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Pelvic inflammatory disease

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ABSTRACT

Pelvic inflammatory disease (PID) is a very common condition among women of reproductive age. It is also a common reason for presenting to the emergency room. Although it often presents with mild symptoms, it is very important to consider it in any sexually active patient in order to start treatment as soon as possible and avoid complications.

Keywords: pelvic inflammatory disease, sexually transmitted diseases, cervicitis, salpingitis, endometritis, infertility

INTRODUCTION

Pelvic inflammatory disease (PID) is an inflammation and infection of the upper female genital tract that includes endometritis, salpingitis, endocervicitis and their complications, tubo-ovarian abscess and pelvic peritonitis [1]. The cause of this disease is an ascending infection from the lower genital tract. The way the infection spreads is from the vagina to the cervix, then to the fallopian tubes and ovaries and finally into the peritoneal cavity [2]. It is a very common pathology among sexually active young women and one of the most common reasons for presenting to the emergency room [2,3]. It is important to be diagnosed rapidly, as it can lead to multiple sequelae and complications, such as ectopic pregnancy, tubal infertility, chronic pelvic pain. Acute PID can also lead to the apparition of tubo-ovarian abscesses that can be life-threatening in case of rupture [4]. Despite being so common, it can cause diagnostic problems because the symptoms are usually mild and non-specific [2].

METHODS

A PubMed, Web of Science systematic electronic search was undertaken using keywords like "pelvic inflammatory disease", "endometritis", "salpingitis", "infertility", "tubo-ovarian abscess", "sexually transmitted diseases". The search included systematic reviews, randomized controlled trials, review articles, meta-analyses and international guidelines and resulted in 75 articles, from which only 20 papers were further reviewed and included in the final review.

ETIOLOGY AND RISK FACTORS

The etiology of PID is closely related to sexually transmitted microorganisms such as *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Mycoplasma genitalium* and gram-negative bacteria [2,5]. It is considered a polymicrobial infection, involving *C. trachomatis* and/ or *N. gonorrhoeae* which must always be taken into consideration. The presence of anaerobes is reported more frequently in recent past years, their pathogenic role not being well known yet [6]. Bacterial vaginosis is present in 2/3 of women diagnosed with PID. Bacterial vaginosis is an imbalance of the vaginal flora with *lactobacilli* normally present in the vagina replaced by a dominant anaerobic flora along with significant concentrations of *Gardnerella vaginalis* and genital mycoplasmas [4]. Bacterial vaginosis is associated with the production of enzymes that degrade cervical

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mucus, thus destroying the cervical barrier and facilitating the spread of microorganisms to the upper genital tract [1,7]. The risk factors for PID are abortion, intrauterine device insertion, hysterosalpingography, *in vitro* fertilization, young age, multiple sexual partners, history of PID, new sexual partner, postpartum period [5,8].

CLINICAL MANIFESTATIONS AND DIAGNOSIS

The onset of severe pain in the lower abdomen is the classic symptom of PID. Atypical mild clinical manifestations have become more common as the frequency of *N. gonorrhoeae* infection decreased [1,9,10]. Symptoms of PID include pelvic pain of varying intensity, dyspareunia, dysuria, abnormal vaginal intermenstrual bleeding, postcoital bleeding, abnormal vaginal discharge [1]. Signs of PID are fever > 38°C, lower abdominal tenderness and adnexal and cervical mobilization tenderness at bimanual palpation [5]. Positive testing for *Gonorrhea*, *Chlamydia* or *M. genitalium* supports the diagnosis. According to Centers for Disease Control and Prevention (CDC) 2021 guideline, most women with PID have either mucopurulent cervical secretion or the presence of white blood cells on microscopic examination of vaginal secretion, increased C-reactive protein and elevated erythrocyte sedimentation rate. The most specific diagnostic criteria are endometrial biopsy that reveals endometritis, transvaginal ultrasound / magnetic resonance imaging (MRI) / computed tomography (CT) that show salpingitis with no fluid in the pelvis or tubo-ovarian abscess, exploratory laparoscopy that reveals PID. Differential diagnosis should be made with functional pain, acute appendicitis, endometriosis, ectopic pregnancy, ovarian cyst, irritable bowel syndrome [5].

MANAGEMENT

PID treatment guidelines have been developed by CDC. Treatment should be instituted empirically as soon as PID is suspected. Delaying treatment can increase the risk of infertility and ectopic pregnancy [11]. The selection of antibiotics is based on the mode of treatment - inpatient / outpatient [12]. The first line of treatment is the outpatient regimen, with oral or intramuscular administration. Hospitalization may be necessary in the following cases: if surgical emergencies such as appendicitis cannot be excluded, pregnancy, tubo-ovarian abscess, severe nausea / vomiting or temperature > 38°C, patient inability to follow or tolerate outpatient oral treatment or having no clinical response to oral or intramuscular medication after 72 hours of therapy [13].

