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TO STUDY THE EFFECT OF ANTIBACTERIAL DRUGS ON THE INTESTINAL MICROFLORA OF NEWBORNS BORN BY CAESAREAN SECTION (USING THE EXAMPLE OF THE SAMARKAND REGION)

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✓ ***Resume***

This article is devoted to the study of the effect of antibacterial drugs on intestinal microbiocenosis in newborns during lactation. The article analyzes the causes and consequences of intestinal microflora disorders as a result of the administration of antibacterial drugs to a mother and a child born by caesarean section at an early age, methods for restoring intestinal microbiocenosis. Factors that cause disorders of intestinal microbiocenosis from the first days of birth in children after cesarean section surgery increase the risk of developing acute infectious intestinal infections in the future. Cesarean section surgery leads to a violation of intestinal microbiocenosis in infancy, when antibacterial drugs are prescribed not only to women, but also to newborns. The administration of antibacterial drugs in the first days of a child's life and a violation of intestinal microbiocenosis is the cause of various infectious diseases in young children.

Keywords: cesarean section, indications, antibiotics, intestinal microflora, acute intestinal infections

ИЗУЧЕНИЕ ВЛИЯНИЯ АНТИБАКТЕРИАЛЬНЫХ ПРЕПАРАТОВ НА МИКРОФЛОРУ КИШЕЧНИКА НОВОРОЖДЁННЫХ, РОДИВШИХСЯ ПУТЁМ КЕСАРЕВА СЕЧЕНИЯ (НА ПРИМЕРЕ САМАРКАНДСКОЙ ОБЛАСТИ)

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✓ ***Резюме***

Данная статья посвящена изучению влияния антибактериальных препаратов на микробиоценоз кишечника у новорожденных в период лактации. В статье анализируются причины и последствия нарушения микрофлоры кишечника в результате назначения антибактериальных препаратов матери и ребенку в раннем возрасте, рожденным путем кесарева сечения, методы восстановления микробиоценоза кишечника. Факторы, вызывающие нарушения микробиоценоза кишечника с первых дней рождения у детей после операции кесарева сечения, повышают риск развития острых инфекционных кишечных инфекций в дальнейшем. Операция кесарева сечения приводит к нарушению микробиоценоза кишечника в грудном возрасте, когда антибактериальные препараты назначают не только женщинам, но и новорожденным. Назначение антибактериальных препаратов в первые дни жизни ребенка и нарушение микробиоценоза кишечника является причиной различных инфекционных заболеваний у детей раннего возраста.

Ключевые слова: операция кесарево сечение, показания, антибиотики, микрофлора кишечника, острые кишечные инфекции

КЕСАР КЕСИШ ЙЎЛИ БИЛАН ТУҒИЛГАН БОЛАЛАРНИНГ ИЧАК МИКРОБИОЦЕНИЗИГА АНТИБАКТЕРИАЛ ПРЕПАРАТЛАРНИНГ ТАЪСИРИНИ ЎРГАНИШ (САМАРҚАНД ВИЛОЯТИ МИСОЛИДА)

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✓ ***Резюме***

Ушбу мақола антибактериал дориларнинг лактация даврида янги туғилган чақалоқларда ичак микробиоценозига таъсирини ўрганишга бағишланган. Мақолада эрта ёшдаги болаларда кесар кесиш йўли билан туғилган она ва болага антибактериал препаратларни қўллаш натижасида ичак микрофлораси бузилиши сабаблари ва оқибатлари, ичак микробиоценозини тиклаш усуллари таҳлил қилинади. Кесар кесиш операциясидан кейин болаларда туғилишининг биринчи кунларидан бошлаб ичак микробиоценозининг бузилишига олиб келадиган омиллар келажакда ўткир юқумли ичак инфекциялари ривожланиш хавфини оширади. Кесар кесиш операциясидан сўнг антибактериал препаратлар нафақат аёлларга, балки янги туғилган чақалоқларга ҳам буюрилади. Бу ҳолат чақалоқлик даврида ичак микробиоценозининг бузилишига олиб келади. Эрта болалик даврида ичак микробиоценозининг бузилиши ёш болаларда турли юқумли касалликларнинг ривожланишига олиб келади.

