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Perioperative antibiotic prophylaxis for abdominal delivery at the regional perinatal center

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Abstract

Aim. To conduct a comparative pharmacoepidemiological study and assess the rational use of antibiotics in women undergoing caesarean section.

Methods. A retrospective analysis of 1,025 birth histories of women after planned and emergency cesarean section was carried out with a detailed assessment of the use of antibiotics in 2007–2009 (523) and 2016–2017 (502) — with an interval of 10 years for which new clinical guidelines, principles of rational pharmacotherapy and evidence-based medicine were introduced. The time of administration of the first dose, duration of administration, consumption of antibiotics were assessed. The significance of differences in relative indicators was assessed according to Pearson (χ^2).

Results. Antibiotics were prescribed to women with planned and emergency caesarean section in 100% of cases in the first period of the study (2007–2009) and prescribed in 98% of women with planned caesarean section and 96% with emergency caesarean section in the second period (2016–2017). In the first period, the first dose of antibiotic was administered: in 110 (44%) cases during surgery and 139 (56%) cases after surgery in planned caesarean section; in 139 (51%) cases during surgery and 135 (49%) cases after surgery in emergency caesarean section. In the second period, antibiotics were administered 30–60 minutes before the operation in 263 (96%) cases in the planned caesarean section and 218 (95%) cases in the emergency; postoperative antibiotics were administered in 7 (2%) women in the planned caesarean section and 2 (1%) women in the emergency ($p < 0.05$). Greater than 5–6 days of antibiotics were used: in 166 (67%) women in the planned operation and 166 (61%) in the emergency for the first period; in 43 (16%) women with the planned operation, and 38 (17%, $p < 0.05$) women with an emergency for the second period. In the first period, 13 antibiotics from 8 pharmacotherapeutic groups were used and in the second period, 7 out of 5 were used.

Conclusion. From 2007 to 2017, the use of antibiotics has become to comply with the implemented clinical guidelines for abdominal delivery: the duration of antibiotic use has decreased, the time of administration of the first dose and the range of antibiotics used changed.

Keywords: pharmacoepidemiology, cesarean section, antibiotic prophylaxis, antibiotic therapy, emergency and planned cesarean section.

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Background. The risk of infections of the pelvic organs, in the surgical incision site, and sometimes in the urinary tract in women post cesarean section (CS) is 5–20 times higher than in women with vaginal delivery. Infectious complications can be very serious and, in rare cases, can even lead to maternal mortality [1].

A single administration of an antibiotic preoperatively has been proven to correspond to infection prevention efficiency to a 5-day course of antibiotic use after CS [2, 3]. Prophylactic antibiotics after umbilical cord clamping are also effective in reducing infectious disease risk [4].

The Cochrane systematic review shows that antibiotic prophylaxis reduces the risk of infectious disease in CS by 50%–70% [5]. In another systematic review, the authors evaluated prophylactic antibiotics before and after umbilical cord clamping in CS. They concluded that antibiotic administration prior to umbilical cord clamping is more

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effective in reducing postoperative infectious complication incidence [6]. Prophylactic administration of antibacterial agents reduces bacterial load. The strict adherence to the timing of administration and recommendations for antibacterial agent prescription plays an important role in patient recovery [7]. Failure to comply with these rules and inappropriate use of antibiotics increase the risk of resistant strains of bacteria [8].

The problem of the irrational use of antibiotics is widespread and is of particular relevance in hospitals in the Russian Federation. Noncompliance with administration timing and the irrational choice of antibiotic are the main errors [9, 10]. Pharmacoepidemiological research is essential to improve the practice of inappropriate drug prescribing. Such studies are the main tool for assessing the drugs' efficacy and safety and obtaining information about their use in clinical practice, making comparisons, and studying the change in the use and consumption of drugs over time to optimize their use [11].

