ANTIMICROBIAL PROPHYLAXIS IN LAPAROSCOPIC
CHOLECYSTECTOMY AND HERNIOPLASTY

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Abstract. The objective of our study was to characterize the pattern of surgical antibioprophylaxis in cholecystectomy and hernioplasty performed in the Surgical Clinic of the Emergency Clinical Hospital. This prospective study was conducted based on using a protocol established according to literature in this field and specific risks associated to surgical procedure. We recommended cefazolin 1g or cefuroxim 1.5g i. v., in a single dose for cholecystectomy. If the patients are allergic gentamicin, 1.7 mg/kg was recommended. We, also, chose cefazolin 1g i.v. in a single dose for hernia repair. Antibiotic was not routinely recommended in case of hernia repair without mesh or in laparoscopic cholecystectomy. Collected data were compared to our protocol and to the National Guide SRATI by conformities rate for each parameter. This study has identified several areas for improvement in SAP. We consider that the protocol should be revised and updated more often in order to improve the quality of the protocol and improvable of the medical staff and, also, to have in view the introduction of new antibiotics to be used. It is important for these medicines to be found in the Romanian market. Lately, we have had difficulty in being supplied with cefazolin therefore, we have used especially cefuroxim. The pharmaceutical varying market proves that the protocol should have a larger choice of antibiotics.

Keywords: cholecystectomy, hernioplasty, antimicrobial prophylaxis

Background

Antibiotics are drugs derived wholly or partially from certain microorganisms and are used to treat bacterial or fungal infections. They are ineffective against viruses. Antibiotics either kill microorganisms or stop them from reproducing allowing the body's natural defenses to eliminate them [1].

Surgical site infections (SSI's) account for approximately 15 % of nosocomial infections and are associated with prolonged hospital stays and increased costs [8]. Infection develops when endogenous flora are translocated to a normally sterile site. Seeding of the operative site from a distant site of infection can also occur (especially in patients with prosthesis or other implant). Factors influencing the development of SSI's include bacterial inoculums and virulence, host defenses, perioperative care, and intraoperative management. Unfortunately, an increasing number of resistant pathogens, such as methicillin-resistant Staphylococcus aureus (MRSA) and Candida species, are commonly implicated in surgical wound infections. For patients who have demonstrated recent infection with MRSA or vancomycin-resistant Enterococcus (VRE), prophylaxis with vancomycin, teicoplanin, linezolid or quinupristin/dalfopristin should be considered.

Antibiotic prophylaxis is designed to achieve effective antibiotic concentration at the time of initial surgical incision, and maintained throughout the vulnerable period of the procedure, the time between skin incision and skin closure [2]. If prophylaxis is given to, early antibiotic levels will be suboptimal when protection is needed. Antibiotics used after skin closure is unlikely to be effective.

Surgical antimicrobial prophylaxis (SAP) involves the administration of a short course of an antimicrobial agent before an operation begins for preventing site infection.

SAP is indicated for clean-contaminated or part of the clean procedures.

It is not recommended for an operations classified as contaminated or dirty.
There is ongoing discussion about whether prophylaxis should be used in clean procedures without foreign-body insertion. There is nearly uniform agreement about the value in clean contaminated procedures and reasonable agreement about use in clean procedures when foreign bodies are inserted.

Prophylaxis is most likely to be effective when given for a short duration against a single pathogen with a known sensitivity pattern.

It is a common misconception that antibiotics used for prophylaxis should not be used for therapy and vice versa.

The only difference between prophylaxis and therapy is the inoculums size and the duration of the antibiotic administration.

In prophylaxis there is no infection, so inoculums is minimal/none and antibiotic are administrated only for the duration of surgical procedure. If multiple organisms exist with a predictable susceptibility pattern, duration of protection is short and efficacy of prophylaxis will be excellent. [3].

With therapy the infections already exists and antibiotics are continued until the infection is eradicated.

When no infection exists prior to surgery single dose prophylaxis is preferred. When infection is present antibiotic are given for more than one day and represent early therapy not prophylaxis.

The appropriate choice of antimicrobial agents, dosage regime, timing, duration and route must be evidence based.

Optimal time to give an antibiotic is 30-60 minutes before incision. For cesarean section it should be delayed until the umbilical cord is clamped.

Optimal duration remains as an area of discussion. For many surgical procedures, a single dose is adequate and for prosthetic device, surgery is recommended 24-48 hours.

If the procedures last several hours, readministration is recommended if the antibiotic has a relatively short half-life. For example based on serum half-life data, in prolonged procedures an additional intraoperative dose of cefazolin should be given at 4 hours, for cefoxitin 2-hours intervals can be used.

