DEPENDENCE OF THE DEVELOPMENT OF HISTOLOGICAL CHANGES IN THE TISSUES OF THE FALLOPIAN TUBES IN ADOLESCENT GIRLS AND YOUNG WOMEN WITH INFLAMMATORY GENITAL DISEASE ON THE TAXONOMIC AFFILIATION OF PATHOGENS

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Summary

The aim. To conduct a comparative analysis of the fallopian tubes’ clinical, microbiological and histological characteristics in adolescent girls and young women with inflammatory genital disease.

Materials and methods. The etiological diagnosis of inflammatory disease was established with the help of complex microbiological and cytological studies of biomaterial from the vagina of teenage girls and the cervical canal of young women before hospitalization and histological examination fragments of fallopian tube – after surgery. The microbiological examination included the cultural detection of bacteria of various taxonomic groups, fungi, mycoplasmas, and ureaplasmas from the biomaterial. A set of methods described in the article was used to detect chlamydia [13]. The degree of bacterial infection of the fallopian tube fragments was assessed by determining the microbial count. Histological examination of biopsy specimens of fallopian tube tissues removed during surgery was performed by the conventional method [9].

Results. In the examination of 29 adolescent girls and young women hospitalized for surgical treatment, a comparative analysis was conducted between the clinical manifestations of inflammatory genital disease, identifiable factors, and histological signs of damaged fallopian tubes. When studying the spectrum of factors in the inflammatory focus (fallopian tube biopsies) in adolescent girls (n=12), enterobacteria (33.3 %), staphylococci (33.3 %), streptococci (8.35 %), and Pseudomonas aeruginosa (8.35 %) were detected; in 16.7 % of adolescent girls, the cultures were sterile. In young women (n=17), microbiological examination of fallopian tube tissues revealed chlamydia (29.4 %), mycoplasma (11.6 %), ureaplasma (5.8 %), gonococci (5.8 %), enterobacteria (5.8 %), fungi (5.8 %); in 6 (35.8 %) of the examined women, no bacterial growth was detected. Among young women who had been operated on for tubo-ovarian inflammatory diseases and ectopic pregnancy, chlamydia were most often (29.4 %) found in the tissues of the fallopian tubes.

Conclusions. The studies have shown that in the development of acute purulent salpingitis in young women, sclerotic changes and signs characteristic of the productive process prevailed in the tissues of the fallopian tubes against the background of genital inflammation, and in adolescent girls, an exudative process was observed against the background of genital inflammation. The peculiarities of the course of genital inflammation depend on the biological properties of pathogens of different taxonomic affiliations.

Key words: infectious pathogens, fallopian tubes, adolescent girls, young women
INTRODUCTION

In the current context, there has been an increase in the frequency of inflammatory genital diseases with high risks of reproductive function disorders, the possibility of affecting the intrauterine fetus, and threats to human health in general [4]. This is associated with the widespread prevalence of this pathology, latent, subclinical forms of the disease course, certain difficulties in clinical and laboratory diagnostics, and the insufficient effectiveness of drug treatment [7].

At the center of attention are adolescent girls, whose reproductive health preservation determines the prospects of future generations. According to the WHO classification, the term «adolescents» encompasses girls aged 10 to 19 years, and the definition of «young women» refers to adolescent girls who begin their sexual life before the age of 19 [1].

The liberalization of sexual relations among adolescent girls, in the context of low sexual culture, has become the main reason for the «silent epidemic» of genital inflammatory diseases, which occur at a rate 2-3 times higher among young girls than among patients aged 25 to 29 [2, 10]. Among sexually inexperienced adolescent girls, genital inflammatory diseases can also develop from menarche as a result of the influence of exo- and endogenous factors on a predisposing background [12].

With the onset of sexual life, among the etiological factors of genital inflammatory diseases, chlamydia, mycoplasmas, Escherichia coli, streptococci, staphylococci, enterococci, and L-forms of bacteria play a leading role, contributing to the formation of anatomical and functional changes in the fallopian tubes [8].

For the first time, Palmer, Mintz, and histologist De Bruk [3, 5] described the histological characteristics of the uterus and fallopian tubes depending on the damage caused by sexually transmitted infections in women of reproductive age, thereby refuting the «myth» about the development of genital inflammatory disease on a provoked premorbid background [6, 14].

However, the lack of data on comparing the microbiological and histological characteristics of the fallopian tubes in inflammatory genital disease in adolescent girls and young women is a factor in conducting inadequate treatment [11].

THE AIM OF THE STUDY

To conduct a comparative analysis of the clinical, microbiological, and histological characteristics of the fallopian tubes in adolescent girls and young women in the context of developing the inflammatory genital disease.

