

Authors Reply

Comments on Ricardo F Savaris' Letter to the Editor regarding the publication in the JBSTM–Brazilian Protocol for Sexually Transmitted Infections, 2020: "Pelvic Inflammatory Disease"

Maria Luiza Bezerra Menezes^[1], Paulo Cesar Giraldo^[2], Iara Moreno Linhares^[3], Neide Aparecida Tosato Boldrini^[4] and Mayra Gonçalves Aragon^{[5],[6]}

[1]. Universidade de Pernambuco, Departamento Materno-Infantil, Recife, PE, Brasil.

[2]. Universidade Estadual de Campinas, Departamento de Tocoginecologia, Campinas, SP, Brasil.

[3]. Universidade de São Paulo, Disciplina de Ginecologia, Departamento de Obstetrícia e Ginecologia, São Paulo, SP, Brasil.

[4]. Universidade Federal do Espírito Santo, Departamento de Ginecologia e Obstetrícia, Vitória, ES, Brasil.

[5]. Ministério da Saúde, Secretaria de Vigilância em Saúde, Brasília, DF, Brasil.

[6]. Universidade Federal do Espírito Santo, Programa de Pós-Graduação em Doenças Infecciosas, Vitória, ES, Brasil.

Reply to the letter to the editor

We would like to thank Dr. Savaris for his relevant comments on our article (https://doi.org/10.1590/0037-8682-0419-2021)¹. His letter emphasizes three basic points: 1) diagnostic criteria for pelvic inflammatory disease (PID), 2) benefits in the use of gentamicin as a single dose rather than in two or three daily doses, and 3) suitability of antibiotic usage prior to intrauterine device (IUD) removal or even the need for its removal for the treatment of PID.

We would like to emphasize that in all our lectures or written articles on female pelvic infections, we always stress the unique characteristics of the 60% to 70% of cases that are asymptomatic². Therefore, to base diagnosis solely on clinical criteria may be insufficient. If the focus is to prevent sequelae, reliance on clinical criteria would result in a delay in early intervention. The more clinical signs that are present, the greater the diagnostic specificity. However, this also corresponds to a lower diagnostic sensitivity. We will fail to treat many women who may have subsequent serious problems with fertility, chronic pelvic pain, or ectopic pregnancy in a timely manner due to the absence of an early diagnosis. In addition, reliance on Dr. Savaris' suggested criteria may increase the number of false positives, as many cases of urinary tract infection or even adnexal cysts can

Corresponding author: Maria Luiza Bezerra Menezes. e-mail: luiza.menezes.24.09@gmail.com bhttps://orcid.org/0000-0001-7001-2005 Received 26 July 2021 Accepted 25 August 2021 cause pain in the lower abdomen and vagina. This consequently results in unnecessary aggressive treatments. Both laboratory and diagnostic imaging components are essential, regardless of whether they are labeled "major" or "minor" criteria. Thus, a presumptive early diagnosis must be based on complementary tests to effectively reduce the occurrence of adverse sequelae.

Regarding the use of gentamicin in a single daily dose, as shown in Figure 5 "Pelvic inflammatory disease treatment" in our publication¹, we emphasize that this is the recommended dosage for in-hospital treatment, as it is at least as effective, or perhaps even more effective, than a fractionated dose. It is of lower cost, requires less intervention, and has lower nephrotoxicity than multiple daily dose regimens. It should be noted that aminoglycosides have historically been administered in multiple daily doses (usually 2-4 times/day). Since toxic effects depend more on the duration of therapeutic levels than on maximum drug levels, and pharmacological efficacy depends more on concentration than on time, frequent administrations should be avoided^{3,4}. However, we caution that single daily regimens are not optimal for all patients. They should not be used in patients with a creatinine clearance above 25 mL/minute, preadolescents, elderly, pregnant or obese women, or in those with burns, ascites, or certain serious infections (such as meningitis, osteomyelitis, skin infection, infection of skin structures, and enterococcal endocarditis)⁵.

The last point raised concerns regarding the removal of an IUD in women with PID. The biological plausibility and similarity with other infections associated with prostheses and orthotics (orthopedic, cardiac, dental, ophthalmic, etc.) support the main recommendation to remove the foreign body. There is always the



possibility that their presence facilitates biofilm formation, which reduces or prevents an adequate treatment response or predisposes patients to relapses. We reiterate, as stated in the article, that IUD removal is not necessary in mild and moderate cases of PID, based on European and UK studies^{6,7}, and the WHO's medical eligibility criteria for the use of contraceptive methods⁸. However, we emphasize that in severe cases, it is essential to remove this foreign body to optimize treatment. Therefore, we follow the recommendation to not remove the IUD during treatment of PID unless the patient requests its removal or when there is no clinical improvement after 72 hours of adequate antibiotic treatment^{9,10}. In cases of severe PID, removal of the IUD is recommendation I-B)⁹.

