

Perioperative antibiotic prophylaxis of infections in abdominal surgery: evidence-based medicine and current trends

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Періопераційна антибіотикопрофілактика інфекцій в абдомінальній хірургії: доказова медицина та сучасні тенденції

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Abstract

Objective. To summarize the results of our own research on the use of perioperative antibiotic prophylaxis in abdominal surgery and modern approaches to antibiotic prophylaxis from the perspective of evidence-based medicine.

Materials and methods. The results of treatment of 415 patients with acute abdominal pathology, of whom 165 developed peritonitis, and current international recommendations for the use of perioperative antibiotic prophylaxis in abdominal surgery were analyzed.

Results. For effective perioperative antibiotic prophylaxis as a key element of infection prevention strategy, it is important to adhere to the basic principles defined by international standards and confirmed by clinical experience.

Conclusions. Perioperative antibiotic prophylaxis for abdominal infections reduces the risk of complications and prevents the development of antibiotic resistance. Antimicrobial monotherapy, such as imipenem-cilastatin, is effective in elective colorectal surgery; in non-elective surgery, a combination of parenteral antibiotics effective against typical intestinal pathogens is recommended. The implementation of control checklists and local protocols for perioperative antibiotic prophylaxis based on microbiological monitoring is recommended. Perioperative antibiotic prophylaxis is a supplement to surgical standards, not a replacement for them.

Keywords: intra-abdominal infection; purulent-septic complications; perioperative antibiotic prophylaxis; antimicrobial monotherapy.

Surgical site infections (SSIs) are a big deal for patients and the healthcare system. In low- and middle-income countries, nearly one-third of patients develop SSIs after surgery, with an overall incidence ranging from 5.6 to 11.8 per 100 surgical procedures [1, 2]. Although the incidence of SSIs is significantly lower in high-income countries, they remain the third most common type of healthcare-associated infection after respiratory and urinary tract infections in Europe and the United States [3, 4], and in some European countries they are even the most common type of healthcare-associated infection. , there are more than 3.5 million patients with healthcare-associated infections in the European Union and the European Economic Area each year, of whom more than 90,000 die [5].

A significant proportion of SSIs are infections following abdominal surgery, accounting for 15 to 25% of all infections associated with healthcare [6–8]. In European countries, the incidence of SSI in the large intestine reaches 9.6% [9]. Therefore, surgeons and infection control specialists pay considerable attention to the prevention of infection

in the abdominal surgical area. In surgical practice, abdominal infections are most often associated with surgical interventions on the digestive tract and are considered one of the main causes of postoperative complications. Thus, after "clean" surgical interventions, the frequency of infections ranges from 3 to 6%, while after operations for acute obstructive colonic obstruction, this figure ranges from 32 to 74%, and after surgical interventions on the large intestine against a background of severe concomitant pathology and with a complicated course, purulent-inflammatory complications occur in 40–75% of patients with a mortality rate of 40–60% [7, 10–12].

Infections arise and spread primarily under conditions of sufficient bacterial contamination, suppression of humoral and cellular resistance factors, and immune reactivity of the body. They can be localized both in the abdominal cavity and in its organs, are usually polymicrobial, and include both aerobic and anaerobic bacteria. The average number of bacterial isolates isolated from patients with abdominal cavity infections ranges from 2 to 5, with a predominance

of obligate and facultative anaerobes [6, 10, 13]. Thanks to modern methods of collection and culture, which have appeared in recent years, knowledge about intra-abdominal infections has been expanded and deepened. Adequate surgical drainage and the use of antibacterial therapy improve the clinical course of these infections and reduce the risk of local complications and septicemia.

According to the study of the etiological structure of infectious complications, the most common pathogens of abdominal infections are: *Escherichia coli* (22.0%), *Staphylococcus aureus* (19.0%), *Staphylococcus epidermidis* (13.0%), *Enterococcus faecalis* (15.0%), *Pseudomonas aeruginosa* (10.0%), *Acinetobacter baumannii* (11.3%). These pathogens are most sensitive to β -lactam antibiotics, in particular meropenem (75–100%) and cefepime (65–100%). Fluoroquinolones are also highly active. However, sensitivity to third-generation cephalosporins (70–85%) and amoxicillin-clavulanate (40–75%) is decreasing. Highly resistant pathogens to ampicillin-sulbactam and first- and second-generation cephalosporins.

