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Review / Derleme

Gynecological chlamydial infections in practice

Jinekoloji pratiğinde klamidial enfeksiyonlar

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Abstract

Chlamydia trachomatis is potentially affecting the women health. The disease doesn't have symptoms or progresses at a light level. Therefore, carrier women constitute a reservoir continuously. It may be result in serious pelvic inflammatory disease, pelvic pain, infertility, and ectopic pregnancy in women. But, the processes that result in these pathologies have not been determine. The aim of this paper, microbiologic, pathophysiological and epidemiologic clinics and diagnosis, treatment, prevention methods and control precautions of the genital chlamydia infections will be reviewed and discussed in terms of various aspects for women.

Keywords: Chlamydia trachomatis, women health, genital infection.

Özet

Clamidya trohomatis enfeksiyonu, belirti vermeden yavaş seyrederek, kadın sağlığını büyük oranda etkilemektedir. Bu yüzden taşıyıcı kadınlarda sürekli olarak başkalarına bulaştırma potansiyeli vardir. Enfeksiyon, kadınlarda pelvik inflamatuvar hastalıklara, kasık ağrısına, kısırlığa ve dış gebeliğe sebep olabilir. Bu hastalıkların sekelleri henüz net olarak belirlenememiştir. Bu yazının amacı, adın sağlığı için, clamidya trohomatis etkenini, mikrobiyolojik, patofizyolojik ve epidemiyolojik olarak incelemek ve tanı, tedavi, korunma yöntemleri ve genital klamidya enfeksiyonlara karşı alınması gereken tedbirleri gözden geçirerek, çeşitli yönleriyle tartışmaktır.

Anahtar sözcükler: Klamidya trohomatis, kadın sağlığı, genital enfeksiyon.

Introduction

Chlamydial infection is one of the common diseases that are transmitted sexually (STD) and it is caused by the chlamydia trachomatis. Mostly, the disease doesn't have symptoms

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or progresses at a light level. Therefore, carrier women constitute a reservoir continuously. Diagnosis of the disease is delayed or not noticed most of the time because of symptom non-presence. As a result, it may lead to serious irremediable problems such as infertility in women [1, 2].

Chlamydia trachomatis is the bacterial infection which is most transmitted sexually in the world [3]. Carrier women are potential infection sources for their partners. The disease is generally encountered in women. This infection leads to urethritis in men and cervicitis, urethritis, and endometritis in women [4].

Mucopurulent cervicitis pioneers at least 3 types of complications [4]:

- Increase in the risk of pelvic inflammatory disease (PID),
- Increase in the risk of cervical cancer,
- Early membrane rupture, chorioamnionitis, preterm birth and neonatal infections (neonatal conjunctivitis and pneumonia etc.) as a result of infection during pregnancy.

HIV-infected individuals in STD-prevalence rate was high observed, and the majority of STDs were asymptomatic [5]. Incidence of the chlamydia infections in women increased dramatically from 79 to 467 per each hundred thousand patients from 1987 until 2003 [6].

It is seen that more than 13.5% of the women below the age of twenty five have the lower genital system infection which is in connection with the chlamydia infection. This rate decreased to 4.4% in women at and above 25 [7]. It has been found out that almost 20-30% of the PID cases are connected to the chlamydia infection in the USA [8]. Recent studies in India have revealed that prevalence of the chlamydia infection was 23% in the gynecology policlinic and 19.9% among the sexually transmitted diseases [9]; during the Oncogenic HPV types and cervical neoplasia formation, presence of other infections transmitted sexually in the cases is considered as a risk factor [10]. Chlamydia infections are among those infections and various molecular, biological and seroepidemiological studies have been conducted in recent years regarding that they may play a role as cofactors in cervical cancers [11, 12].

According to the USA National Health and Nutrition Research survey, there are roughly 2.291.000 people carrying diseases in the USA [1, 13]. In a research attended by 695 women between the ages of 15 and 44 in İstanbul/Turkey in 1996, chlamydia was found in 4.89% of the individuals [9]. Prevalence of the chlamydia infection is also high among the sex workers. High incidence of chlamydia trachomatis and lack of regular condom usage among sex workers are revealed in the studies [14].

Microbiologic, pathophysiological and epidemiologic clinics and diagnosis, treatment, prevention methods and control precautions of the genital chlamydia infections will be reviewed in terms of various aspects for women here.

Microbiology

Chlamydia is a small gram-negative obligate intracellular bacterium which can exist in all the spherical or oval places. Intracellular parasitism of the chlamydia differs from the

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other bacteria. Differently from viruses, chlamydia contains both DNA and RNA. They have a cell wall similar to the bacteria. They differ from viruses with their susceptibility to the antibiotics and mitosis. Their metabolic active form called reticular body adds basic small organs and gets penetrated into the cells within 6-8 hours. These forms create great inclusions in the cells. Reticular bodies are then reorganized in the basic small organs and the cell is ruptured within 2-3 days; newly formed basic organs are released. Release of the basic organs initiate the replicative process and this is a form that can infect the new epithelial cells. They have a peptidoglycan cell wall and are sensitive to various antimicrobial agents [15].