Калит сўзлар: кесар кесиш, кўрсатмалар, антибактериал препаратлар, ичак микробиоценози, ўткир ичак инфекциялари

Introduction

In recent years, there has been a tendency to increase the indications for cesarean section surgery to prevent maternal and perinatal mortality [1,3,5]. The growth of extra-genital and genital pathologies among women, increase in the number of unwanted pregnancies, increase in the level of sexually transmitted diseases determine the relevance of this problem. The number of both planned cesarean sections and unplanned ("emergency") operations has increased. In this regard, the World Health Organization published a statement on the incidence of caesarean sections in 2015 [3,4], in which they called for further research to better understand the health consequences of caesarean sections, including long-term manifestations in children. At the same time, the incidence of surgical delivery continues to increase in both developed and developing countries due to many reasons: expansion of indications for cesarean section for the benefit of the fetus, performance of cesarean section for the slightest deviation from the normal course of labor. In addition, cesarean sections have become optional. Thus, no significant decrease in the frequency of this operation should be expected in the coming years [6,7,13].

The global increase in the number of caesarean sections, especially in developed countries, remains a subject of debate in the medical community. Not only are the reasons for the increasing frequency of abdominal delivery discussed, but also its consequences for the health of mother and child. Undoubtedly, cesarean section is a life-saving operation in case of certain complications during pregnancy and labor. According to statistics, in the following years there has been a sharp increase in the number of people born by caesarean section operation, both in foreign countries and in Uzbekistan. Analysis of cesarean section operations for 2018-2020 in districts and cities in Samarkand region showed that this indicator increased from 20% to 100%. It is known from the literature that in children born after cesarean section operation, the formation of intestinal microflora continues for a long time compared to children born normally. The occurrence of primary microbial colonization of the organism of a child who is sterile

before birth is associated with the ingestion of the microflora of the skin and vagina of the mother by the natural birth canal during delivery [11,13].

Children born by caesarean section are affected by a variety of physical, hormonal, bacterial and medical influences in the intrapartum and early postnatal period. They are often exposed to antibacterial drugs both before and after birth [3,9,10].

The development of diarrhea caused by side effects of antibiotics in early childhood is associated with the content of intestinal microflora in children [6,12]. The incidence of antibiotic-induced diarrhea, according to different authors, ranges from 5 to 39%, reaching up to 62% in some observations [4, 7,12]. Disturbances of intestinal microflora during this period are often caused by such drugs as clindamycin, lincomycin, aminopenicillin, cephalosporins, tetracycline, erythromycin [2,3]. According to some authors, when using cephalosporins, antibiotic-induced diarrhea is observed in 3-9% of cases, amoxicillin/clavulanate - 23%, other broad-spectrum penicillins - 11%, erythromycin - 16%, when prescribing other macrolides - 8% of cases [4,8,9,12].

Thus, from the first days in children born after cesarean section operation, the risk of purulent-inflammatory diseases in the postpartum period will also be higher, because the risk of microbial colonization is higher. The normal intestinal microbiocenosis or normal autoflora consists of a complex combination of microorganisms that influence each other's vital activity and are in constant contact with the body. This balance of different microbial populations that maintain biochemical, metabolic, and immunologic balance is necessary to maintain health [6,12].

It is known from the literature that observation and preparation of bermen for labor, psychoprophylaxis, demonstration of useful aspects of natural childbirth lead to an increase in the number of physiological births [3,9,10]. An important aspect of cesarean section operation is its planned preparation. Taking this into account, we set a goal to analyze the indications of those who underwent cesarean section operation in Samarkand region, and also, the postoperative effect of antibacterial drugs on intestinal microflora in newborns was studied.

Purpose of the study: to analyze the indications for caesarean section operation and antibacterial drugs used after the operation in women and their impact on intestinal microflora in newborns in Samarkand region.

Materials and methods

Case history reports of 40 women who underwent cesarean section in Samarkand region were taken as material for the study. Also in Samarkand city maternity complex No. 1 during 2021, the protocols of case histories of 40 infants born by cesarean section were obtained. The materials for the study were blood, urine, feces. General blood, urine, feces, and bacteriologic methods were performed as research methods. The results were analyzed retrospectively.

Results and discussion

Based on the results of the analysis of indications for surgical intervention in women who underwent cesarean section and the impact of antibacterial drugs used after surgery on the intestinal microflora of newborns in Samarkand region. In addition, a comparative analysis of the intestinal microbiocenosis in children born after cesarean section surgery was carried out in relation to physiologic labor (control group).

When we analyzed the indications for surgical intervention among pregnant women who underwent surgery, it was found that the main reasons were uterine scar, maternal pelvis not matching the weight of the fetus, prolongation of the anhydrous period longer than 24 hours, and induction of labor.