The major pathogen in postoperative clean surgery is S. aureus. Because first generation cephalosporins are more active against S. aureus, are less expensive and have narrower spectrum of in vitro activity, has few side effects, these agents are prefers for most surgical procedures. [4].

If MRSA is present or if the patient is allergic to cephalosporins is often used vancomycin.

Parenteral cephalosporin has are commonly used for surgical prophylaxis, and ordinarily given as a bolus injection i.v. 15-60 minutes prior to the procedures.

Prophylaxis with vancomycin or gentamicin is given by slow i.v. infusion over 1-2 hours, starting 1-2 hours prior to the procedure [5].

Giving prophylaxis to patients who are having procedures for which this protocol does not recommend prophylaxis can be justified if the surgeon believes the patient to be at particularly high risk from SSI.

However, the ultimate decision rests with the surgeon's assessment of risk and benefit.

**Objective**

A prospective study Hospital was performed in the Surgery Clinic of the Emergency Clinical Hospital Bucharest to evaluate the appropriateness of surgery antibioprophylaxis practice in terms of compliance with the protocols and antibiotic susceptibility.

The goal of this study was to evaluate the impact of antibioprophylaxis protocol to improve antibioprophylaxis practice.

The aim of this protocol is, also, to identify the operations for which routine prophylaxis is supported by evidence.

**Material and Methods**

The protocol established by us was based on literature in this field, according to specific risks associated to surgical procedures. [8, 11, 2, 4, 12].

The US Centers for Disease Control's (CDC), NNIS (National Nosocomial Infections Surveillance) risk index is the method of risk adjustment most widely used internationally. Comorbidities/ the NNIS risk index is scored as zero, one, two or three according to the number of risks present (ASA score, wound class, duration of operation). The infection rate increases with increasing risk score.

Risk adjustment is based on three major risk factors:

- The American Society of Anesthesiologists. (ASA) score, reflecting the patient's state of health before surgery;
- wound class, reflecting the state of contamination of the wound;
- duration of operation, reflecting technical aspects of the surgery.

The American Society of Anesthesiologists has devised a preoperative risk score based on the presence of co morbidities at the time of surgery. An ASA score >2 is associated with increased risk of wound infection and this risk is additional to that of classification of operation and duration of surgery.

**ASA score Physical status**
1. A normal healthy patient
2. A patient with a mild systemic disease

3. A patient with a severe systemic disease that limits activity, but is not incapacitating

4. A patient with an incapacitating systemic disease that is a constant threat to life

5. A moribund patient not expected to survive 24 hours with or without operation

This protocol applies to all elective operations in the clean, clean-contaminated or contaminated categories.

Recommendations for prophylaxis of emergency surgery are limited to clean operations (for example, emergency repair of abdominal aortic aneurysm or open fixation of a closed fracture) and clean-contaminated operations (for example emergency caesarean section and facial trauma).

The protocol development group considered that antibiotic therapy for emergency operations with contaminated or dirty wounds is standard therapy rather than prophylaxis and as such is beyond the scope of this protocol.

Operations can be categorized into four classes with an increasing incidence of bacterial contamination and subsequent incidence of postoperative infection.

**Classification of operation**

**Clean**: operations in which no inflammation is encountered and the respiratory, alimentary or genitourinary tracts are not entered. There is no break in aseptic operating theatre technique.

**Clean contaminated**: operations in which the respiratory, alimentary or genitourinary tracts are entered but without significant spillage.

**Contaminated**: operations where acute inflammation (without pus) is encountered, or where there is visible contamination of the wound. Examples include gross spillage from a hollow viscous during the operation or compound/open injuries operated on within four hours.

**Dirty**: operations in the presence of pus, where there is a previously perforated hollow viscous or compound/open injury more than four hours old.

Duration of surgery is positively associated with risk of wound infection and this risk is additional to that of the classification of operation.

In the operations that lasted longer than the 75th percentile for the procedure were classified as prolonged.

Some surgical procedures are associated with specific risks, for example, the insertion of an orthopedic implant increases the risk of SSI (Surgical Site Infection). Procedures performed endoscopically have been associated with a lower risk of infection.

Risk factors are depending of patient: extremes of age, poor nutritional state, obesity (> 20 % ideal bodyweight), diabetes mellitus, smoking, coexisting infections at other sites, bacterial colonization (e.g. nose colonization with *S. aureus*), immunosuppression (steroid or other immunosuppressive drug use).

