ejpmr, 2023,10(9), 341-345

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

SEXUALLY TRANSMITTED DISEASES

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Article Received on 16/07/2023 **Article Revised on 06/08/2023** **Article Accepted on 27/08/2023**

ABSTRACT

Sexually transmitted diseases (STD) are a variety of infections which are caused by the microorganisms including viruses that are acquired through sexual contact. These infectionsare manifested as various group of symptoms or syndromes. Early diagnosis and complete treatment is the keystone for reducing the burden and preventing transmission. Health care providers must be well versed with the strategy of treatment and prevention of these STDs.

KEYWORDS: Sexually transmitted diseases, Syphillis, Etiology, Epidemiology, Pathogenesis, Treatment,signs and symptoms, Diagnosis.

INTRODUCTION

Sexually transmitted diseases, previously known as sexually transmitted diseases, involve thetransmission of an organism between sexual partners through different routes of sexual contact, either oral, anal, or vaginal. STIs become a concern and burden on healthcare systems, as many infections go untreated and lead to potentially serious complications. The natural history and patterns of spread of the most common sexually transmitted infections will be discussed as well as disease prevention, evaluation, diagnosis, and treatment.

Chlamydia

Chlamydia is the most common bacterial sexually transmitted disease in females, caused by Chlamydia trachomatis, an obligate intracellular gram-negative bacterium. The disease is commonly asymptomatic.

Chlamydia trachomatis is an obligate intracellular bacterium. During its unique developmental cycle, two different forms are observed, elementary bodies (EBs), which are infectious but notable to divide, and reticulate bodies (RBs), which are metabolically active and able to multiply. Persistent forms can also be present under particular conditions.[1]

Etiology

Chlamydia trachomatis is an obligate intracellular bacterium that infects mainly ocular and genitourinary epithelium.There are at least 18 serologic variants (serovars), including the oculogenital serovars A – K and the lymphogranuloma venereum serovars L1, L2, and L3.

Management of lymphogranuloma venereum (LGV) serovars are excluded from this protocol but are covered in the Manitoba Health, Seniors and Active Living Lymphogranuloma Venereum protocol.[2]

Epidemiology

In the USA in 2006, more than one million cases of chlamydial infection, which is a notifiable disease, were reported to the CDC, corresponding to a rate of 347.8 cases/ 100 000, an increaseof 5.6% as compared with the rate in 2005.With the exception of LGV, chlamydial infections are widely diffused among the general population, affecting mainly young people between 16 and 24 years of age. Risk factors include high frequency of partner change, multiple partners, unprotected sex, and being unmarried.

Chlamydial infection is not a notifiable disease, screening studies showed large differences according to the population tested, ranging from 6–11% in individuals attending family planning centres to 1–3% in individuals attending preventive medical centres of universities.[3-5]

Pathogenesis

Chlamydiae exhibit a unique biphasic developmental cycle consisting of the conversion of EBs to RBs, the division of RBs, and the reorganization of RBs back into EBs. The persistent cycleseems to be the norm.

Chlamydial persistence has been described as a longterm association between chlamydiae and their host cells in which these bacteria remain in a viable but culture-negative state.

Characteristically, C.trachomatis infection is frequently low-grade or asymptomatic, and repeated infection is

common, indicating that natural immunity is limited. The major sequelae arise as a result of inflammation and fibrosis. A key question is whether persistent forms of chlamydiae play a role in the immunopathology of disease. In vitro, some factors inducing the development of aberrant persistent forms of chlamydiae, e.g. nutrient depletion, antibiotics and cytokines, have been identified. Chlamydial interaction with the cytokine system of the host is likely to be central to disease, as the inflammation following chlamydial infection and exacerbated by re-infection leads to tissue damage and scarring.

Moreover, continued chlamydial Hsp60 expression secondary to the action of interferon-c produced by the cellmediated immune response might ultimately drive chronic inflammatory responses associated with the severe sequelae of chlamydial infection. The presence of Chlamydia-specific anti-Hsp antibodies has been proposed as a marker of chronic C. trachomatis infection. Antibody response to the surface antigen, MOMP, is an important mediator of immunity. Antigenic variation can arise in response to antimicrobial and/or immune pressure, and may play a role in persistence and disease pathogenesis.[5-6]

Complications

In women: Include pelvic inflammatory disease, endometritis, salpingitis, tubal infertility, ectopic pregnancy, reactive arthritis and perihepatitis.

In men: Include epididymo-orchitis and reactive arthritis.[6]

Signs and Symptoms

Symptoms of uncomplicated chlamydial infection in women may include abnormal vaginal discharge, dysuria, and post-coital and intermenstrual bleeding.

Symptomatic men usually present with urethral discharge and dysuria, sometimes accompanied by testicular pain. Rectal infection may manifest as a rectal discharge, rectal pain or blood in the stools, but is asymptomatic in most cases.[7]

Diagnosis

Diagnosis is based on a combination of history, physical examination and laboratory investigation. A diagnosis of chlamydia should be considered in anyone with signs or symptoms compatible with chlamydia.

