2). Rational use of drugs according to standard guidelines could be evaluated by Drug Utilization Evaluation (DUE) studies (3). Results of DUE studies could be used as a guide to correct the use of drugs in order to reach cost-effective and beneficial programs (4).

Among gynecological surgeries, hysterectomy and cesarean section are the most common (5, 6). Cesarean section is a surgical procedure that has increased steadily over the past three decades and has reached 25% in some countries (7). Infection is one of the most important risk factors following cesarean section, and hysterectomy which can lead to maternal death (8, 9). Maternal and neonatal mortality due

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to infection is ranked after bleeding, which has caused 15% of all maternal deaths (9, 10). Surgical Site Infections (SSI) could result in increased hospital stay, delayed retrieval, and patients' psychological problems (11). Antibiotics should be used to prevent SSIs before gynecological surgeries that involve manipulating the female reproductive system, such as a hysterectomy or surgeries where the peritoneal cavity may be infected through the vagina. In the case of infectious abortion, antibiotic administration should be done(12). Although the use of surgical and preventive antiseptics is associated with an overall reduction in infection, contamination of the surgical site is inevitable (13).

Since antimicrobials make up 13 to 37 percent of the cost of medicines in hospitals, the proper use of these drugs is important in terms of cost ,and on the other hand inappropriate administration of antibiotics as prophylaxis, will cause many complications such as disruption of the natural microbial flora of the body, super infection, growth of antibiotic-resistant bacteria and, increased risk of drug adverse effect, and drug interactions (14).

Due to lack of information about prophylactic regimens in Alzahra hospital; this study was designed to evaluate the rational use of antibiotics in this center. Considering the importance of these drugs in treatment of infectious diseases and the consequences of irrational use, the present DUE study can help to identify defects of antibiotics utilization, and develop rational antibiotic implementation protocols to prevent emerging resistance.

Methods

The present study was a cross-sectional prospective study was done from July 2017 to December 2017, in Alzahra hospital, a tertiary and referral center for gynecological surgeries affiliated to Tabriz University of Medical Science, Tabriz, Iran. The study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences under the code of ethics IR.TBZMED.REC.1397.211. All patients aged 18-70 who receive preoperative antibiotic as prophylaxis during the study period was enrolled. The data included patient demographic information, diagnosis, antibiotic therapy received (agents, rout of administration, doses, durations of administration, start time of administration in relation to the time of surgery, dose intervals, number of doses). Compliance with the recommendations and defined standards AHFS drug information. SPSS (v. 24) software was used for statistical analysis. The qualitative variables were presented by their frequency and percentage.

Results

A total of 210 patients who underwent common gynecological surgeries were enrolled in this study. The mean age of patients was 35.3 ± 10.9 years. 58.6% (n=123) and 28.1 (n=59) patients underwent cesarean section and hysterectomy, respectively (Table 1). Forty-one (33.3%) of patients who had a cesarean section underwent premature rupture of membranes (PROM).

Table 1. Demographic data, and number of patients who underwent gynecological surgeries.

	patients (n=210)
age (year)	35.3±10.9
Weight (Kg)	73.6±50.2
Past Medical History	n (%)
None	161 (76.6)
HTN	10 (4.8)
Hypothyroidism	36 (17.1)
Anemia	3 (1.4)
Type of surgery	n (%)
Cesarean section	123 (58.6)
EP	1 (0.5)
Hysterectomy	59 (28.1)
Laparoscopy	15 (7.1)
Infectious abortion	12 (5.7)

Data is presented as Mean ± SD or n (%), HTN Hypertension

Twelve (5.7%) of patients did not receive a prophylaxis regimen. The most frequently prescribed classes of antibiotics were cephalosporin (94.4%) followed by metronidazole (11.6%). Among preoperative prophylaxis regimens, 71.4% (n=150) patients received 1 g cefazolin, intravenously. According to the AHSP guideline, other prophylactic regimens other than cefazolin were not used correctly (Table 2). The correct prescribed dose was observed only for metronidazole and clindamycin, but on the other hand, the mentioned antibiotics were prescribed with the wrong regimens. Nine (4.2%) patients had type 1 allergy to beta-lactam, which also did not receive the correct alternatives.

Seventy-eight percent of patients (n=156) received a single drug for prophylaxis while 4 patients (2.0%) received two drugs. Thirty-eight patients (19.1%) received three drugs for prophylaxis. In more than 40% of patients, the one-hour interval between antibiotic injection and the start of surgery was not observed. Patients receiving cefazolin

received the drug for a minimum of 24 hours and a maximum of 72 hours (Table 3).