Among the women who underwent cesarean section, 4.3% took antibacterial drugs in the form of tablets and 95.7% of women received antibacterial drugs in the form of injections (Figure 1). The anamnesis revealed that women who gave birth by cesarean section received antibiotics almost immediately after the operation.

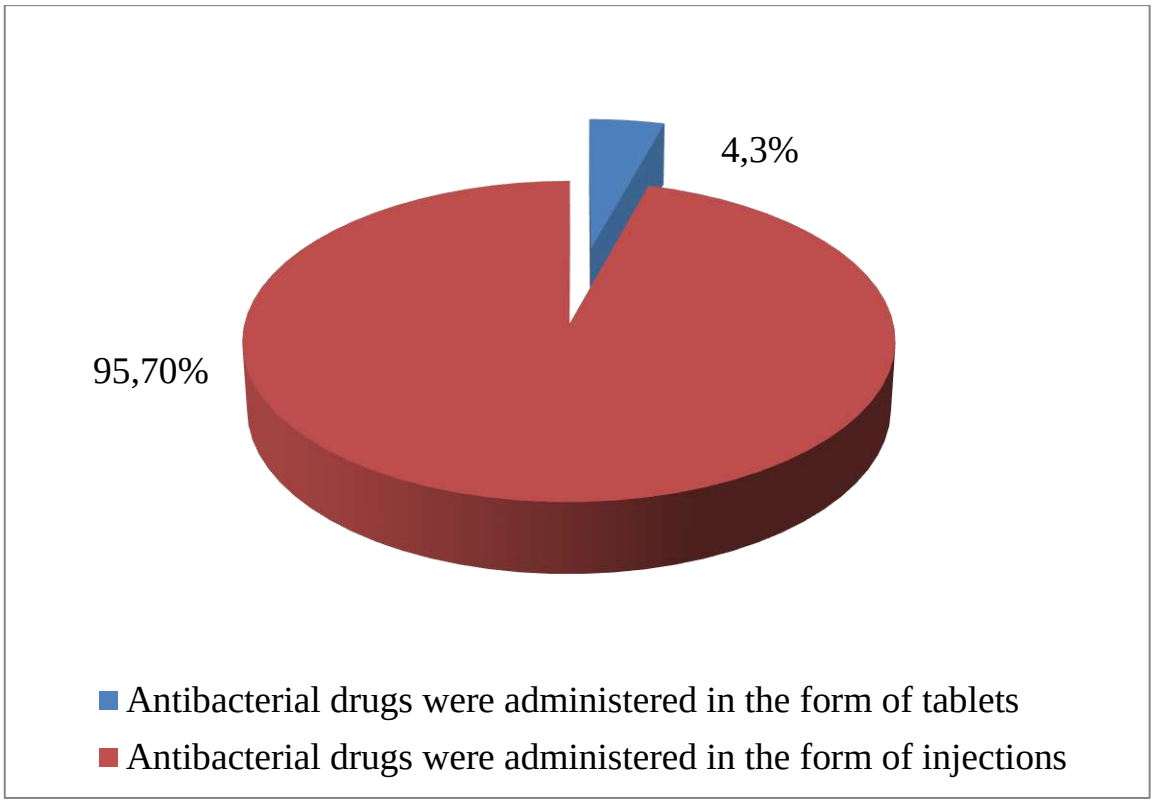

Figure 1. Types of antibacterial drugs prescribed to women after cesarean section