Immunopathogenesis

Chlamydia is a strong antigen and leads to cellular and humoral immune response. In addition to the immunogenic antigens, the course of the chlamydia infection depends on the balance and interaction of the cytokines released by the active lymphocytes. When the disease susceptibility enhances together with the increase in the IL 10 secretion, Interferon gamma becomes the most important defense factor in the host against the chlamydia [16].

Changes or deformations in the immune system induced by the chlamydia cause it to survive in the host and lead to recurrent infections. A critical characteristic of the chlamydia organisms is the short term immunity to the infection. As a result, re-infection or persistent infection is common. Chlamydia infections can be in form of primary or chronic recurrence/re-infection.

Risk factors for the chlamydia infection

Demographically, chlamydia infection is encountered below the age of 20 most frequently [17]. The age of the patients is a strong determiner of the chlamydia infection; adolescents and young adults are at the highest risk [18, 19]. This can be explained with the anatomic cervical differences in young women. Here, squamo columnar junction changes structurally; it is the primary settlement place for the chlamydia and it is more exposed to the chlamydia after the change. Because the cervical region isn't ripened fully in women at especially younger ages, the transmission possibility of the disease is higher. The disease can also be carried with homosexual relationships because it can be transmitted anally or orally [1].

The below-stated risk factors have been determined in women for the chlamydia infection [17, 19-23]:

- Adolescents and young adults
- Multi-partner life style
- Irregular use of barrier contraceptives
- Clinical presence of mucopurulent cervicitis
- Cervical ectropy
- Being unmarried
- Previous history of a sexually transmitted disease
- Low socioeconomic level
- Black race

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- Use of oral contraceptive.

Epidemiology

It is predicted that approximately 4 million chlamydia infection cases appear in the United States of America every year [24, 25]. Chlamydia was discovered in 19.9% of the patients who applied to the STD clinic and in 23% who applied to the Gynecology policlinic in the clinical research conducted in New Delhi [26]. Chlamydia was detected in 28.1% of the infertile women. Chlamydia was found in 4% of the asymptomatic women and 30.4% of the symptomatic women who applied to the Gynecology clinics [27]. It is predicted that chlamydia infection existed in between 5% and 12% of the women whose pregnancies are terminated in Europe [28]. Chlamydia screening of the young women has been proved to be a cheap and effective method to prevent the PID. Routine chlamydia screening is suggested for women below the age of 24. But no sufficient evidence has been found for or against the routine screening in asymptomatic men [29].

Diseases caused by the Chlamydia Trachomatis are given below.

- Genital infections
- Conjunctivitis
- Pelvic inflammatory disease (PID)
- Pneumonia in babies
- Urethritis
- Fitz-Hugh-Curtis Syndrome
- Reiter syndrome
- Lymphogranuloma venereum (subclass L1, L2, L3)
- Abortus
- Stillbirth
- Prematurity

Urogenital system infections are formed by D-K subclasses.

According to the research conducted by the World Health Organization, 101 million chlamydia infections are found annually worldwide [3]. It is assumed that the chlamydia infection will be the primary cause of the PID and female infertility. Sequels of the chlamydia infection in women such as PID, infertility and ectopic pregnancy make it the most costly sexually transmitted disease following the HIV or AIDS [18].

Diagnosis

Clinical diagnosis can be misleading because the chlamydia infection is asymptomatic in 70-80% of the women and 50% of the men. Odorless and non-itchy mucoid vaginal secretion is seen in patients who aren't complicated with the chlamydia infection. If the urethra is held, the patient has dysuria complaints. In patients with the development of the PID, severe abdominal pain, disparaneu and menstrual irregularity are observed together with high fever. During the examination, yellow, dense and mucoid cervicitis is observed. Cervix is prone to bleeding during the smear test because it is fragile. In the urine test, leucocyte can be observed above 5 in each area. This reminds us of the diagnosis of urethritis. Urethral infection caused by the chlamydia isn't discriminated from the urethral infections of the other bacteria in terms of clinical findings. The amine

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test can be used to distinguish the chlamydial infections from the other lower genital infections; but its specifity is low [29]. Because the disease is asymptomatic and the infection spectrum enhances increasingly, reliable and sensitive laboratory methods are needed. Collecting and carrying samples are more important than anything else to make the correct diagnosis. Reliability of the diagnosis is directly proportional to the sufficiency of the sample taken. Because the chlamydia is an obligate intracellular pathogen, samples collected from the hosting cell that includes the organism must contain the chlamydia; especially the techniques must be used where the organism is directly seen. Sample areas must be selected from places where pathogen may get settled. Chlamydia is detected by 10-20% further when the cervical and urethral samples are taken together instead of the sample taken only from the cervix [30]. In female patients, chlamydia infection sampling is frequently performed as urethral and rectal swab and first urine sampling in addition to the endocervical swab, vaginal/intraoital swab and vulvar swab [31].