Regulatory, administrative, and educational interventions, such as clinical guidelines, orders of the Ministry of Health of the Russian Federation, and postgraduate courses in clinical pharmacology for physicians on the rational use of drugs, in particular antibacterial agents, contribute to improved drug use [12–14].

This study aimed to conduct a comparative pharmacoepidemiological analysis of the practice of using antibacterial agents in CS with a 10-year period.

Materials and methods. The study was conducted in the Perinatal Center of the Republican Clinical Hospital of the Ministry of Health of the Republic of Tatarstan. The source of information was the labor and delivery medical records of women after elective and emergency CS.

We performed a quasi-random sampling of the labor and delivery medical records of women who underwent elective and emergency CS surgery. A retrospective analysis of antibiotic prophylaxis and therapy in 1025 women who underwent CS surgery was performed.

The quasi-random sampling method consisted of selecting the labor and delivery medical records from stacks of folders arranged by month in alphabetical order. From each stack corresponding to an alphabet letter, every fifth record was selected according to their arrangement in the stack.

We sampled the labor and delivery medical records in two time intervals (periods), namely, 2007–2009 and 2016–2017 (with a 10-year interval). These records were distributed by year: 222, 301, 198, and 304 medical records in 2007, 2009, 2016, and 2017, respectively. The period 1 sample consisted of 523 labor and delivery medical records (elective CS: 249 cases; emergency CS: 274 cases), while period 2 consisted of 502 medical records (elective CS: 275 cases; emergency CS: 227 cases).

For research, we created a database in Excel workbook format. Information from the labor and delivery medical records was entered into the database manually. The electronic record for each puerpera in the database included the following:

– Medications prescribed before, during, and after surgery (doses, routes, time of administration, duration of use)
– Age
– Diagnosis
– Gestational age at delivery
– Duration of hospital stay
– Clinical state indicators of the mother (blood pressure, body temperature, leukocyte laboratory tests, erythrocyte sedimentation rate before and after surgery) and the newborn (Apgar score, height and weight at birth, weight loss)

The study was approved by the local ethics committee of the Kazan (Volga region) Federal University (protocol no. 01/32/67 of December 28, 2017).

Statistical analysis included the calculation of mean values (median), range of values (minimum and maximum values), and relative values (the proportion (%) of the total number of patients). To assess the significance of the differences in relative indicators, the Pearson χ^2 test was used. The differences between the samples were considered significant at $p < 0.05$. The test assesses the statistical significance of the differences between two or more relative indicators (frequencies, proportions) when analyzing the sample. Statistical processing was performed using the Microsoft Excel software package.

The volume of consumption of antibacterial agents before, during, and after the surgery and their total consumption were assessed according to the Anatomical Therapeutic Chemical classification/Defined Daily Dose (ATC/DDD) methodology with the calculation of the number of DDDs per parturient woman. To calculate the consumption of the drug used in the hospital during the stay, the total dose in milligrams/grams was divided by this antibacterial agent's DDD, adopted by the World Health Organization [11, 15].

The calculation of DDDs per postpartum women per day was performed according to the equation:

$$\text{DDD/puerpera/day} = \frac{\text{total antibiotic dose (mg)/DDD (mg)}}{\text{the number of puerperas who received antibiotic/day}}$$

Results. The age range of patients enrolled in the study is 17–45 years, of which the age of the

Table 1. Time of administration of the dose 1 of antibiotic, n (%)

Time of administration of the dose 1 of antibiotics	Time period 1, 2007–2009, n = 523		Time period 2, 2016–2017, n = 502	
	Elective CS, n = 249	Emergency CS, n = 274	Elective CS, n = 275	Emergency CS, n = 227
30–60 minutes before surgery	0	0	263 (96)*	218 (95)*
During surgery	110 (44)	139 (51)	0*	0*
After surgery	139 (56)	135 (49)	7 (2)*	2 (1)*
Not administered	0	0	5(2)	7 (4)
Total	249 (100)	274 (100)	275 (100)	227 (100)

Note: *$p < 0.05$ when comparing elective versus elective and emergency versus emergency CS in the time periods 1 and 2.

