Management of Pelvic Inflammatory Disease in Clinical Practice

Introduction

- Pelvic inflammatory disease (PID) refers to acute and subclinical infection of the upper genital tract in females, involving any or all of the uterus, fallopian tubes, and ovaries; this is often accompanied by involvement of the neighboring pelvic organs. It results in endometritis, salpingitis, oophoritis, peritonitis,perihepatitis, and tubo-ovarian abscess.
- PID is both a clinical and public health concern due to its potential to result in infertility and morbidities like chronic pelvic pain, ectopic pregnancy, and recurrence in undiagnosed or poorly treated cases.
- In the past, C. trachomatis and N. gonorrhoeae were responsible for most PID diagnoses but now days approximately half of PID cases are polymicrobial and involve enteric pathogens, respiratory pathogens and pathogens responsible for bacterial vaginosis
- Knowledge of the role of novel organisms like Mycoplasma genitalium (M. genitalium) in the pathogenesis of PID has been evolving

CLINICAL FEATURES

Patients at risk

- women ≤25 years
- history of STIs
- having two or more sexual partners
- inconsistent condom use
- History of prior PIDs

Symptoms and Signs

The clinical presentation of PID can vary widely from an asymptomatic or mild clinical picture to severe disease.

- lower abdominal or pelvic pain
- mucopurulent discharge
- cervical motion tenderness or adenexal tenderness on the bimanual examination
- Patients may also report fever, metrorrhagia, urinary symptoms, or dyspareunia on review of systems.

Laboratory findings

In recognition of the non-specifcity of the clinical signs, many treatment guidelines recommend supporting clinical diagnosis with laboratory investigations.

Nucleic acid amplifcation tests (NAAT) , Wet prep microscopy
testing for STIs, eg, T. vaginalis HIV and syphilis should be considered.
Other labs can provide supportive information such as:

- Leukocytes on wet prep saline microscopy of mucocervical secretions
- a urinalysis may be positive for leukocyte esterase and white blood cells
- ESR, CRP , and white blood cell counts, may also be elevated in patients

Laparoscopy can provide a defnitive diagnosis of PID, but it is invasive, costly, and rarely needed.

Treatment

	CDC	CNGOF & SPILF	European Guidelines
Outpatient regimens	Single dose Ceftriaxone 250mg IM & Doxycycline 100mg orally twice daily for 14 days **with or without** Metronidazole 500mg orally twice daily for 14 days **Or** Single-dose cefoxitin 2g I.M. and Doxycycline 100mg orally twice daily for 14 days **with or without** Metronidazole 500mg orally twice daily for 14 days 1–2 doses of Azithromycin 500mg IV daily, then Azithromycin 250mg orally for 12–14 days **with or without** Metronidazole 500mg orally twice daily for 14 days *Levofloxacin 500mg orally once daily **Or** *Ofloxacin 400mg twice daily **Or** *Moxifloxacin 400mg orally once daily **with or without** Metronidazole 500mg orally twice daily for 14 days	Single-dose Ceftriaxone 1g I.M. and doxycycline 100mg orally twice daily and Metronidazole 500mg twice daily for 14 days **Or** Oral ofloxacin 200mg daily and metronidazole 500mg twice daily with or without single dose ceftriaxone IM **alternatives** oral levofloxacin 500mg daily and metronidazole 500mg twice daily for 10 days with or without single ceftriaxone 1g IM **Or** Oral moxifloxacin 400mg daily for 10 days **with or without** single dose ceftriaxone 1g I.M.	Single dose ceftriaxone IM 500 mg and oral doxycycline 100 mg twice daily with metronidazole 500 mg twice daily for 14 days **Or** Oral ofloxacin 400 mg twice daily and oral metronidazole 500 mg twice daily for 14 days (ofloxacin may be replaced by levofloxacin 500 mg once daily **Or** Oral moxifloxacin 400 mg once daily for 14 days
Inpatient regimens	Cefotetan 2g IV 12 hours and Doxycycline 100mg orally or IV 12 hours **Or** Cefoxitin 2g IV 6 hours and Doxycycline 100mg orally or IV 12 hours **Or** Clindamycin 900mg IV 8 hours and Gentamicin IV/IM loading dose at 2mg/kg, then dose 1.5mg/kg 8 hours or single daily dosing of 3–5mg/kg Ampicillin/Sulbactam 3g IV 6 hours and Doxycycline 100mg orally or IV 12 hours	Single dose ceftriaxone 1g IV & Oral/IV doxycycline 100mg and oral metronidazole 500mg twice daily for 10 days **Or** IV doxycycline 100mg and Cefoxitin 2g for twice daily **replaced by** doxycycline 100mg twice daily and metronidazole 500mg twice daily for 10 days **Alternative** Clindamycin 600mg and gentamicin 5mg/kg/day IV for 3 days, then clindamycin 600mg three times daily oral for 10 days	Ceftriaxone IV/IM 1g once daily and Oral/IV Doxycycline 100 mg twice daily and oral Metronidazole 500 mg twice daily for 14 days **Or** Clindamycin 900mg 3 times daily and Single daily dose gentamicin (3–6 mg/kg) and clindamycin 450 mg four times daily for 14 days **Or** Oral doxycycline 100mg twice daily and oral metronidazole 500 mg twice daily for 14 days