A key element of the SSI prevention strategy in abdominal surgery is perioperative antibiotic prophylaxis (POAP). Its effectiveness in "clean" and "conditionally clean" surgeries has been proven in many randomized controlled trials and meta-analyses [14–17]. It is important to distinguish between antibiotic prophylaxis and antibiotic therapy. The goal of POAP is to prevent colonization and entry of bacteria into the wound, not to treat an existing infection [18]. In case of violation of the timing, dosage, suboptimal choice of drug, or duration of POAP, not only its ineffectiveness is possible, but also the development of antibiotic resistance of pathogens, prolongation of the patient's hospital stay, and an increase in the financial burden on the healthcare system [19].

The relevance of the topic is also due to the need to update local protocols, taking into account current international recommendations, the regional microbial landscape of circulating strains and their resistance, as well as the realities of the Ukrainian healthcare system in conditions of war, resource shortages, and forced reorganization of healthcare facilities.

The aim of the study: to summarize the results of our own research on the use of POAP in abdominal surgery and modern approaches to antibiotic prophylaxis from the perspective of evidence-based medicine.

Materials and methods

The results of treatment of 415 patients with acute abdominal pathology were analyzed, of which 165 had complications of peritonitis. Its occurrence in 32 patients was caused by acute appendicitis, in 37 – perforated gastroduodenal ulcer, in 39 – acute intestinal obstruction, in 19 – acute pancreonecrosis, in 17 – acute cholecystitis, in 12 – traumatic injuries of the abdominal cavity, and in 9 – pathological perforation of the colon. In 251 patients, the microflora of wound exudates was assessed by culture. The sensitivity of isolates from patients to antibiotics was determined by the disk diffusion method.

We studied modern international and national guidelines and scientific publications found through a selective search in PubMed on approaches to the use of POAP for the prevention of SSI in abdominal surgery and its principles.

Results

The occurrence and nature of postoperative infectious complications depended on the nature of the pathogen isolated from the site of infection. The main pathogens of purulent-inflammatory complications in patients with pancreatitis were associations of aerobic and anaerobic microbes. Wound infection after surgical interventions on the abdominal organs was more often caused by *Escherichia coli* in monoculture – 43% of cases, and in association with *staphylococcus* and *proteus* – 27%.

Most of the isolated strains of microorganisms were resistant not only to aminoglycosides and cephalosporins, but also to fluoroquinolones.

Therefore, one of the principles of POAP, based on international clinical guidelines developed by the World Health Organization, the US Centers for Disease Control and Prevention, and the Enhanced Recovery After Surgery (ERAS) Society, was the correct selection of antibiotics [2, 20, 21]. The basis for choosing an antibiotic is the type of intervention, the expected spectrum of pathogens and regional data on their sensitivity to antibiotics (the results of microbiological monitoring are used), patient safety and tolerance to the drug. International guidelines recommend first choosing first- and second-generation cephalosporins (e.g., cefazolin) for most "clean" and "conditionally clean" surgeries, and in the presence of anaerobic flora (colorectal surgery), a combination with metronidazole. If there is an allergy to β -lactams, clindamycin or vancomycin in combination with aminoglycosides or fluoroquinolones may be substituted.

Our experience confirms the importance of choosing the right antibiotic depending on the type of surgery. For high-risk surgical procedures (perforated ulcer, acute intestinal obstruction, destructive cholecystitis, etc.), patients should be prescribed short-term prophylaxis (third- or fourth-generation cephalosporins or combinations with aminoglycosides). With regard to colorectal surgery, it should be noted that *Escherichia coli* is the most common pathogen, so prophylaxis should be aimed at combating this pathogen.

In patients with peritonitis who had suppressed T-cell immunity, antibacterial therapy was combined with immunomodulatory drugs. Experience with the use of these drugs in combination with immunocorrectors (immunofan, laferobion) in patients with peritonitis indicates a faster recovery of T-cell immunity and the phagocyte system than with other drugs. In accordance with the concept of immune distress based on the systemic inflammatory response syndrome, it is mandatory to include drugs that regulate the production of anti-inflammatory cytokines, prevent the aggregation of blood cells, suppress the production of low-molecular-weight inflammatory mediators, and stimulate the ability of the endothelium to

respond to high concentrations of microbial products in the immunocorrective therapy regimen. For this purpose, we widely use diclofenac sodium, dipyridamole, and pentaxifylline in therapeutic concentrations for 5–7 days.

Another important principle of POAP is the timing of antibiotic administration. The optimal time for antibiotic administration is 30–60 minutes before the incision is made, so that its therapeutic concentration in the tissues is reached at the moment of possible contamination. When using vancomycin or fluoroquinolone, the infusion should be started 60–120 minutes before surgery, taking into account the duration of administration of the drug.