Table 2. Duration of antibacterial agent usage after CS in the time periods 1 and 2, n (%)

Duration of course	Time period 1, 2007–2009, n = 523		Time period 2, 2016–2017, n = 502	
	Elective CS, n = 249	Emergency CS, n = 274	Elective CS, n = 275	Emergency CS, n = 227
Single administration	13 (5)	12 (4)	150 (55)*	103 (44)*
Within 3 days	20 (8)	22 (8)	42 (15)	41 (18)
Within 4 days	49 (19.5)	47 (17)	36 (13)	36 (16)
Within 5–6 days	166 (67)	166 (61)	43 (16)*	38(17)*
Within 7–8 days	1 (0.5)	27 (10)	1 (0.5)	2 (1)
Not administered	0 (0)	0 (0)	5 (2)	7(4)
Total	249 (100)	274 (100)	275 (100)	227 (100)

Note: *$p < 0.05$ when comparing elective versus elective and emergency versus emergency CS in the time periods 1 and 2.

female patients in periods 1 and 2 were 28 (18–44) years and 30 (17–45) years. The parturient women included in the two time periods compared did not differ in age and number of previous births. In the time period 1, there were 315 primiparas and 208 multiparas. In the time period 2, there were 208 primipara and 294 multiparas ($p > 0.05$).

An analysis of the frequency of prescribing antibiotics to women who underwent elective and emergency CS surgeries revealed that in the study period 1, antibiotics were prescribed in 100% of cases. In the period 2, antibacterial agents were prescribed in 98% of cases (n = 270) with elective CS and were not prescribed in 2% of cases (n = 5). In the case of emergency CS, antibacterial agents were prescribed in 96% of cases (n = 220) but not in 4% of cases (n = 7).

We analyzed the time of administration of the dose 1, the duration of antibiotic prescription, and the amount of antibacterial agents prescribed. We calculated the total consumption rate (total DDD) for all antibiotics (before and after surgery) and the total antibacterial load (antibiotic consumption during the entire hospital stay) and also compared these indicators in two time intervals (periods) (Table 1).

In the analyzed period 1, antibiotics were prescribed mainly empirically. Thus, the dose 1 of the antibiotic was administered in 110 (44%) and 139 (51%) cases with elective and emergency CS, respectively, during surgery after umbilical cord clamping. In about half of the cases, the dose 1 was administered after CS, i.e., 139 (56%) cases with elective CS and 135 (49%) cases with an emergency CS.

Current clinical guidelines [13] substantiate the rationality of the use of antibacterial agents 30–60 minutes preoperative. The analysis of the time of administration of the dose 1 in the labor and delivery medical records of women in the analyzed period 2 revealed that antibiotics were predominantly administered preoperative in 263 (96%) and 218 (95%) cases with elective and emergency CS, respectively, which is in line with clinical guidelines [13]. In seven (2%) and 2 (1%) cases of elective and emergency CS, antibiotics were prescribed postoperative. Antibiotic prophylaxis was not performed in five and seven cases with elective and emergency CS, respectively.

When analyzing the duration of antibacterial agent usage, the statistical difference was in a single administration of an antibiotic 30–60 minutes preoperative when comparing the time periods 1 and 2, as in the case of elective and emergency CS surgeries (Table 2).