MATERIALS AND METHODS

An examination of 29 adolescent girls and young women, aged 15 to 18 years, urgently hospitalized in the gynecological department for surgical treatment due to complications of inflammatory pelvic disease was conducted. A retrospective analysis of the obtained data was performed. Surgical treatment was performed in 9 (31.3 %) adolescent girls due to acute appendicitis complicated by acute pelvic peritonitis and the development of tubo-ovarian formations, and in 5 (10.3 %) cases due to unilateral hemato- and hydrosalpinx. In 11 (37.9 %) young women, inflammatory pelvic disease with bilateral hydrosalpinx and pyosalpinx was detected, complicated by acute pelvic peritonitis, and in 6 (20.6 %) cases, ectopic pregnancy was observed.

The etiological diagnosis of inflammatory pelvic disease was established using a comprehensive microbiological and cytological examination of biomaterial from the vagina and cervical canal of adolescent girls and young women before hospitalization, and fragments of the fallopian tubes were examined after surgery.

Microbiological testing included the cultural detection of bacteria from various taxonomic groups, fungi, mycoplasmas, and ureaplasmas in biomaterial. To detect chlamydia, a complex of methods was applied: immunofluorescence reaction, DNA diagnostics in PCR, cytoscopic smear staining according to Romanovsky-Giemsa [13]. The degree of bacterial infection of the fallopian tube fragments was assessed by determining the microbial count.

Histological examination of the biopsy specimens of fallopian tube tissues removed during surgical intervention was conducted using the commonly accepted method with staining of preparations by hematoxylin-eosin according to Van Gieson and picronfuchsin, as well as by the Hodge-McManus method using Schiff’s iodine acid [9].

RESULTS

In the etiological spectrum of factors isolated from the vagina in adolescent girls, representatives of conditionally pathogenic flora predominated (Enterobacter sp. – 25.0 %, Pseudomonas aeruginosa – 8.3 %, Staphylococcus sp. – 16.75 %, Streptococcus sp. – 16.75 %, Proteus vulgaris – 8.3 % in monocolture, and St. haemolyticus in association with St. aureus – 8.3 %, Klebsiella pneumoniae in association with E. coli – 8.3 %, Enterococcus sp. in association with Proteus vulgaris – 12.5 %), which were determined with critical (from 1 x 104 to 9 x 104 CFU/ml) and high (not less than 1 x 105 CFU/ml) microbial counts.

In young women, biomaterial from the cervical canal was dominated by sexually transmitted factors, which were found both in monocolture and in microbial associations (C.trachomatis in 5.8 % in monocolture and 23.6 % in association; M.hominis in 11.6 % in monocolture
Inflammatory genital disease resulting in tubo-ovarian complications was observed in the right adnexa in the form of tubo-ovarian inflammatory formations. The purulent-necrotic process was characterized by its limitation and was represented by a conglomerate of connected fallopian tube and ovary with purulent content.

The inflammatory process involving the organs of the pelvis that are anatomically adjacent to the appendix and respond to its changes has been considered by us as secondary.

In 3 of the examined adolescent girls, the fallopian tubes were surgically removed and were characterized by the following anatomical changes: in 2 cases, these were hydrosalpinx due to the twisting of the tube and cystic changes in the ovary, and in one case, it was hematosalpinx as a result of the direct twisting of the fallopian tube. Inflammatory changes in the fallopian tubes, resulting from the disruption of the local organ (fallopian tube) hemodynamics, were accompanied by the development of stasis, swelling, and the exudation of fluid into the tube’s lumen.

In young women who underwent surgery due to inflammatory genital disease resulting in tubo-ovarian formations (11 patients), the fallopian tubes on both sides were significantly dilated in diameter, ranging from 2 to 6 centimeters, mainly in the distal part. The tube’s wall was hyperemic and swollen. In eight cases, the fimbrial end of the tube was adhesively sealed. Thick adhesions were visualized between the uterine appendages, intestinal loops, omentum, and the posterior leaf of the broad ligament. Fluid was found in the tube’s lumen, ranging from turbid and thin to viscous and cream-like (pus). In nine young women with altered fallopian tubes, they were intimately connected to the ovary, where single or multiple cavities with purulent contents were identified. Accumulation of fluid was observed in the Douglas space, with pus – in 7 cases, serosanguinous fluid in 3 cases, and clear yellowish fluid in 1 case.

In 6 young women, surgical treatment was performed due to a ruptured tubal pregnancy. The fallopian tubes in these patients were hyperemic and dense with numerous cysts, mainly located closer to the fimbrial end. These signs indicate a prolonged latent course of inflammatory genital disease with pronounced anatomical changes in the fallopian tubes.