Medication should cover *N. gonorrhoeae* and *C. trachomatis*, even when cultures are negative, because this does not exclude an upper genital tract infection. Metronidazole is important in the treatment regimen because it acts on anaerobic germs in the upper genital tract. Doxycycline is preferable to be administered orally if possible because it has the same bioavailability and intravenous perfusion is painful. If after 24 hours of parenteral treatment improvement is already seen, it is recommended to switch to oral therapy for 14 days [11,13].

Recommended intramuscular and oral regimens

First line of treatment that should be taken into consideration is Ceftriaxone 500 mg IM in a single dose (for persons weighing > 150 kg with documented gonococcal infection 1 g of Ceftriaxone) PLUS Doxycycline 100 mg orally 2 times / day for 14 days WITH Metronidazole 500 mg orally 2 times / day for 14 days. Second option could be Cefoxitin 2 g IM in a single dose and Probenecid 1 g orally administered concurrently in a single dose PLUS Doxycycline 100 mg orally 2 times / day for 14 days WITH Metronidazole 500 mg orally 2 times / day for 14 days. Third option may be another third-generation cephalosporin (Ceftizoxime / Cefotaxime) PLUS Doxycycline 100 mg orally 2 times / day for 14 days WITH Metronidazole 500 mg orally 2 times / day for 14 days.

In case of cephalosporin allergy, if risk of gonorrhea is low, the following treatment is recommended: Levofloxacin 500 mg orally once daily WITH Metronidazole 500 mg orally 2 times / day 14 days, or another treatment options Moxifloxacin 400 mg orally once daily WITH Metronidazole 500 mg orally 2 times / day 14 days or Azithromycin 500 mg IV daily, 1 - 2 doses, followed by 250 mg orally daily in combination with Metronidazole 500 mg 2 times / day for 12 to 14 days.

If a gonorrhea culture is positive, treatment should be based on antimicrobial susceptibility testing, and if it is quinolone-resistant, an infectious disease specialist should be consulted.

Parenteral treatment

In case parenteral treatment is the best option, therapy should be one of the following: Ceftriaxone 1 g IV every 24 hours PLUS Doxycycline 100 mg orally or IV every 12 hours PLUS Metronidazole 500 mg orally or IV every 12 hours or Cefotetan 2g IV every 12 hours PLUS Doxycycline 100 mg orally or IV every 12 hours or Cefoxitin 2g IV every 6 hours PLUS Doxycycline 100 mg orally or IV every 12 hours. An alternative parenteral treatment is available: Ampicillin-Sulbactam 3 g IV every 6 hours PLUS Doxycycline 100 mg orally or IV every 12 hours or Clindamycin 900 mg IV every 8 hours PLUS Gentamicin loading dose IV / IM 2 mg/kg body weight, followed by a maintenance dose 1.5 mg/kg

body weight every 8 hours; single daily dosing 3-5 mg/kg body weight can be used also.

After a clinical improvement, switch can be made to oral therapy with Doxycycline 100 mg orally 2 times / day plus Metronidazole 500 mg 2 times / day to complete the 14 days of treatment. In the case of alternative parenteral regimens (Clindamycin and Gentamicin) the transition is made to Clindamycin 450 mg orally 4 times / day or Doxycycline 100 mg orally 2 times / day.

If tubo-ovarian abscess is present, for a better control over anaerobic microorganisms, Doxycycline 100 mg orally 2 times / day either with Clindamycin 450 mg orally 4 times / day or Metronidazole 500 mg orally 2 times / day should be used with alternative parenteral regimen [11,12].

People who had sexual intercourse with a woman with PID in the last 60 days prior to the onset of her symptoms should be tested and treated for *Chlamydia* and *Gonococcus*, even if they are asymptomatic [14].

At 48-72 hours after treatment initiation or after discharge from hospital, the patient should be reevaluated and tested for all sexually transmitted diseases, including syphilis, HIV, hepatitis. Patients should be advised not to have sexual intercourse until the end of the treatment and disappearance of symptoms [13,15].

COMPLICATIONS

Delaying PID treatment is often associated with complications, although they can appear anyway. Chronic pelvic pain occurs in one-third of patients with PID. This can occur due to the inflammation and adhesions caused by the infectious process, being the most common in recurrent PID [16]. Another important complication is infertility, the infection severely affecting the fallopian tubes leading to their obstruction or to loss of epithelial cells. Infertility risk increases if PID treatment is delayed, if the pathogen agent is *Chlamydia* and if the patient has repeated episodes of PID. Last but not least, ectopic pregnancy is also a complication of PID, respectively of the fallopian tubes' sequelae [17-20].

CONCLUSIONS

PID is very common among women at reproductive age. Women should be instructed how to prevent catching sexually transmitted diseases, this being possible through the implementation and development of health educational programs. Also, women with PID should be diagnosed rapidly and treated effectively. The diagnosis of PID remains difficult because of the nonspecific symptoms. Empirical treatment should reduce the development of long-term sequelae.

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