Table 3. List of antibacterial agents prescribed of the study's time period 1

Pharmacotherapeutic group	International nonproprietary name	Trade name	Dosage
Inhibitor-protected aminopenicillins J01C	Ampicillin + sulbactam	Ampicillin	1000 mg + 500 mg
	Amoxicillin + clavulanic acid	Amoxiclav	1000 mg + 200 mg
Cephalosporins J01D A (generations I–III)	Cefazoline (I)	—	1000 mg
	Cefuroxime (II)	—	1500 mg
	Cefoperazone (III)	Cefobid, medacef	1000 mg
	Cefotaxime (III)	—	1000 mg
	Ceftriaxone (III)	Lendacin	1000 mg
Macrolides J01F	Azithromycin	Sumamed	500 mg
Fluoroquinolones J01MA	Ciprofloxacin	—	500 mg
	Ciprofloxacin	—	200 mg/100 ml
Aminoglycosides J01G	Gentamycin	—	80 mg/2 ml
Lincosamides J01FF	Clindamycin	Dalacin	100 mg
Other antibacterial agents G01AF01	Metronidazole	—	500 mg/100 ml
Antifungal agents A07AA02	Nystatin	—	500,000 U

Table 4. List of antibacterial agents prescribed of the study's time period 2

Pharmacotherapeutic group	Drug name	Dosage
Cephalosporins J01D A	Cefazoline (I)	1000 mg
	Ceftriaxone (III)	1000 mg
Inhibitor-protected aminopenicillins J01C	Amoxicillin + clavulanic acid	1000 mg + 200 mg
Fluoroquinolones J01M A	Levofloxacin	500 mg
	Ciprofloxacin	200 mg/100 ml
Macrolides J01F	Erythromycin	500 mg
Other antibacterial agents G01AF01	Metronidazole	500 mg/100 ml

In the time period 2, since antibiotics were administered preoperative (single administration) in emergency CS (103 (44%) cases) and elective CS (150 (55%) cases), there was a 45% decrease in antibiotic prescription in the postoperative period ($p < 0.05$).

In the time period 1, the duration of antibiotic use was generally more than 5–6 days (in 166 cases (67%) with an elective CS and 166 cases (61%) with an emergency CS). In the time period 2, it was in 43 (16%) cases with an elective CS and 38 (17%) cases with an emergency CS ($p < 0.05$) (Table 2).

It can also be noted that the duration of antibiotic use in two time periods was more than 7–8 days, typical for patients with an exacerbation of chronic infectious and inflammatory processes.

Antibacterial agents from different groups were used: 13 names of drugs from 8 pharmacotherapeutic groups in the time period 1 and 7 names of drugs from pharmacotherapeutic groups in the time period 2 (Tables 3 and 4).

In the time period 1, inhibitor-protected aminopenicillins, cephalosporin antibiotics, metronidazole, and the antifungal agent nystatin were often prescribed (Table 5).

Among penicillins, ampicillin + sulbactam was mainly used during surgery after umbilical cord clamping (13% of the cases) and postoperative (29% of the cases), while amoxicillin + clavulanic acid was used less frequently. Among cephalosporins, cefazoline was most often prescribed during surgery after clamping (3.5% of the cases) and after surgery (11% of the cases). In the range of the third generation cephalosporins, cefoperazone was prescribed after surgery postoperative (3% of the cases), ceftriaxone during surgery after umbilical cord clamping (0.5% of the cases), and postoperative (0.7% of the cases). There were

Table 5. The frequency of prescribing antibacterial agents in the time period 1, n (%)

Drug name	During surgery	After surgery
Ampicillin + sulbactam	67 (13)	152 (29)
Amoxicillin + clavulanic acid	11 (2)	15 (3)
Cefazoline (I)	18 (3.5)	55 (11)
Cefuroxime (II)	1 (0.2)	1 (0.2)
Cefoperazone (III)	—	16 (3)
Cefotaxime (III)	—	2 (0.4)
Ceftriaxone (III)	3 (0.5)	4 (0.7)
Ciprofloxacin	5 (1)	19 (3)
Gentamycin	—	2 (0.3)
Clindamycin	—	6 (1)
Azithromycin	—	1 (0.2)
Metronidazole	9 (2)	38 (7)
Nystatin	—	48 (9)

also isolated cases of cefuroxime and cefotaxime administration.