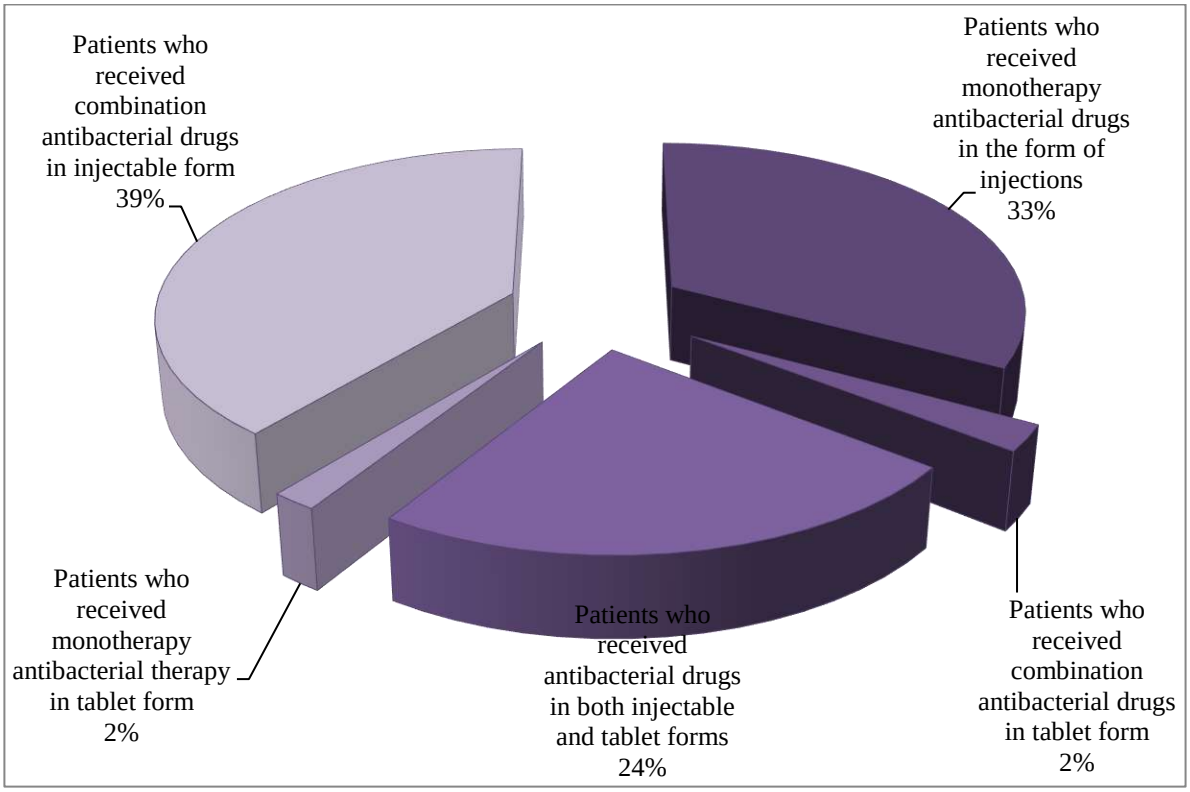

Figure 2. Distribution of combinations of antibacterial drugs in women who underwent cesarean section

Table 1

Types of antibacterial drugs and their frequency of use in women after cesarean section

№	Group and name of antibacterial medications		2018 y	2019 y	2020 y	2021 y
1.	**Cephalosporin group**	Cefazolin	18%	9,20%	2,30%	2,50%
		Ceftriaxone, cefotaxime, ceftazidime	12,20%	11,50%	4,60%	4,10%
		Ceftriaxone-sulbactam, Cefoperazone-sulbactam	6,20%	6,60%	10,70%	11,30%
		Cefepime, cefepime-sulbactam	2,20%	3,80%	9,50%	11,70%
2.	**Fluoroquinolone group**	Ciprofloxacin	4,40%	5,70%	4,80%	3,90%
		Ofloxacin	2,50%	3,80%	3,50%	4,80%
		Norfloxacin	1,10%	2,30%	2,40%	3,80%
		Levofloxacin	0,30%	2,40%	5,58%	6,50%
		Gatifloxacin	-	-	0,58%	1,10%
		Moxifloxacin	-	-	0,13%	1,20%
3.	**Macrolide group**	Azithromycin	5,50%	5,90%	7,1%	4,50%
		Erythromycin	3,40%	2,30%	1,10%	1,58%
		Clarithromycin	2,20%	3,70%	2,59%	3,80%
		Roxithromycin	2,40%	3,25%	6,29%	6,70%
4.	**Penicillin group and combination of penicillin-containing antibiotics**	Penicillin	2,20%	2,30%	0,58%	-
		Ampicillin	3,20%	2,30%	0,58%	-
		Amoxicillin	1,58%	2,30%	0,58%	0,20%
		Amoxiclav	1,20%	2,30%	3,58%	1,67%
5.	**Glycopeptide group**	Vancomycin	-	-	1,58%	1,20%
6.	**Aminoglycoside group**	Streptomycin	-	-	0,58%	-
		Gentamicin	3,50%	3,30%	1,20%	1,10%
		Tobramycin	-	-	0,45%	-
		Amikacin	7,50%	8,60%	6,80%	7,70%
7.	**Nitroimidazole group**	Metronidazole	9,50%	7,60%	2,5%	1,30%
8.	**Sulfonamide and trimethoprim group**	Biseptol (injection)	4,60%	3,58%	2,68%	1,56%
9.	**Tetracycline group antibiotics**	Doxycycline	-	-	1,46%	1,10%
		Unidox solutab	-	-	1,36%	1,58%
10.	**Carbapenem group**	Imipenem and cilastatin	-	-	1,37%	2,30%
		Meropenem	-	-	3,20%	4,30%
11.	**Combination antibacterial drugs**	Levofloxacin and ornidazole	-	0,68%	1,10%	2,30%
		Ciprofloxacin and ornidazole	0,78%	0,88%	0,98%	-
		Ofloxacin and ornidazole	0,30%	0,58%	1,68%	-
		Ciprofloxacin and tinidazole	-	-	0,25%	-
12.	**Nitrofuran group**	5 -NOK	1,10%	2,30%	3,30%	1,50%
		Furadonin	1,60%	1,80%	1,90%	2,30%
		Furamag	2,38%	1,10%	1,20%	2,50%
			100,0%	100,0%	100,0%	100,0%