Table 2. Frequently used combinations of antimicrobial agents for surgical prophylaxis (N=198)

Antibiotic	n (%)
Cefazolin 1g IV	150(71.4)
Ampicillin 2g IV Gentamicin 80mg IM Metronidazole 500mg IV	1(0.5)
Cefazolin 1g IV Ceftriaxone 1g IV	1(0.5)
Ampicillin 2g IV	1(0.5)
Gentamicin 80mg IM	4(1.9)
Gentamicin 80mg IM Ampicillin 2g IV	1(0.5)
Gentamicin 80mg IM Ampicillin 2g IV Clindamycin 900mg IV	3(1.4)
Metronidazole 500mg IV	1(0.5)
Metronidazole 500mg IV Ceftriaxone 1g IV	10(4.8)
Cefazolin 1g IV Ampicillin 2g IV	15(7.1)
Cefazolin 1g IV Metronidazole 500mg IV	11(5.2)

Data is presented as n (%)

Table 3. Timing of administration of prophylactic antibiotic in patients who underwent gynecological surgeries.

Antibiotic	Single dose, n (%)	24h n (%)	72h n (%)
Cefazolin	10 (6.4%)	111(70.7%)	9(5.7%)
Ampicillin		4(23.5%)	5(29.4%)
Gentamicin	2 (5%)	14(35%)	7 (17.5%)
Clindamycin		4 (22.2%)	6 (33.3%)
Metronidazole		6 (13.3%)	16 (35.6%)
Ceftriaxone		2 (10%)	10 (50%)

Discussion

The advantage of preoperative antibiotic prophylaxis is well defined. Several guidelines are available for prevention of SSI in patients who undergo an operation regarding the optimal antibiotic prophylaxis (15-18). Unfortunately, the reviews have shown that optimal practice isn't accomplished in numerous hospitals (19).

In this study, the compliance of the prophylaxis regimen before common gynecological surgeries with the ASHP guidelines was evaluated. The reason for choosing this topic was the high consumption and extension of duration of antibiotic administration of antibiotics after surgery by surgeons. In the current study conformity of the selected antibiotic type, dose of administration, timing, and during of administration with ASHP guidelines was investigated. The results of this study indicate that the administration of prophylactic antibiotics in this center is not in accordance with the ASHP guidelines.

The antibiotic prophylaxis regimen in 71.4% (n= 150) patients out of 198 antibiotic recipients were cefazolin which is in full compliance with the ASHP guidelines in terms of the type of antibiotic. Cefazolin is a beta-lactam antimicrobial that is used most often for surgical antibiotic prophylaxis in patients with no prior allergy to beta-lactam antibiotics, and history of MRSA infection, Unless, depending on the type of surgery, cefazolin alone does not cover potential microorganisms. This agent is active against common skin pathogens such as Staphylococcus aureus, and Streptococcal species (20). In cases where antibiotics other than cefazolin were used for prophylaxis, suitable alternative was not administered, according to the ASHP guideline. In a study conducted in India, the choice of prophylactic antibiotics was not correct in all women undergoing cesarean section and did not comply with standard guidelines(21). In a study of 13 Dutch hospitals, out of 1,763 cases, the choice of antibiotic did not comply with the ASHP guidelines in any of the cases. The main reason for not choosing the right antibiotic prophylaxis regimen was the use of a hospital guideline by surgeons, which was different from the standard guidelines (22).

According to the ASHP protocol in cesarean section and hysterectomy, prophylactic regimens in which more than one type of antibiotic is prescribed are gentamicin+ clindamycin/metronidazole. If one drug would be used as a prophylaxis for infection, it does not make sense to use two or more drugs because of the potential for increased drug side effects, increased drug interactions, bacterial resistance, superinfection, and increased treatment costs (23).

None of the 9 patients with a history of penicillin allergy received the correct antibiotic prophylaxis regimen according to the ASHP guidelines. Alternative regimens based on the AHSP guideline for cesarean

section are clindamycin, vancomycin, or clindamycin with aminoglycosides. In hysterectomy, clindamycin or vancomycin can be used with aminoglycoside, aztreonam or fluoroquinolone, or a combination of metronidazole plus aminoglycoside or fluoroquinolone.