In addition, metronidazole was prescribed in 9% and 7% of the cases during and after surgery, and nystatin and ciprofloxacin were prescribed in 9% and 4% of the cases, which is considered a contraindication for this category. Other classes of antibacterial agents (macrolides, lincosamides, aminoglycosides) were prescribed less frequently (Table 6).

In the time period 2, from cephalosporin antibiotics preoperative, cefazoline and ceftriaxone was predominantly prescribed as a single dose (99% and 1% of the cases). Postoperatively, cefazoline administration was continued in 14% of the cases, and ceftriaxone was used for subsequent use in 32% of the cases.

Fluoroquinolone and amoxicillin + clavulanic acid (0.6% and 0.4% of the cases) prescriptions were associated with the risk of chronic endometritis exacerbation (Table 6). Erythromycin was prescribed due to an allergic reaction to cephalosporins.

At the next stage, using the DDD methodology, we calculated the consumption volume in DDD of all antibacterial agents used for antibiotic prophylaxis and antibiotic therapy in the time periods 1 and 2 and calculated the total antibacterial load (all the days that the patient received antibacterial agents) and the consumption volume in DDD for 1 day. The results are presented in Tables 7 and 8.

The consumption of antibacterial agents differed in the time periods 1 and 2.

When comparing amoxicillin + clavulanic acid consumption in the time period 1, the drug DDD is

Table 6. The frequency of prescribing antibacterial agents in the time period 2, n (%)

Drug name	Before surgery, n = 490	After surgery, n = 490
Cefazoline (I)	487 (99)	69 (14)
Ceftriaxone (III)	3 (1)	158 (32)
Amoxicillin + clavulanic acid	—	2 (0.4)
Levofloxacin	—	2 (0.4)
Ciprofloxacin	—	1 (0.2)
Erythromycin	—	1 (0.2)
Metronidazole	—	9 (0.18)

eight times higher (2.5 DDD) than that of the time period 2 (0.3 DDD), since amoxicillin + clavulanic acid was often used in the time period 1. The total consumption of cefazoline and ciprofloxacin showed equal DDD in both time periods, i.e., 3.3 and 0.9 DDD, respectively. For the ceftriaxone consumption, there was a difference of 0.4 DDD (4.6 and 5 DDD in the time periods 1 and 2). The consumption data of other antibacterial agents is presented in Tables 7 and 8.

The total antibacterial load in the time periods 1 and 2 was 3.4 and 2.5 DDD, i.e., the consumption of antibacterial agents decreased by 0.9 DDD in the time period 2.

Discussion. The rational prescription of antimicrobial drugs for women of childbearing age group is of great importance. Its rational use is influenced by drug policy instruments regulating and changing significantly the drug prescription practice, leading to the use of drugs in correct dose and mode of administration, hence prevents misprescription [12, 13]. The time of dose 1 administration of the drug affects the duration of hospital stay of patients, as well as the economic costs.

In a major multicenter study conducted in the Russian Federation in 2006, the timing of the dose 1 administration and the choice of antibiotic were assessed. The study results show the prevalence of inappropriate use of antibiotics. The results of our study of the time period 1 demonstrate the prevalence of inappropriate choice of antibiotics [9, 10].

For the time period 1, our study results confirmed that the precise time for the dose 1 administration was not observed, the duration of antibiotic intake lasted more than 5–6 days, and the choice of antibiotic was irrational. Metronidazole and nystatin were also frequently prescribed, which should be considered excessive.