Other risk factors are depending of operation such as: length of surgical scrub, skin antisepsis, preoperative shaving, preoperative skin preparation, length of operation, antimicrobial prophylaxis, operating theatre ventilation, inadequate instrument sterilization, foreign material in surgical site, surgical drains, surgical technique including haemostasis, poor closure, tissue trauma, postoperative hypothermia.

Extrinsic risks or patient care practices include preoperative skin care, perioperative practices and postoperative wound care.

This prospective study was conducted based on using of cefazolin 1g or cefuroxim 1.5 g i. v., in a single dose for cholecystectomy. If the patients are allergic gentamicin, 1.7 mg/kg was recommended. We, also, chose cefazolin 1 g i. v. in a single dose for hernia repair. Antibiotic was not routinely recommended in case of hernia repair without mesh.

Collected data were compared to our protocol and to the National Guide SRATI [6] by conformity rate for each parameter.

The antibiotics were chosen depending on the present germs such as *S. aureus*.

It was not necessary to use antibiotics, which covers anaerobes germs.

During this study frequency of pathogens detection and pathogens causing surgical site infection were performed.

The choice of antibiotic took into account local resistance patterns.

Descriptive, univariate and multivariate analysis were carried out using GraphPad version [7].

**Results and discussions**

**Laparoscopic cholecystectomy**

In the protocol established by us the application of antibioprophylaxis is recommended just in high risk interventions such as senior citizens over 60 years, obstructive jaundice, acute cholecystitis, cholangitis, common duct stone, previous biliary surgery, nonfunctioning gall bladder.

We did not recommend antibioprophylaxis in laparoscopic cholecystectomy.

Our protocol recommended using of 1 g cefazolin or 1.5 g cefuroxim in a single dose administrated at induction of anesthesia. In allergic patients, we recommended 1.7 mg/kg gentamicin by slow i. v. perfusion (1-2 hours) started 1-2 hours before procedure.

SAP was not applied in cholangitis, chole-
cystopancreatitis, pyocholecystitis, and immune deficiency patients.

81 patients undergoing cholecystectomy were included in our prospective study. In all the cases was used laparoscopic technique.

SAP prescription was similar in any point with our protocol for 17 cases (20.98%), for another 51.8% of cases SAP was prolonged to 24 hours and in other 27.6% cases SAP was completely stopped after 48 hours (Figure 1).

The most common antimicrobial agent used was cefuroxim in 34 cases which represent 41.9%, followed by ampicillin 17.28%, cefazolin 13.5%, amoxicillin/clavulanic acid 11.1%, ampicillin/sulbactam 3.27%, ampicillin+gentamicin 3.27%, ampicillin+gentamicin+metronidazol 3.27%, ciprofloxacin 1.23% (Figure 2).

Hospital stay was 4.1 days in the case of using 1.0 g cefazolin single dose. In other cases when antibiotic was administrated 24 hours hospital stay was 3.95 days for cefuroxim, 3.75 days for amoxicillin/clavulanic acid and 3.88 days for ampicillin (Figure 3).

The rate of hospitalization was higher in the case of using cefuroxim during 48 hours (5.45 days) in compare with its use (3.93 days) 24 hours (p = 2.794, t = 0.09807).

No significant difference was seen between hospital stay in case of administration ampicillin during 24 hours (3.88 days) and during 48 hours (3.8 days). (p = 3.95, t = 0.09807).

On the average, it cost 5.15 lei for using single dose cefazolin and 6.15 lei for ampicillin, 15.66 lei for amoxicillin/clavulanic acid, 25.44 lei for cefuroxim administrated 24 hours (Figure 4).

Extremely difference was found between the costs of the antibiotics administrated in single dose and during 24 hours (p < 0.001).

There was no infection in any of the cases analyzed.

The administration of gentamicin instead of using cephalosporin has, in allergic patients was ignored.

It was considered that by using aminoglicosides along side neuromuscular blocking drugs muscular relaxation was increased [8].

The reduced cost of ampicillin does not recommend it as being preferable to microbial prophylaxis due to its moral wear and resistance [9].

At present ampicillin is not recommended in the antibioprophylaxis guides.

It may be said that the choice of antibiotics depended on the experience, knowledge and wish of the doctor has to use medicines recently introduced in therapy. The choice depending on the established by the guide appears as a last one.

We noticed that the protocol was respected in 20.98% cases in our study.

Cefuroxim was the most frequently used antibiotic. It is preferable to use cefazolin or cefuroxim in single dose regarding cost/benefit and benefit/risk for microbial prophylaxis in cholecystectomy.