Cadham Provincial Laboratory (CPL) performs assays for both chlamydia and gonorrhea only on genitourinary specimens and eye swab specimens submitted for Nucleic Acid Amplification Testing (NAAT). All other sources will only have chlamydia testing performed and reported by NAAT. CPL is currently the sole laboratory provider of NAAT diagnostic and screening services in Manitoba for chlamydia and gonorrhea. NAAT results are acceptable for medico-legal purposes in Manitoba for diagnosis of chlamydia. In rare circumstances, residual specimens may be sent to the National Microbiological Laboratory or another external reference laboratory for repeat testing.

Nucleic acid hybridization tests DNA probing (with Pace 2, Gen Probe) was the first molecular DNA test for C. trachomatis,and was largely used before the advent of NAATs. The performance of these tests is comparable to that of the better antigen detection and cell culture methods. Pace 2 can be used with endocervical or urethral swabs,but is not recommended for use with noninvasive specimens. The Digene Hybrid Capture II test is a nucleic acid hybridization test that is signal amplification based. Its sensitivity is substantially higher than that of the Pace 2 test and is comparable to that of PCR.[8]

Treatment

Complicated genitourinary chlamydia infection should be treated with azithromycin (Zithromax; 1 g, single dose) or doxycycline (100 mg twice daily for seven days; Studies indicate that both treatments are equally effective. Although dual therapy to cover gonorrhea and chlamydia recommended when patients are diagnosed with gonorrhea, additional coverage for gonorrhea is not required with the diagnosis of chlamydia alone.

Alternative regimens for uncomplicated chlamydia infection include erythromycin (500 mg four times daily for seven days), erythromycin ethylsuccinate (800 mg four times daily for seven days), levofloxacin (Levaquin; 500 mg oncedaily for seven days).

Ceftriaxone 250 mg IM in a single dose followed by Doxycycline 100 mg orally twice a day for 14 days with or without Metronidazole 500 mg orally twice a day for 14 days.[9-10]

Genital herpes

Genital herpes is a sexually transmitted infection which is seen throughout the world and continues through life. It is the most common cause of diseases accompanied by genital ulceration. Genital herpes is a serious health problem because the infection continues throughlife with remissions and relapses, it causes recurring painful ulcers, the virus transmitted frommother to infant causes serious neonatal infections, and there is no known cure for it.

First infection with either herpes simplex virus type 1 (HSV-1) or type 2 (HSV-2) is termed primary infection and results in either symptomatic disease at the site of viral entry (i.e. on the face or genital area) or asymptomatic, and thus unrecognised, infection. Herpes simplex viruses (HSV) are the most common human pathogens causing infections in orofacial and genital regions.[11]

Epidemiology

Genital HSV infections are among the most commonly seen sexually transmitted infections inthe world. The real

prevalence of the genital herpes infection is unknown due to asymptomatic cases. The most common cause of the genital herpes infection is HSV-2, but the number of primary genital herpes cases induced by HSV-1 is on the rise.

The prevalence of infections induced by HSV-1 and HSV-2 varies between countries. While HSV-1 prevalence is about 60–80% worldwide, its prevalence in developing countries varies between 70 and 100%. HSV-2 prevalence is reported to vary between 7 and 80% depending on the country, age group, and sexual life characteristics. More than 500 million people are estimated to be infected with HSV-2 worldwide, which corresponds to 16% of the world population in between the ages of 15–49. It is also estimated that 20 million new cases occur every year.

HSV-1 is typically transmitted during childhood and with non-sexual contact. While HSV-1- induced genital herpes prevalence varies between geographical regions, almost half of all new genital herpes cases are caused by HSV-1 in European countries. HSV-1 seropositivity is estimated to be 40–63% in the United States, while HSV-2 seropositivity is estimated to be 50 Fundamentals of Sexually Transmitted Infections 16–18%.

However, HSV-1 seroprevalence was found to increase in those who were diagnosed with genital herpes only. Having orofacial HSV-1 infection during childhood may protect against genital HSV-1 infection in later years and silent HSV-2 seroconversion occurs more frequently in individuals with HSV-1 immunity. [12]

Pathophysiology

Host's immune system is the most important factor which determines the transmission, severity, and frequency of recurrence of the infection. Humoral and cellular immune systems limit the spread of the virus in immune-competent individuals. In experiments with both humans and rats, CD4+ and CD8+ T lymphocytes, macrophages, natural killer cells, and inflammatory cytokines such as interferon-γ were shown to be involved in protection against HSVs.

While individuals with mild cellular immune deficiency experience frequent recurrences and slower resolution, individuals with severe immune deficiency are at a higher risk of disseminated, treatment-resistant, and chronic disease. More frequent and severe recurrent herpes infections in acquired immunodeficiency syndrome (AIDS) patients indicate the importance of cellular immunity, CD4+ T cells in particular.