During the laparoscopy, endotubal swab, endometrial aspiration and biopsy from the fimbrial end are reliable methods to use for the diagnosis of the chlamydia [15]. Centers of Disease Control and Prevention (CDCP) strongly suggest the routine screening of the women below 25 who are sexually active and carry a high risk in respect of chlamydia. However, this is not suggested for men. Besides, it is recommended for all the pregnant women in the USA to have the chlamydia test [1, 32].

The following methods are used for the laboratory diagnosis of the chlamydia [33].

- Specific tests:
  - Cell culture
  - Direct fluorescent test
  - Elisa
  - Cytology
- Molecular methods
  - Non-specific tests
  - Leucocyte esterase test
- Rapid test:
- Serology

They cannot be produced in the chlamydia synthetic medium. They reproduce in the ovum yolk-sac with embryo in the best way. Afterwards, Mac Coy and HeLa cell cultures are used for isolation. Traditionally, tissue culture is necessary for the diagnosis, that is, the diagnosis is made with the cell culture in chlamydia infections. There are now quick and cheap screening tests available for chlamydia.

New strains of the chlamydia

Chlamydia variant strain has been isolated in Sweden recently [34]. When these strains are encountered in the tests used for the diagnosis of the chlamydia, it is highly possible to get a wrong result from the test. Symptoms and treatment of these amended strains are not different from the normal chlamydia. Clinicians and microbiologists must be careful with the correctness of the diagnosis when negative results are obtained in doubtful cases and there is a decrease in the positive results which cannot be explained.

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Chlamydia and pelvic inflammatory disease

PID develops in 20% of the women with lower genital system infection connected to the chlamydia and chronic pelvic pain develops in 4% [4, 35]. Clinic spectrum of the chlamydia infections can range from the subclinical endometritis to the salphingitis, tubo-ovarian abscess, pelvic peritonitis and perihepatitis. However, symptomatic chlamydia infections can constitute a part of all the chlamydia infections, because most of its infections are asymptomatic.

Chlamydia and pregnancy

Chlamydia frequency in pregnant women progresses between 2% and 35% [30]. Negative effects on the pregnancy and the post-partum PID risk have increased in women who have chlamydia infection. Sequels like stillbirth, low birth-weight newborn, preterm birth and premature membrane rupture have been reported and post-partum endometritis may develop almost 6 weeks after the birth. Moreover, contamination risk is high during the birth in newborns [17]. Tubal pregnancy was discovered in 9% of the women who had PID in connection with the chlamydia infection [36]. Asymptomatic chlamydial infections may lead to early pregnancy losses or habitual abortus through the immune mechanism [36]. In a study, anti-chlamydial IgG antibodies were indicated in 10% of the healthy women, 50% of women with bad obstetric history and 68% of infertile women [37].

Chlamydia and infertility

PID which develops in connection with the chlamydia is the most significant preventable cause of the infertility. As a result of the infection which emerges in connection with the chlamydia, infertility develops in approximately 3% of the women. Risk related to the tubal factor increases up to 10% after the first attack of the PID. The rate is doubled at every repeating attack. Although most of the patients with the chlamydia infection are asymptomatic, tubal damage is higher in the chlamydia infections compared to the other agents in case of re-infection/chronic infection [38]. During the studies conducted to control the chlamydia, women were encountered by 70-80% and asymptomatic men by up to 50%. Non-diagnosed carriers can transmit the infection to their sexual partners [39]. If the PID is the cause of the infertility, the factor is the chlamydia by 30% [40].

Chlamydia and other infections

Chlamydia infections of the genital tract facilitate the HIV transmission. This has been proved in many studies. Chlamydia increases the HIV infection possibility of the female patients 5 times [39.18.41.3]. These infections may partially be in an epidemiological relationship, because these two sexually transmitted diseases contain the common sexual/behavioral risk factors. But chlamydia and HIV may be in a relationship independently from the common risk factors that allow the sexual transmission [42].

A possible relationship was indicated between the chlamydia and HIV infection.

- Damaging of the genital epithelium by the chlamydia due to the invasive intracellular pathogenesis facilitates the HIV infection.
- HIV infection increases because of the immunological change in the chlamydia infections.

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On the other hand, chlamydia infections which are connected to the immunosuppression in the HIV-like PID-progress more aggressively. Therefore, early diagnosis and treatment of the chlamydia infection is important for the prevention of the HIV and clinical damages.