The antibiotics chosen by us are to be found in the guide of the experts in type as well as duration and doses. Regarding allergic patients, experts recommended the association of 3.0 mg/kg gentamicin and 600 mg clindamycin, in contrast with 1.7 mg/kg gentamicin in monotherapy chosen by us. When we established the protocol clindamycin had not yet been registered in our country. There

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**Figure 1.** SAP prescription in laparoscopic cholecystectomy

**Figure 2.** The most common antibiotics used in cholecystectomy

**Figure 3.** Hospital stay (days) in cholecystectomy

**Figure 4.** The average costs of antibiotics used
is a difference between the doses we recommended and that of the experts who recommended higher doses of gentamicin.

The National Guide SRATI recommend antibioprophylaxis both in open and laparoscopic intervention.

The choice of one antibiotic or another to be introduced in the guide is up to the local Therapeutic Committee.

Hernioplasty

Cefazolin was the antibiotic recommended by our both protocol and SRATI Guide.

It was used 1 g cefazolin i.v. in a single dose at induction of anesthesia.

We did not recommend the antibiotic to be routinely used in case of intervention without mesh. The experts recommend 1 g cefazolin in a single dose applying only in intervention with mesh and do not refer at all to the cases in which a mesh is not used. Regarding allergic patients, experts recommended the association of 3.0 mg/kg gentamicin and 600 mg clindamycin, in contrast with 1.7 mg/kg gentamicin in monotherapy chosen by us.

We analyzed 85 patients scheduled for hernioplasty of which 19 patients (22.3 %) did not received antibioprophylaxis. In 12 cases (14.14 %), the patients received antibiotics in a single dose using cefuroxim (4 patients), amoxicillin/ clavulanic acid (4 patients) or cefazolin (4 patients). In 25 cases (29.4 %) antibiotic therapy was stopped after 24 hours.

In nine patients (10.58 %) was given antibiotic for 48 hours. In other 25 patients (26.8 %), SAP was completely stopped after 48 hours (Figure 5).

In 23 cases the protocol was respected which means 27 %.

If we take into account the eight cases in which was given amoxicillin/clavulanic acid or cefuroxim the percentage increase to 36.

Hospitalization lasted for 4.3 days in the cases in which the antibiotic was not used, 4.4 days in the cases of using single dose of antibiotic, 3.96 days in the cases in which the antibiotic was given 24 hours, 3.66 days in the cases of using antibiotic during 48 hours and 6.1 days in the cases in which antibiotic was given more than 48 hours.

The statistics showed that the average hospitalization was significant in case of using the antibiotic more than 48 hours and the one in which the antibiotic was not given (p < 0.05). The statistics, also, showed as being insignificant the administration of antibiotic during 24, 48 hours or a single dose compare with the group in which was not given (p > 0.05).

Concerning the high costs of the use of antibiotic over 48 hours, the difference is significant in comparison with that of using antibiotic in a single dose or 24 hours.

It can be said that the efforts of the doctors were concentrated on the operative technique, monitoring of the evolution and less on monitoring the resources used.

The regimes used varied markedly in SAP dosage, type of antibiotic and length of used.

Surgical site infection rate occurred 1-5 %. The distribution of pathogens isolated from surgical site infection was in accordance with the evidences.

Conclusions

This study has identified several areas for improvement in SAP.

Many surgeons often did not distinguish between prophylactic and therapeutic use of antibiotics.

When SAP was prescribed in accordance with protocol the main mistakes in its modalities of prescriptions was choice of molecule, excessive postoperative duration of the SAP or inappropriate use of broad-spectrum antimicrobials.

We consider that the protocol is valid from point of view of efficiency, safety and pharmacoeconomic. We propose the promotion, respecting and applying it.

We, also, propose the revision of the protocol regarding the alternatives in case of allergic patients.

The reevaluation of the protocol should stress the involvement of all the participants in the medical performance and the importance of implementing such a protocol.

We consider that the protocol should be revised and updated more often in order to improve the quality of the protocol and improvable of the medical staff and, also, to have in view the introduction of new antibiotics to be used.
It is important for these medicines to be found in the Romanian market.

Lately, we have had difficulty in being supplied with cefazolin therefore, we have used especially cefuroxim.

The pharmaceutical varying market proves that the protocol should have a larger choice of antibiotics.

The local Therapeutic Committee can use the results of our study when they check up the guide.

We wish to stress the National Guide (SRATI) appeared a few years after we established, settled and carried out our study.

It could be say that the practices in SAP are still imperfect. but it may be perfectible.

Last, but not least we propose there ought to be clear criteria of measuring the quality of guide.

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