Humoral immune system, on the other hand, does not affect disease severity. However, it is involved in reduction of virus titer in inoculation region and neural tissues during primary infection. Another cell that is primarily affected in genital herpes and involved in immune response against HSV-2 52 Fundamentals of Sexually Transmitted Infections is keratinocytes. Keratinocytes infected with HSV-2 show up-regulation of antiviral cytokines such as interferon alpha, beta, tumor necrosis factor-alpha (TNF-α), colony-stimulating factors, growth factors, defensins, selectins, lymphocyte function-associated antigens, and receptors.

Primary HSV infection results from a previously unexposed person having close contact with someone who is actively shedding the virus from skin or secretions. There may be a prodrome of hours to days consisting of pain, tingling, itching, or burning at the site of exposure.

Epithelial damage at the portal of entry leads to eruption of vesicles that open, ulcerate, and reepithelialize during an outbreak that lasts about two weeks. During initial infection, viral DNA travels by axon to the spinal cord sensory ganglion where it persists for life.8 Reactivation of HSV causes migration back through the axon, its branches, or contralateral axons to the skin and mucosa.[13-15]

Pathogenesis

The pathogenesis of HSV-1 and HSV-2 infections in humans and animal models has some general similarities and some important differences. HSV-1 is primarily associated with orolabial lesions, stromal keratitis, and occasionally encephalitis. HSV-2 primarily causes genital infections but is also capable of necrotizing stromal keratitis, encephalitis, meningitis, and neonatal ophthalmic, and neurologic complications in infants surviving infection. In animal models, HSV-2 is significantly more neurovirulent than HSV-1 by all routes ofinfection.

HSV-1 mutants lacking *vhs* function have a significantly reduced capacity to replicate in the cornea, trigeminal ganglia, and brains of mice and show impaired establishment and reactivation from latency in a murine eye model of latency and pathogenesis. UL41 mutant viruses, however, remain highly immunogenic, suggesting that deletion of *vhs* may be a useful property for live-attenuated herpesvirus vaccines. The *vhs* proteins of HSV-1 and HSV-2 are 87% identical at the amino acid level, although the shutoff activity of HSV-2 is significantly faster than that of HSV-1. The kinetics of *vhs* activity, however, do not correlate with virulence, since replacement of the *vhs* from HSV-1 with the higher-activity *vhs* allele from HSV-2 failsto alter the virulence of the HSV-1 recombinant. In addition, *vhs* from HSV-2 in combination with ICP47 has been shown to block antigen presentation by class I major histocompatibility complex (MHC).[15]

Complications

- Acute urinary retention (particularly in women).
- Aseptic meningitis (including a recurrent form).
- Disseminated herpes.
- Encephalitis Hepatitis.

- Neonatal infection.
- Pelvic inflammatory disease.

Pneumonitis.[16]

Signs and Symptoms

- Pain or itching around the genitals.
- Small bumps or blisters around the genitals, anus or mouth.
- Painful ulcers that form when blisters rupture and ooze or bleed.
- Scabs that form as the ulcers heal.
- Painful urination.

Discharge from the urethra, the tube that releases urine from the body, Discharge from the vagina.[17]

Diagnosis

Detection of type-specific HSV IgG antibodies is a rapid, effective, and reliable method in infection diagnosis. Although it does not provide information related to infection time, it is possible to support primary infection diagnosis in individuals who are believed to have the first genital herpes attack. Discharge from the vagina.

Laboratory diagnosis

Laboratory confirmation is recommended in all patients with suspected genital herpes, using methods that directly demonstrate the virus in genital specimens; typically swabs should be taken from the base of the lesion (vesicles should be unroofed with a needle or scalpel blade) (Ib, A).Viral detection in early disease (for both first episodes and recurrences) are much morelikely to be successful. Swabbing for laboratory confirmation should not be delayed if at all possible.

Detection of type-specific HSV IgG antibodies is a rapid, effective, and reliable method in infection diagnosis. Although it does not provide information related to infection time, it is possible to support primary infection diagnosis in individuals who are believed to have the first genital herpes attack.

The most commonly preferred methods are cell culture and PCR, which is a NAAT method. It is possible to distinguish between HSV-1 and HSV-2 using these two methods. It is absolutelynecessary to distinguish between HSV-1 and HSV-2 in newly diagnosed genital herpes cases. Discharge from the vagina.[17]

Treatment

First-episode genital herpes

- Acyclovir 400 mg three times a day, or
- Acyclovir 200 mg five times a day, or
- Famciclovir 250 mg three times a day, or

Valaciclovir 500 mg two times a day Discharge from the vagina.

Recurrent genital herpes

- Acyclovir 800 mg three times daily for two days, or
- Famciclovir 1 g twice daily for one day, or50
- Valaciclovir 500 mg twice daily for three days (Ib, A)

Alternative longer five-day courses include

- Acyclovir 400 mg three times daily for 3–5 days, or
- Acyclovir 200 mg five times daily, or
- Valaciclovir 500 mg twice daily or

Famciclovir 125 mg twice daily Discharge from the vagina.[18]

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