Another important principle is the duration of prophylaxis. It has now been conclusively proven that continuing antibiotic prophylaxis after surgery is not only ineffective but can also be harmful. Most international guidelines strongly recommend a single dose of the drug [2, 20].

POAP can be administered orally or parenterally. If elective surgery on the large intestine is to be performed, oral administration of the drugs is useful. The advantages of oral administration of drugs are that poorly absorbed drugs can be used, which affect microorganisms in the lumen of the large intestine and do not develop bacterial resistance. Various combinations are used: erythromycin with neomycin, metronidazole with kanamycin, and tetracycline with neomycin. The absolute success of oral drugs is indicated by mechanical cleansing of the large intestine from fecal masses.

In the case of non-elective colon surgery, combinations of parenteral antimicrobial drugs effective against pathogens commonly found in the colon flora are preferred for the prevention of infections.

If preventive treatment is prescribed orally, the patient should take antimicrobial drugs 24 hours before surgery. However, for all patients being prepared for surgery, the parenteral route of antibiotic administration is preferable. With intravenous administration of antimicrobial drugs, high concentrations in the blood serum and intestinal tissue are achieved during surgery within a short period of time.

The next POAP principle is to re-administer antibiotics only if necessary. This may be necessary if the operation lasts more than 3–4 hours, there is significant blood loss (more than 1.5 liters), obesity, or a large volume of infusion therapy. This approach allows the necessary concentration of the drug to be maintained in the tissues throughout the operation.

Another important principle of POAP is avoiding the unjustified use of antibiotics. POAP is only appropriate when indicated. Unjustified use of antibiotics (e.g., in "clean" surgeries without risk factors) leads to the development of antibiotic resistance, increased treatment costs, and an increased risk of side effects (e.g., the development of *Clostridium difficile* infection).

Thus, the effectiveness of POAP directly depends on compliance with all the key principles outlined above. Ignoring the latter not only reduces the preventive value of POAP, but also increases the risk of antibiotic resistance

in circulating strains, which is why compliance with POAP protocols is considered a necessity in modern surgical practice.

Discussion

Proper POAP significantly reduces the risk of SSI in abdominal surgery. Ukrainian clinical protocols are largely consistent with international protocols [22, 23]. However, Ukrainian standards and international recommendations are being implemented in clinical practice with certain difficulties, particularly in the Ukrainian healthcare system [24]. Russia, in its war against Ukraine, is destroying healthcare facilities, causing a shortage of medical personnel and, as a result, a heavy workload for doctors, an increase in the frequency of emergency operations due to the large number of wounded, disrupted logistics chains for the supply of medicines, and, among other challenges for the healthcare system and surgical practice, an increase in antibiotic resistance of infectious agents [25, 26]. According to K. Yu. Belka and co-authors [24], problems of incomplete compliance with medical care protocols and standard operating procedures, as well as the use of reserve antibiotics for antibiotic prophylaxis, are widespread in Ukrainian healthcare facilities, contributing to the development of antibiotic resistance in strains.

Today, many surgical healthcare facilities do not have their own clinical protocols for POAP based on microbiological monitoring results that determine the spectrum and sensitivity of the microbial landscape. This leads to chaotic and unregulated antibiotic prescribing, often "just in case" [27]. Irrational use of POAP can lead to an increase in the incidence of SSIs caused by hospital-acquired antibiotic-resistant strains; longer hospital stays and higher treatment costs; increased risk of mortality, especially among elderly and frail patients in high-risk groups; loss of clinical effectiveness of key antibiotics on a national scale.

According to the Standard "Parenteral Perioperative Antibiotic Prophylaxis" [22], the use of first- and second-generation cephalosporins (cefazolin, cefuroxime) is recommended for POAP in abdominal surgery, which is entirely justified. However, in our conditions, the results of microbiological monitoring indicate a high level of antibiotic resistance of pathogens to this group of antibiotics, therefore we use third- and fourth-generation cephalosporins, the effectiveness of which has been confirmed by clinical practice. In international practice, third- and fourth-generation cephalosporins are also used for POAP in colon surgery [28]. D. W. Bratzler et al. [15] believe that during operations where SSI is likely to be caused by enterobacteria or anaerobes (e.g., colorectal surgery), a combination of second-generation cephalosporins (e.g., cefuroxime) with metronidazole is appropriate. Drugs with a complicated route of administration (e.g., slow infusion over 2 hours) and/or poor tissue penetration (e.g., vancomycin) should also be avoided if possible. Similarly, broad-spectrum antibiotics such as meropenem are suitable for empirical treatment of

severe infection but should not be used routinely for POAP. Given the uniqueness of the spectrum of surgical procedures, the microbial landscape of pathogens, and the characteristics of infection control and prevention in each individual clinic, we believe that it is very important for surgical clinics to have their own POAP protocols based on international and national protocols and taking into account the local characteristics of the healthcare facility.