The microbiological and histological examination of damaged fallopian tube tissues in adolescent girls and young women was conducted. The results of the microbiological studies are presented in Figure 1.

According to the data presented in Figure 1, in the microbiological examination of tissues from damaged fallopian tubes in adolescent girls, conditionally pathogenic microorganisms (Enterobacter spp. – 33.3 %, Staphylococcus spp. – 33.3 %, Streptococcus spp. – 8.35 %, Pseudomonas aeruginosa – 8.35 %) were detected with a high microbial count (not less than 1 x 10⁵ CFU/ml).

When comparing the results of the microbiological examination of vaginal biomaterial before surgery with the data obtained during surgical intervention when studying fragments of fallopian tubes in adolescent girls, a match in the spectrum of isolated microbial cultures was observed only in 1 case (8.35 %) – Enterobacter spp. with a high microbial count.

The conducted research indicates that in adolescent girls, inflammatory changes in the fallopian tubes were unilateral and formed as a result of inflammatory diseases of adjacent organs, provided that the blood supply to the tube was disrupted (during acute appendicitis; torsion of the fallopian tube). It should be assumed that the overlay of microbial factors and their involvement in the development of pathological changes in the focus of damage (fallopian tubes) in non-pregnant adolescent girls was secondary.

In young women, microbial factors transmitted through sexual contact were detected in 52.2 % of fallopian tube tissue samples: C.trachomatis in 5 (29.4 %), N.gonorrhoeae in 1 (5.8 %), M.hominis in 2 (11.6 %), and U.urealyticum in 1 (5.8 %). Additionally, Enterobacter spp. was found in 1 (5.8 %) sample, and Actinomyces israelii in 1 (5.8 %) sample. Bacteria were not isolated in 6 (35.8 %) of the examined fallopian tube tissue samples during microbiological analysis.
The analysis of microbiological studies from the focus of damage (fallopian tubes) in 17 young women showed a match in results with 8 (47.0 %) patients compared to the microbiological data obtained during examination before surgery. Simultaneously, C. trachomatis, M. hominis, and U. urealyticum were found in biomaterial from the cervical canal and directly in fallopian tube biopsies. The data obtained indicate the causal role of these microorganisms in the formation of inflammatory changes in the pelvic organs and their involvement in the development of pathological changes in the reproductive system organs. C. trachomatis was most frequently detected (in 29.4 %), and it was isolated in 2 (11.6 %) cases of ectopic pregnancy and in 3 (17.4 %) young women with tubo-ovarian inflammatory disease in the damaged fallopian tube tissues. The data suggest the primary role of sexually transmitted agents in fallopian tube damage among young women.

DISCUSSION

Microbiological studies of biological material obtained directly from the focus of the inflammatory process confirmed the role of microorganisms in the development of inflammatory changes in the pelvic organs in both adolescent girls and young women. The final conclusion regarding the nature of fallopian tube damage by conditionally pathogenic bacteria, as well as chlamydia, mycoplasmas, ureaplasmas, and gonococci, in comparison with the course of the clinical process, allowed for an assessment of the pathogenic activity of the inflammation factors and the determination of their impact on the histological structure of the tube.

In the development of secondary inflammation in the fallopian tube on the background of gangrenous-perforated appendicitis complicated by acute pelvic peritonitis in adolescent girls, purulent inflammation of the tube with signs of exudative processes was identified. Microscopically, a diffuse leukocytic infiltration of the stroma was observed in the submucosal layer against the background of disrupted internal organ blood circulation. Inflammatory changes were also found in the muscular layer of the tube and were accompanied by disruptions in internal organ blood circulation due to the expansion and hemorrhage of intermuscular vessels, along with pronounced leukocytic infiltration. The fimbriae of the fallopian tube exhibited necrotic changes and deformation (Figure 2).

In 17 young women, the fallopian tubes were macroscopically dilated with diameters ranging from 2 to 4 cm, and in 8 of them, they were adhesively fused in the distal segment, surrounded by flat adhesions with pronounced vascular patterns that extended to the ovaries and pelvic walls. In young women with chlamydial etiology tubo-ovarian inflammation (out of 3 examined), pseudobulbous eruptions on the parietal peritoneum and the accumulation of gelatinous yellow fluid in the Douglas pouch were visualized.
In the examination of the fallopian tubes damaged by C. trachomatis in young women who underwent surgery for ectopic pregnancy, profound changes in the organ’s stroma occurred 6-12 months after the onset of infection (coinciding with sexual debut). These changes were characterized by structural alterations in the histoarchitecture of the tube, with a predominance of sclerotic changes in the submucosal and mucosal layers, gradual disappearance of cilia, fibrotic destruction of the organ, which, in our opinion, became the cause of functional inadequacy of the fallopian tubes (Figure 3). These described changes should be characterized as irreversible.