The dose of the antibiotic prophylaxis regimen was only correctly prescribed in the two drugs metronidazole 500 mg and clindamycin 900 mg and complied with the ASHP guidelines, but in general, in none of the single or multidrug prophylaxis regimens the dose of all drugs was not in accordance with the guideline did not exist. Cefazolin was the most common antibiotic used in this center, which was prescribed in all cases in a dose of one gram, while according to the ASHP protocol, 2g is the recommended dose for cefazolin in patients who weight <120 kg and 3 g for patients' weight >120 kg. Gentamicin was administered in all prescribed doses at a dose of 80 mg, while the recommended dose in ASHP was 5 mg per kg body weight, which unfortunately was not the appropriate dose in any of the cases. hence the proper antimicrobial selection, the appropriate duration, and dose of treatment play an important role in the improvement of outcomes and the efficacy of antibiotics in future infections (24).

Classen et al., (25) Stated that the lowest incidence of SSI in heart surgery is when prophylactic antibiotics are used within one hour before surgery. Stone et al., (26) Confirmed the same time frame for abdominal surgery.

In more than 40% of cases, the optimal time interval between prophylactic antibiotic injection and the incision was not observed and often there was more than 1 hour, Based on previous studies, it seems that they have not benefited much from prophylaxis (25, 26) According to ASHP instructions, this interval is one hour before the surgical incision. In the past, according to guidelines for cesarean section, prophylactic antibiotic administration was done during umbilical cord clamping. However, according to the latest version of the ASHP guideline, there is no difference between this type of surgery and other surgeries in terms of the time of antibiotic administration, and the surgical incision is recommended just one hour before.

Out of 210 patients undergoing gynecological surgery, 6 patients did not receive antibiotics after surgery. Of the 204 recipients, 58.8% (n=120) received cefazolin. These individuals received antibiotics for at least one day after surgery and for a maximum of 72 hours after surgery. According to the examinations and questions from the ward staff, the reason for prescribing antibiotics after surgery for more than 24 hours was the patient's bleeding, excessive manipulation of the surgical site during surgery, or having a preoperative infection. However, this seems a long time antibiotics administration after surgery. Metronidazole was administered up to 48 hours after surgery in 51.1% of cases or clindamycin was continued up to 48 hours in more than 40% of cases and up to 72 hours after surgery in 33.3% of cases. In 70.7% of cases, cefazolin was discontinued less than 24 hours after surgery.

A study of 377 patients in the surgical ward of a hospital in Riyadh, Saudi Arabia, who were admitted with a diagnosis of acute appendectomy showed that there is no significant difference in incidence of SSI between patients who received only one dose of antibiotics before surgery and patients who received Antibiotics before and after surgery (27). A study of 339 patients with maxillofacial fractures at the Hospital of Bern University of Medical Sciences, Switzerland, found no difference in the incidence of postoperative infection in a group of patients who received antibiotics the day after surgery with patients who the prophylaxis was continued for 5 days after surgery.

According to the ASHP guidelines, antibiotics are re-administered to ensure that the serum concentration is sufficient. So that if the duration of surgery is more than 2 half-life of antibiotics or the patient has extensive bleeding during surgery, then it seems necessary to re-dose the antibiotic.

Regarding the half-life of drugs used in Al-Zahra Medical Center (cefazolin half-life is 1-1.9 hours, gentamicin half-life is 2-3 hours, clindamycin half-life is 2-4 hours and metronidazole half-life is 6-8 hours) and the duration of the surgeries, which was recorded in the operation sheet in the patient's medical record, was not more than 2 hours in any of the studied cases. Therefore, there is no need for re-dosing of administered antibiotics.

In general, studies show that continuing antibiotics for more than 24 hours after surgery has no benefit in reducing infection after surgery (28, 29). On the other hand, previous studies have shown that long-term administration of antibiotics, in addition to developing antibiotic resistance, increases the side effects of antibiotics (30-32)

The pattern of prophylactic antibiotic administration pattern, including the choice of antibiotic type, prescribed antibiotic dose, time of prophylactic antibiotic administration before surgery, and duration of prophylaxis in Al-Zahra Medical Center, does not comply with the ASHP guideline. This pattern of antibiotic use, in addition to imposing short-term and long-term costs on the health system, leads to the development of multidrug-resistant microorganisms. We believe that the preparation of practical instructions and monitoring of their observance and holding numerous workshops and continuous training of physicians will help to make better use of antibiotics.

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