In the time period 2, antibiotics were administered 30–60 minutes preoperative, recognized as a good clinical practice, since it reduces the fre-

Table 7. Consumption of antibacterial agents of systemic action in the time period 1 of the study in units of DDD, Me (min-max)

Medicinal product name (international nonproprietary name)	2007–2009, n = 523		
	Before surgery	After surgery (number of DDDs per day)	Total antibacterial load (number of DDDs for the entire period of hospitalization)
Ampicillin + sulbactam	0.5 (0.25–0.5)	0.5	3 (0.5–6)
Amoxicillin + clavulanic acid	0.8	0.8 (0.8–1.0)	2.5 (1.2–4.5)
Cefazoline (I)	0.7 (0.3–0.7)	0.7 (0.3–1.0)	3.3 (0.3–5.0)
Cefuroxime (II)	0.5	0.5	1.0
Cefoperazone (III)	0.5	0.5	2.0 (1.0–3.0)
Cefotaxime (III)	—	0.5	1.5
Ceftriaxone (III)	0.5	1.1 (0.5–1.5)1	4.6 (3.0–7.0)
Ciprofloxacin	0.25	0.6 (0.3–2.0)	0.9 (0.25–2.5)
Gentamycin	—	1.0	3.0
Clindamycin	—	3.0 (2.0–6.0)	11.0 (10.0–12.0)
Azithromycin	1.0	2.0	2.0
Metronidazole	0.3	0.7 (0.3–1.0)	1.2 (0.3–2.0)
Nystatin	—	1.3	5.3 (2.6–8.0)

Table 8. Consumption of antibacterial agents of systemic action in the time period 2 of the study in units of the defined daily dose (DDD), Me (min – max)

Medicinal product name (international nonproprietary name)	2016–2017, n = 502		
	Before surgery	After surgery (number of DDDs per day)	Total antibacterial load (number of DDDs for the entire period of hospitalization)
Cefazoline (I)	0.3	0.8 (0.65–1.0)	3.3 (0.7–5.0)
Ceftriaxone (III)	0.5	1.3 (1.0–2.0)	5.0 (1.0–10.0)
Amoxicillin + clavulanic acid	—	0.3	0.3
Levofloxacin	—	2.0	6.0
Ciprofloxacin	—	0.3	0.9
Erythromycin	—	1.0	1.0
Metronidazole	—	1.0	3.0

quency and severity of postoperative complications and complies with international standards of evidence-based medicine worldwide.

The Russian clinical guidelines for antibiotic prophylaxis recommend first- to second-generation cephalosporins (cefazoline at 1 g and cefuroxime at 1.5 g intravenously) and inhibitor-protected aminopenicillins (amoxicillin + clavulanic acid at 1.2 g, amoxicillin + sulbactam at 1.5 g, ampicillin + sulbactam at 1.5 g intravenously) as drugs of first choice, being the most effective and safe. If patients have a history of allergic reactions to penicillins and/or cephalosporins, a combination of clindamycin (600 mg) and gentamycin (80–120 mg) intramuscularly, drip-feed intravenously is recommended.

Also, current clinical guidelines substantiate the rationality of antibacterial agent administration 30–60 minutes preoperative, and the irrelevance of continuing prophylactic antibacterial agent administration for more than 24 hours postoperative is justified by the fact that this does not increase the efficiency [14].

In our study, in the time period 2, cefazoline (1 g) was prescribed preoperative, corresponding to the clinical guidelines' recommendations, but ceftriaxone prescription in the postoperative period in 32% of the cases remains a common unsolved problem; in two cases, it was prescribed in combination with fluoroquinolones and metronidazole due to the risk of chronic endometritis exacerbation [16]. In the time period 2, inhibitor-protected aminopenicillins were not prescribed for prophylaxis preoperative. In the time period 1, they were prescribed more often, both during and after the surgery.

The United Kingdom National Institute for Health and Care Excellence reported in 2016 that the drug of choice is intravenous cefuroxime in a single dose of 750 mg, which is used for prophylaxis in both elective and emergency CS. A repeated dose is sometimes prescribed for patients with risk factors [17, 18].

The American College of Obstetricians and Gynecologists clinical guidelines recommend cefazoline administration at a dose of 1 g 60 minutes preoperative. In the case of allergic reactions to cephalosporins, clindamycin is recommended [19]. Intravenous preoperative administration of antibiotics for prophylaxis in CS reduces significantly the incidence of infectious complications in the postpartum period in the mother as compared to the administration after umbilical cord clamping [2].