In the microbiological examination of the tissues of the fallopian tubes in 3 (17.4 %) young women, M. hominis and U. urealyticum were isolated. Microscopically, destructive changes in the cilia of the fallopian tubes were noted, along with disruptions in the intraorgan blood circulation due to the dilatation and increased blood filling of vessels, as well as hemorrhages within the vessels themselves and in the intermuscular and interstitial layers (Figure 4).

Among 6 young women who underwent surgery for tubo-ovarian inflammatory formations, microbial agents were not detected in the bacteriological examination of the fallopian tube tissues. During the surgical intervention, it was found that under these conditions, the fallopian tubes were dilated with diameters ranging from 2 to 6 cm, with thin walls and filled with viscous and turbid content. The mucosal lining of the tube was atrophic. Histologically, the following findings were prominent in the tube wall: atrophy of the cilia of the fallopian tubes, dystrophic changes in the muscular layer of the tube, and local proliferation of ciliated epithelium. The serous membrane of the tube was thickened due to edema.
The described changes indicate significant anatomical and functional disruptions in the histoarchitecture of the tube under the influence of microbial factors. Over time, especially after the administration of prolonged, often empirically unjustified antibiotic therapy, these changes may disappear and may not be detectable in the cervical canal or directly at the site of injury. In these patients, L-forms of bacteria were found at the site of injury, which was associated with diagnostic difficulties in detecting infectious agents.

In 2 young women, Enterobacter spp. and E. coli were detected during microbiological examination of the fallopian tubes. In the submucosal layer, there was diffuse leukocytic infiltration against the background of disturbances in intraorgan blood circulation due to significant vessel dilation and proliferation of cellular elements in the mucosal lining. Epithelial cells with signs of dystrophic changes, such as granular and vacuolar degeneration, were predominantly observed.

In a young woman who had multiple sexual partners, histological examination revealed acute purulent salpingitis with pronounced diffuse inflammation infiltrating all layers of the fallopian tube, accompanied by signs of granulomatous inflammation. The infiltrate consisted of polymorphonuclear leukocytes, lymphocytes, plasma cells, fibroblasts, among which large cells with numerous nuclei were found. The surface epithelium over a significant area was desquamated and infiltrated with inflammatory cells. The cilia of the tube were severely deformed and thickened due to the previous inflammatory process. Significant hemorrhages in the submucosal layer were also observed. Microbiological examination of the fallopian tube contents isolated N. gonorrhoeae (Figure 5).
Therefore, the presented data indicate the histological characteristics of tissue damage in the fallopian tubes according to the spectrum of identified inflammatory factors. In adolescent girls, inflammatory changes in the fallopian tubes were unilateral, developed against the background of impaired blood supply, pathology of adjacent organs, colonization by opportunistic flora, and were accompanied by the development of an exudative inflammatory process.

The irreversible destructive histological changes in the fallopian tubes damaged by sexually transmitted pathogens in young women were generalized and characterized by the following spectrum of morphological alterations:

- In cases of chlamydial damage, sclerotic destruction of the fallopian tubes was observed, accompanied by fibrotic deformation of the organ;
- In cases of mycoplasmal and ureaplasmal inflammation, the primary feature was disturbances in intraorgan blood circulation (interstitial hemorrhages), accompanied by lymphoid cell infiltration of the muscular and serous layers of the tube, along with signs of moderate sclerotic destruction of the organ;
- In cases of gonococcal infection, microscopic examination revealed diffuse leukocytic infiltration of all layers of the tube with signs of granulomatous inflammation, which developed against the background of sclerotic changes in the mucosal and muscular layers of the tube;
- In cases of bacterial salpingitis caused by enterobacteria and staphylococci, there was a predominance of local leukocytic infiltration of the organ’s stroma against the background of edema, localized disturbances in hemodynamics with the proliferation of epithelial cells, as well as signs of dystrophic changes, such as granular and vacuolar degeneration;
- In aseptic inflammation, atrophy of the ciliary apparatus was observed, accompanied by hypertrophy of the muscular layer of the fallopian tube.

Thus, the conducted research allowed for the identification of the specific characteristics of fallopian tube damage in adolescent girls and young women based on the etiological factors of inflammation. Despite the young age of the subjects and the relatively short duration of the disease (6-12 months), the development of tubo-ovarian inflammatory processes was accompanied by the formation of irreversible histological changes in the fallopian tubes of young women.