Finally, we wish to clarify that our article was prepared based on the Clinical Protocol and Therapeutic Guidelines for Comprehensive Care for People with Sexually Transmitted Infections (PCDT-IST), published by the Ministry of Health of Brazil¹¹. Clinical Protocol and Therapeutic Guidelines (PCDT) are documents that establish the criteria for diagnosing infections, diseases, or health problems. They further recommend treatment with medications and other products, list appropriate dosages, and suggest protocols for clinical control mechanisms and for the monitoring and verification of therapeutic results by health professionals and managers of the Brazilian National Health System. The PCDT criteria are based on scientific evidence and criteria of efficacy, safety, and cost-effectiveness of the recommended technologies. They are periodically reviewed every two years. PCDT documents undergo analysis and approval by Conitec (National Commission for the Incorporation of Technologies in the Brazilian National Health System), created by Brazilian Law nº 12.401, of April 28, 2011, which provides for therapeutic care and the incorporation of health technology within the scope of the Brazilian National Health System¹². The points discussed here may be useful for revisions in the next PCDT-IST update.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

ORCID

Maria Luiza Bezerra Menezes: 0000-0001-7001-2005

Paulo Cesar Giraldo: 0000-0003-4365-9879

Iara Moreno Linhares: 0000-0002-7846-6885

Neide Aparecida Tosato Boldrini: 0000-0003-1140-5057

Mayra Gonçalves Aragon: 0000-0001-6631-1790

REFERENCES

- Menezes MLB, Giraldo PC, Linhares IM, Boldrini NAT, Aragon MG. Brazilian Protocol for Sexually Transmitted infections, 2020: pelvic inflammatory disease. Rev Soc Bras Med Trop. 2021;54:e2020602.
- Pinto VM, Szwarcwald CL, Baroni C, Stringati LL, Inocencio LA, Miranda AE. *Chlamydia trachomatis* prevalence and risk behaviors in parturient women aged 15 to 24 in Brazil. Sex Transm Dis [Internet]. 2011 Oct [cited 2020 Oct 2];38(10):957-61. Available from: https://doi. org/10.1097/olq.0b013e31822037fc
- Beers MH et al. Manual Merck: diagnóstico e tratamento; [tradução Paulo Cesar Ribeiro Sanches et al.]. – São Paulo: Roca, 2008.
- Savaris RF, Fuhrich DG, Duarte RV, Franik S, Ross J. Antibiotic therapy for pelvic inflammatory disease. Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD010285. DOI: 10.1002/14651858. CD010285.pub2.
- Gentamicina injetável. Medicina Net [Internet], 2021. Available from: https://www.medicinanet.com.br/conteudos/medicamentos/431/ gentamicina injetavel.htm
- Ross J, Cole M, Evans C, Deirdre L, Dean G, Cousins D. United Kingdom national guideline for the management of pelvic inflammatory disease (2019 interim update) [Internet]. United Kingdom: British association for sexual health and HIV BASHH; 2019 [cited 2020 Jul 22]. Available from: https://www.bashhguidelines.org/media/1217/pid-update-2019.pdf
- Ross J, Guaschino S, Cusini M, Jensen J. 2017 European guideline for the management of pelvic inflammatory disease. Int J STD AIDS [Internet]. 2018 Feb [cited 2020 Oct 2];29(2):10814. Available from: https://doi.org/10.1177/0956462417744099
- WHO, World Health Organization. Family Planning: a global handbook for providers. Updated 3rd edition. WHO, 2018. Available from: http:// apps.who.int/iris/bitstream/handle/10665/260156/9780999203705-eng. pdf?sequence=1
- Caddy S, Yudin MH, Hakim J, Money DM; Infectious Disease Committee; Special Contributor. Best practices to minimize risk of infection with intrauterine device insertion. J Obstet Gynaecol Can [Internet]. 2014 Mar [cited 2020 Oct 2];36(3):266-74. Available from: https://doi.org/10.1016/s1701-2163(15)30636-8
- Esposito CP. Intrauterine Devices in the Context of Gonococcal Infection, Chlamydial Infection, and Pelvic Inflammatory Disease: Not Mutually Exclusive. J Midwifery Womens Health 2020 Jul;65(4):562-566. doi: 10.1111/jmwh.13120. Epub 2020 Jun 27. Available from: https:// pubmed.ncbi.nlm.nih.gov/32592523/
- 11. Brasil, Ministério de Saúde. Secretaria de Vigilância em Saúde. Departamento de Doenças de Condições Crônicas e Infecções Sexualmente Transmissíveis. Protocolo Clínico e Diretrizes Terapêuticas para Atenção Integral às Pessoas com Infecções Sexualmente Transmissíveis (IST) – Brasília: Ministério da Saúde, 2020. Disponível em: http://www.aids. gov.br/pt-br/pub/2015/protocolo-clinico-e-diretrizes-terapeuticas-paraatencao-integral-pessoas-com-infeccoes
- 12. Brasil, Presidência da República. Lei Nº 12.401, de 28 de abril de 2011. Altera a Lei nº 8.080, de 19 de setembro de 1990, para dispor sobre a assistência terapêutica e a incorporação de tecnologia em saúde no âmbito do Sistema Único de Saúde - SUS. Brasil, 2011. Disponível em: http:// www.planalto.gov.br/ccivil 03/ ato2011-2014/2011/lei/112401.htm