No oral antibacterial drugs are recommended for prophylaxis in all international and national guidelines. Also, according to the Cochrane systematic review, oral adjunctive therapy use following clinical improvement in uncomplicated endometritis treated with intravenous therapy has not been shown to be effective [20].

International and global clinical guidelines for antibiotic prophylaxis use in women who underwent CS in relation to infection prevention in the surgical area state that antibiotic prophylaxis should be performed before skin incision, with no additional doses after the surgical incision needed [21].

The National Clinical Guidelines, developed by the Scottish Intercollegiate Network of Guidelines for Antibiotic Prophylaxis in Surgery, recommend using one standard dose of a narrow spectrum antibiotic for infection prevention [22]. Clinical practice guidelines approved by the Executive Committee and Board of the Society of Obstetricians and Gynecologists of Canada recommend using a single dose of the first-generation cephalosporin 15–60 minutes before the skin incision, without additional doses, which is consistent with Russian clinical guidelines and current antibiotic prescribing practice [23].

National and international guidelines recommend using a single dose of antibiotic to prevent infections. Cephalosporin antibiotics are preferred. However, according to the Cochrane review, inhibitor-protected aminopenicillins are in no way inferior in efficiency [24].

In the study's time period 2, the administration of inhibitor-protected aminopenicillins was registered only in two cases. Over the years, antibiotics of the cephalosporin group have become the most often prescribed and have almost completely displaced inhibitor-protected aminopenicillins from practice.

A large prospective study was conducted in Switzerland, where the scientists evaluated the effect of antibiotic administration preoperative and after clamping the umbilical cord on the risk of developing an infectious complication in the surgical incision area. The authors concluded that antibiotic administration preoperative and after umbilical cord clamping is associated with the same risk of infectious complications [25].

Authors from India evaluated the efficacy of intravenous cefazoline in combination with placebo and cefazoline in combination with azithromycin preoperative for CS. They concluded that the cefazoline administration with azithromycin is much more effective and helps to reduce costs [26].

Our study presents the practice of prescribing antibacterial agents in two time periods with a 10-year interval. The differences in the time of dose 1 administration, the duration of antibacterial agent administration, and the range of antibiotics used in these two periods were revealed. In the period 1, the antibiotic dose 1 was administered in 110 (44%) and 139 (51%) cases with elective and emergency CS during surgery after umbilical cord clamping. In about half of the cases, the dose 1 was administered after CS in 139 (56%) and 135 (49%) cases with elective and emergency CS.

In the period 2, antibiotics were predominantly administered preoperative in 263 (96%) and 218 (95%) cases with elective and emergency CS. Moreover, due to the fact that antibiotics were administered preoperatively (single injection), with emergency and elective CS in 103 (44%) and with 150 (55%) cases, there was a decrease in the antibiotic prescription in the postoperative period by 45% ($p < 0.05$).

The results of our study can contribute to the revision of the Russian clinical guidelines.

CONCLUSIONS

The use of antibiotics in the 10-year range varied in the following aspects.

1. The time of administration of the dose 1 of antibiotic. In the time period 1, the drug was administered mainly during and after the surgery. In the time period 2, it was administered preoperative.

2. The duration of antibiotic use. In the study's time period 1, antibiotics were administered predominantly for more than 5–6 days. In the time period 2, they were administered only on day 1.

3. The range of antibiotics used. In the time period 1 of the study, antibiotics of different groups were administered, while in the time period 2, mainly antibiotics of the cephalosporin series were used.

4. The difference in the total antibacterial load in the two time periods was 0.9 of the DDD.

5. Over a 10-year period, antibiotics of the cephalosporin series have almost completely replaced inhibitor-protected aminopenicillins from practice. The excessive use of the third generation cephalosporin ceftriaxone remains a common unsolved problem.

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