Variations in Treatment Guidelines

- Though largely similar, guidelines for PID treatment tend to vary minimally by country, prevalent organisms, antibiotic susceptibility, and cost.
- The US and French guidelines recommend using 3rd generation cephalosporins in addition to doxycycline and metronidazole as frst-line treatment for mild to moderate PID.
- Though similar, the guidelines differ in the recommended treatment duration and the addition of metronidazole to treatment regimens
- Like the US, the French guidelines reserve the use of fluoroquinolones for patients with cephalosporin allergies or when no alternatives are available.
- All three guidelines recommend a combination of twice-daily dosing of ofloxacin as alternate first-line regimens in uncomplicated PID.

Current Challenges in PID Management: Novel Organisms

M. genitalium is a diminutive pathogenic bacteria frst isolated in 1981.

In a meta-analysis conducted by Lis et al, M. genitalium infection caused a 2-fold risk of infertility and increased the risk for spontaneous abortions, preterm births, and PID.

In a survey of 1139 women with asymptomatic bacterial vaginosis recruited from fve clinics across the US, one in five (20.5%) women were positive for M. genitalium at baseline.

Unfortunately, the sensitivity of M.genitalium to azithromycin is waning due to rising antimicrobial resistance to macrolides. However, the organism currently remains sensitive to moxifloxacin.

Although using doxycycline as frst-line treatment is recommended until antibiotic sensitivity results become available.

Vaccination Against STIs

It is estimated that 10–15% of chlamydial PID progress to tubal factor infertility. a vaccine against C. trachomatis serovars D-K, can potentially avert an estimated 1 million chlamydial-associated tubal factor infertility annually.

Research into chlamydial vaccines has been focused on mostly live attenuated vaccine trials and used laboratory mice.

Protein-based subunit vaccines against C. trachomatis were developed to address the challenges of whole vaccines.

MOMP is a protein that makes up the greater part of the outer membrane of chlamydia and is the antigen primarily responsible for generating innate and adaptive immune responses. Cell-mediated immunity through Thelper 1cells is most important for preventing C. trachomatis infection.

For the first time in decades of research, a vaccine has reached the frst phase of human trials

Novel Approaches to Treatment

Rising antibiotic resistance has become a driving factor in identifying alternative approaches to PID treatment, and novel treatment strategies that utilize non-pharmacological therapies are being considered.

For example,

the effect of Ozone therapy on inflammatory processes in PID has been assessed and shown to progressively decrease inflammation through a reduction in the concentrations of pro-inflammatory interleukin-6 and improvements in the sonographic features of PID.

these fndings may represent the future of PID management and help overcome the challenges of growing antimicrobial resistance.

Conclusion

- PID affects women of reproductive age across the globe.
- Prevention strategies such as asymptomatic screening have reduced PID prevalence, but non-adherence to treatment guidelines and antimicrobial resistance pose challenges for the management of affected women.
- Advances in bench science to produce anti-chlamydial vaccines and alternative antimicrobial therapies may be vital to overcoming these challenges moving into the future.

Thank you
for your
attention