Upon analyzing the distribution of methods and combinations of antibacterial drug administration to women who underwent cesarean section, the following was identified (Figure 4):

- Women who received monotherapy antibacterial drugs in tablet form: 1.8%;
- Women who received multiple antibacterial drugs in tablet form: 2.5%;
- Women who received antibacterial drugs in both injectable and tablet forms: 23.7%;
- Women who received antibacterial drugs in injectable form: 32.9%;
- Women who received multiple antibacterial drugs in injectable form: 39.1% .

Analysis revealed that 62.8% of women who underwent cesarean section received multiple antibacterial drugs in a combination form thereafter. The types of antibacterial drugs used after cesarean section and their frequency of use are presented in Table 1.

As can be seen from the table 1, the frequency of use of the latest generation cephalosporins, carbapenems, and fluoroquinalone groups has increased in recent years. Treatment with antibacterial drugs in the observed women averaged 7-12 days. In the course of the study, children born with cesarean section operation were also taken under observation, and they were divided into 2 groups:

The first group was the main group (20 infants born after cesarean section) and they were recommended probiotics, 20 infants from the control group were not prescribed probiotics.

In order to determine the causes of disturbance of the normal process of biocenosis formation in children of both groups, the diet of the women who gave birth, the peculiarities of lactation development, and the peculiarities of antibacterial drugs and groups of medications were also studied. Since the majority of children in the main and control groups reported cases of hypogalactia after cesarean section, 76.5% of children were switched to artificial feeding during the first week. The children were put to the mother's breast much later, by the end of the second day or at the beginning of the third day.

To analyze the impact of antibacterial agents on the intestinal microbiota of newborns in both groups, fecal samples were taken for bacteriological culture. The following was revealed during the study: in the main group, children exhibited a lack of stool formation after meconium passage. Among children in this group, liquid green stools were consistently observed (67.8%). In the control group, stool formation after meconium passage was noted, but no frothy discharge was detected.

These results may indicate the potential impact of antibacterial agents on the formation of intestinal microbiota in newborns, necessitating further investigation and assessment of potential consequences for children's health.

When analyzing the daily stool count in children of the main group it became known: during the day the frequency of stool up to 5-6 times was determined in 52.1% of cases, up to 7-10 times - in 31.5%, more than 10 times - in 16.4% of cases. Also in children of this group there were cases of periodic intestinal colic (78.9%), allergic diathesis (34.5%). When analyzing the frequency of feces in children of the control group were as follows: up to 2-3 times in 52.1%, 3-5 times in 41.5%, more than 5 times in 6.4%. Body weight was measured in children of both groups for 5-7 days. Physiologic weight loss in children in the main group of children amounted to more than 10%, and the recovery process was observed relatively late. This condition may be aggravated by the action of antibacterial drugs. In children of the control group the weight loss index was 7-8%.

It was found out from the analyses that bacteriologic sowing in children from the main group revealed relatively less Clostridium spp. and Candida albicans. Antibacterial drugs used after cesarean section operation, to a greater or lesser extent, caused the development of conditionally pathogenic flora, as well as disruption of intestinal microflora.

Conclusions

Taking antibacterial drugs by the mother from the first days leads to predisposition to disorders of intestinal microbiocenosis and acute infectious intestinal infections in children born after cesarean section. Selective use of antibacterial drugs in early infancy and the recommendation of probiotics, which help prevent gut microbiocenosis disorders, may help prevent various infectious diseases occurring in young children.

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