A comparison of POAP practices in different countries shows that not only the choice of antibiotic is key, but also the time of its administration, the duration of prophylaxis, adherence to clear protocols, and the infrastructure of healthcare facilities [2, 10, 14–17, 19–21].

According to C. Eckmann et al. [29], POAP is clearly indicated in cases of surgery with a high risk of SSI (e.g., colorectal surgery). Define the basic principles of POAP, which are that it should be administered by the anesthesiology team within 60 minutes before surgery, before the incision is made, and usually as a single injection. Continuation of POAP after surgery leads to increased toxicity, bacterial superinfections, and antibiotic resistance [19, 29, 30].

To improve the effectiveness of POAP, it is advisable to create checklists for clinical audit and internal control in surgical departments of healthcare facilities based on the orders of the Ministry of Health [22, 23].

Modern approaches to POAP in abdominal surgery involve striking a balance between effective infection prevention and the containment of antimicrobial resistance. According to the results of recent studies and clinical guidelines, the use of antibiotics should be personalized, short-term, and strictly justified. Individual patient characteristics should be taken into account, such as obesity, diabetes, and chronic diseases that may alter the pharmacokinetics of drugs. Individual risk factors for SSI should be assessed before any surgical procedure. The odds ratio for SSI increased to 1.35 (1.28; 1.41) in patients with a body mass index above 30 kg/m² and to 3.29 (2.99; 3.62) if the patient also had immune suppression [29]. Unfortunately, however, there are no randomized controlled trials of POAP in morbid obesity, nor are there any high-quality data [31].

Scientists are discussing the need for mechanical bowel cleansing before surgery. According to a systematic review and meta-analysis of 38 randomized controlled trials, mechanical bowel preparation with oral antibiotics is the best way to reduce the risk of SSI in patients after colorectal surgery. These data are consistent with our practice. The advantages of a strategy for preparing for elective intestinal surgery using intravenous antibiotics with oral antibiotics are also pointed out [32, 33]. The use of therapeutic drug monitoring and pharmacogenetic approaches is considered a promising direction [15, 34, 35]. Highly specialized antibiotics with low toxicity and high activity against surgical pathogens are also being developed. Nanotechnology for delivering antibacterial drugs to the site of intervention is also of interest [36, 37]. Current trends in improving antibiotic prophylaxis

include the development of alternative forms, the study of the possibilities of local application of antimicrobial solutions, impregnated dressings (e.g., chlorhexidine or silver solutions), and the use of probiotics to restore the intestinal microflora after antibacterial exposure [38, 39].

Despite the high effectiveness of POAP, it should be emphasized that it does not replace compliance with surgical standards of asepsis, sterility, and other measures for the prevention of SSI, but rather complements them.

Conclusions

1. Perioperative prevention of abdominal infections aims to reduce the risk of their development both in the surgical area and beyond, as well as to optimize the use of antibiotics to prevent unwanted complications resulting from their misuse and to curb the development of antibiotic resistance in pathogens.

2. Antimicrobial monotherapy is effective against both aerobic and anaerobic bacteria and is a powerful component of the concept of simplifying treatment regimens. Imipenem–cilastatin may be recommended as a single prophylactic antimicrobial agent in elective colorectal surgery. In non-elective colorectal surgery, it is recommended to use a combination of parenteral antimicrobial drugs that are effective against pathogens commonly found in the colon flora.

3. The key principles of effective POAP are: selection of an adequate drug and the correct dose, taking into account its pharmacokinetics and the patient's body weight; optimal duration of antibiotic administration and prophylaxis; re-administration of the drug if necessary; avoidance of unnecessary use of antibiotics.

4. POAP does not replace compliance with surgical standards of asepsis, sterility, and other SSI prevention measures, but is an important addition to them.

5. It is advisable for surgical healthcare facilities to develop their own clinical protocols for POAP based on the results of microbiological monitoring to determine the spectrum and sensitivity of the microbial landscape, as well as checklists for clinical audit and internal control.

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