**CONCLUSIONS**

The comparative analysis of clinical, microbiological, and histological characteristics of genital inflammatory disease development in adolescent girls and young women has revealed significant differences, primarily attributed to the etiological factors.

In the histological examination of fragments of the fallopian tubes in adolescent girls, it was determined that genital inflammatory disease caused by opportunistic pathogens was accompanied by an exudative process with subsequent development of tubo-ovarian disease.

The inflammatory process in the genital area of young women induced by sexually transmitted pathogens was generalized and characterized by both disruptions in the histoarchitecture of the fallopian tubes and the development of their anatomical and functional inadequacy, accompanied by corresponding histological changes.

Justification for the principles of early diagnosis and adequate treatment of genital inflammatory diseases in adolescent girls and young women should be conducted with an understanding of the specific spectrum of etiological factors involved in the development of inflammation and considering the peculiarities of the pathomorphosis based on the root causes of the disease. In addition to appropriate antibiotic therapy, treatment for such patients should be supplemented with immunomodulatory agents, interventions aimed at improving blood rheology, restoring the urogenital microbiota, and the use of physiotherapeutic methods.

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**COMPLIANCE WITH ETHICAL REQUIREMENTS**

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Резюме

ЗАЛЕЖНІСТЬ РОЗВИТКУ ГІСТОЛОГІЧНИХ ЗМІН ТКАНИН МАТКОВИХ ТРУБ У ДІВЧАТ-ПІДЛІТКІВ ТА ЮНІХ ЖІНОК ІЗ ЗАПАЛЬНОЮ ХВОРОБОЮ ГЕНІТАЛІЙ ВІД ТАКСОНОМІЧНОЇ НАЛЕЖНОСТІ ЗБУДНИКІВ

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Мета. Провести порівняльний аналіз клініко-мікробіологічної та гістологічної характеристик маткових труб у дівчат-підлітків та юних жінок з умови розвитку запальної хвороби геніталій.

Матеріали та методи. Етіологічний діагноз запальної хвороби встановлювали за допомогою комплексного мікробіологічного та цитологічного дослідження біоматеріалу із вагіни у дівчат-підлітків та цервікального каналу у юних жінок перед госпіталізацією, а гістологічне дослідження фрагментів маткових труб – після операції. Мікробіологічне дослідження включало культуральне виявлення з біоматеріалу бактерій різних таксономічних груп, грибів, мікоплазм, уреаплазм. Для виявлення хламідій застосовували комплекс методів [13]. Оцінку ступеня інфікування бактеріями фрагментів маткових труб проводили за визначенням показників мікробного числа. Гістологічне дослідження біоптатів тканин маткових труб, видалених під час хірургічного втручання, проводили загальноприйнятим методом [9].

Результати. При обстеженні 29 дівчат-підлітків та юних жінок, госпіталізованих на хірургічне лікування, проведено порівняльний аналіз між клінічними проявами захворювання, діагностованими чинниками та гістологічними ознаками ушкоджених маткових труб. При вивченій спектру чинників у вогнищі запалення (біоптатах маткових труб) у дівчат-підлітків (n=12) виявлено представників Enterobacterium spp. (33,3 %), Staphylococcus spp. (33,3 %), Streptococcus spp. (8,35 %), Pseudomonas aeruginosa (8,35 %); у 16,7 % дівчат-підлітків посіви були стерильними. У юних жінок (n=17) при мікробіологічному дослідженні тканин маткових труб було виявлено Chlamydia trachomatis (29,4 %), Mycoplasma hominis (11,6 %), Ureaplasma urealyticum (5,8 %), Gonococcus (5,8 %), Enterobacterium spp. (5,8 %), гриби роду Candida(5,8 %); у 6 (35,8 %) обстежених росту бактерій не встановлено. Серед юних жінок, яких було прооперовано з приводу тубооваріальних запальних захворювань та позаматкової вагітності, найчастіше (29,4 %) в тканинах маткових труб виявляли C. trachomatis.

Висновки. Проведені дослідження показали, що при розвитку гострого гнійного сальпінгіту у юних жінок в тканинах маткових труб на тлі гострого гнійного запалення переважали склеротичні зміни та ознаки, властиві продуктивному процесу, а у дівчат-підлітків – на тлі запалення спостерігався ексудативний процес. Особливості перебігу запального процесу геніталій залежать від біологічних властивостей збудників різної таксономічної належності.

Ключові слова: інфекційні збудники, маткові труби, дівчата-підлітки, юні жінки