Prevention of the chlamydia infection

Because chlamydia is seen very often and doesn't present any symptoms, application of safe sex, living as a monogamist, using a single towel and taking precautions against sexually transmitted disease are particularly significant. Control of the sexually transmitted diseases is one of the primary public health problems.

Five main concepts have been defined to get protected following the CDCP [36]:

- Sexual behavioral education and consultancy for individuals at risk
- Determination of asymptomatic individuals and diagnosis and treatment services for symptomatic people.
- Effective diagnosis and treatment of infected people.
- Evaluation, consultancy and treatment of the partners of individuals who have sexually transmitted diseases.
- Vaccination for immunization before the contact with the infection agent for the purpose of preventing sexually transmitted diseases

Prevention of the chlamydia infection can be achieved at the primary, secondary and tertiary levels. The first prevention includes activities like prevention of exposure to the chlamydia infection agent, health education, life consultancy etc. Unfortunately, the primary protection method couldn't gain the necessary popularity in the developing world [43].

The secondary protection method is to determine the patients with the screening tests to prevent the sequels of the asymptomatic chlamydial infections.

Tertiary protection of the upper genital tract with acute or chronic chlamydial infections results in failure to a large extent, because a serious tubal damage already occurs in patients when the upper genital tract is affected.

Treatment of the urogenital chlamydia infection

Chlamydia infection depends on the infected area, age of the patients and whether the infection is complicated. Treatment of the chlamydia changes during pregnancy. Chlamydia can easily be treated with antibiotics. Azithromycin and doxycycline are generally the suggested antibiotics. Sexual relationship must be avoided and chlamydia tests must be applied to the partners during the treatment [1].

CDCP recommends 1g single-dose oral azithromycin or 100 mg oral doxycycline twice a day for 7 days for non-complicated chlamydia infection. Alternatively, it recommends 500 mg erythromycin in four doses per day or 300 mg oral ofloxacin twice a day for 7 days.

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When compared to the conventional therapy, azithromycin is more advantageous than others in terms of the adaptation of the patient. All the other treatment regimens present similar profiles in respect of treatment rates and side effects. Patients must avoid sexual relationship for 1 week after the beginning of the treatment. It is necessary to treat the sexual partners together with the patients simultaneously to prevent re-infections. If the symptoms discontinue or re-infection isn't suspected, there is no need to apply a test again following the treatment of the patient.

Chlamydia infection progressing with the PID

Recurrent chlamydia infections increase the risk factors available for the development of the PID and ectopic pregnancy. PID is a disease that can be treated under the policlinical conditions.

However, the patient must be hospitalized if

- The disease progresses severely,
- The patient has nausea and vomiting,
- The patient has high fever,
- A tuba ovarian abscess has developed,
- Intolerance and non-response are observed against the oral treatment.

For such patients, the CDCP recommends 400 mg oral ofloxacin twice a day or 500 mg oral metronidazole twice a day or only 500 mg oral levofloxacin as a single dose per day for 2 weeks. In case of intolerance against the aforementioned treatment, the following are recommended: 250 mg im ceftriaxone or 2g im cefoxitin as a single dose, in addition, initiation of 1 g probenecid orally as a single dose together with 100 mg doxycycline (2x1) containing or not containing 500 mg metronidazole for 2 weeks [29].

Treatment of the chlamydia during pregnancy

Levofloxacin, ofloxacin and doxycycline are contraindicated during pregnancy. Therefore, 1 g oral single-dose azithromycin or 500 mg oral (3x1) amoxicillin is recommended. It was reported that amoxicillin was more effective and had less side effects than erythromycin. Alternatively, erythromycin (4x1) 500 mg is a safe and effective treatment [29]. The test must be applied 3 weeks after the completion of the treatment for the control of the treatment efficiency. If the re-exposure risk is high, the patient must be followed up during pregnancy and re-screening tests must be repeated.

Vaccination

Vaccination is mainly more effective than the other biomedical interventions in the control of the epidemics of the chlamydia infections. Currently, the best public health intervention is the increase in the treatment and screening rates of the infected individuals. Protective vaccination of the adolescents before their first sexual experiences helps with a substantial decrease in the chlamydia prevalence. This drop in the prevalence, which is obtained through vaccination, cannot be achieved even by screening 100% of the adolescents with the screening tests [43].

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Serious genitourinary system complications of the chlamydia infection are clearly admitted for both men and women. It is known to ease the transmission of the HIV infection. Despite all, the most valid intervention is still the early diagnosis and treatment of the infected cases and their sexual partners with the screening method. However, the desired intervention against the chlamydia infection is the development and use of an effective vaccine - although still requires a long way - by conducting more extensive researches.

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