Clostridioides difficile Treatment Protocol and Healthcare Burden

Protocolo de Tratamento e Encargos em Saúde da Infeção por Clostridioides difficile

Keywords: Clostridium Infections; Fidaxomicin; Health Care Costs; Portugal

Palavras-chave: Controle de Gastos em Saúde; Fidaxomicina; Infecções por Clostridium; Portugal

In a previous edition of Acta Médica Portuguesa two original articles focused on an important topic – *Clostridioides difficile* infection (CDI).^{1,2}

The epidemiology of *Clostridioides* infection in Portugal reveals that most patients were aged over 70 years-old and most episodes (56%) occurred in hospitalized patients. This infection is associated very frequently with recent antibiotic exposure. There is a recurrence rate between $12\%^1$ and 14%.²

However, neither of the articles focused on the treatment protocol used.

Vancomycin and metronidazole have been considered the main treatment of *Clostridioides* infection. However, in the latest update of the American guidelines on management of clostridioides difficile infection in adults., fidaxomicin has been stated as the preferred treatment in initial infection.³ On the other hand, National Institute of Health and Care Excellence (NICE) guidelines recommend use of fidaxomicin as a second-line treatment and/or if there is a relapse within 12 weeks.⁴ Fidaxomicin is a narrow spectrum macrocyclic antibiotic approved for the treatment of CDI, but is a more expensive drug, which could restrict its access in clinical practice.

A standard treatment course of fidaxomicin is estimated to cost on average between €3866.95 and €4128.92 euros, while a standard course of oral vancomycin costs on average between €61.47 and €328.06 euros.⁵ However, costeffectiveness studies have found fidaxomicin to be cost effective in most scenarios, regardless of the severity of the infection.⁶

We would like to add to this reflection that prolonged length of stay in internal medicine wards, which sometimes occurs due to social issues, may increase the risk of nosocomial infection and the use of large spectrum antibiotics, and could consequently increase the risk of *Clostridioides* infection.

Besides the evidence, from our experience, the preferred treatment in Portugal is still vancomycin. Even in relapsing infection, use of fidaxomicin has not been allowed, and prolonged pulsed regimens of oral vancomycin have been advocated by local antibiotic stewardship

REFERENCES

 Nazareth C, Leitão I, Reis E, Inácio H, Martins F, Ramalheira E, et al. Epidemiology of clostridioides difficile infection in Portugal: a retrospective, observational study of hospitalized patients. Acta Med commissions, leading to longer length of hospital stay.

We wonder if the overall costs of occupying a hospital bed on prolonged treatment with oral vancomycin would not be higher than the costs of using fidaxomicin for 10 days.

According to a national cost-effectiveness study of this drug, the bulk of the costs stems from the hospital stay. Although the cost of treatment is higher with fidaxomicin compared with vancomycin (\in 2736 vs \in 71), the overall cost in the following year including length of stay, complications and outpatient appointments is similar between the two drugs. Additionally, the number of recurrences is lower with fidaxomicin.⁷ So, as suggested by Gouveia *et al* in a study using a Markov model to compare one group under vancomycin treatment and another under fidaxomicin, the ratio of the increased costs over the health gain is favorable to the use of fidaxomicin.⁸

So, apart from focusing only on medication costs, we would like to raise awareness to the overall costs of *Clostridioides* infection. We understand that, although vancomycin is an interesting option in case of initial infection, in relapsing infection, and depending on the overall costs associated with prolonged length of stay, fidaxomicin should be a more accessible treatment. Developing national recommendations and standardization of clinical practice would be useful to guide physicians and infection control committees.

AUTHORS CONTRIBUTION

ICC, MA: Draft and approval of the final version of the manuscript.

TF: Conception and approval of the final version of the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors have followed the protocols of their work center on the publication of data. The data was anonymized and none of the authors had access to patient identification. The study was conducted in accordance with the Helsinki Declaration updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

All authors declared no competing interests.

FUNDING SOURCES

The authors received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Port. 2022;35:270-8.

2. Barbosa-Martins J, Mendonça J, Carvalho C, Sarmento H, Mota P, Coutinho C, et al. Clostridium difficile severity and outcome at a north of Portugal healthcare facility. Acta Med Port. 2022;35:279-85.

- Johnson S, Lavergne V, Skinner AM, Gonzales-Luna AJ, Garey KW, 3. Kelly CP, et al. Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 focused update guidelines on management of clostridioides difficile infection in adults. Clin Infect Dis. 2021;73:755-7.
- National Institute for Health and Care Excellence. Clostridioides difficile 4. infection: antimicrobial prescribing NICE guideline 2021 [cited 2022 May 13]. Available from: https://www.nice.org.uk/guidance/ng199.
- 5 Mercer J, Finoli L. Management of clostridioides difficile infection in

Isabel CRUZ CARVALHO 1, Mariana ALVES^{1,2}, Teresa FONSECA^{1,2}

1. Servico de Medicina III. Hospital Pulido Valente. Centro Hospitalar Universitário Lisboa Norte. Lisboa. Portugal

2. Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal

Autor correspondente: Isabel Cruz Carvalho. isabelcruzcarvalho21@gmail.com

Recebido/Received: 17/05/2022 - Aceite/Accepted: 31/05/2022 - Publicado/Published: 01/09/2022 Copyright © Ordem dos Médicos 2022

https://doi.org/10.20344/amp.18578

adults: literature review and 2021 IDSA/SHEA Foc - Pennsylvania Society of Health-System Pharmacists. [cited 2022 Apr 02]. Available from: https://www.pshp.org/news/591183/Management-ofClostridioides-difficile-Infection-in-Adults-Literature-Review-and-2021-IDSASHEA-Foc.htm.

- 6. Stranges PM, Hutton DW, Collins CD. Cost-effectiveness analysis evaluating fidaxomicin versus oral vancomycin for the treatment of clostridium difficile infection in the United States. Value Health. 2013;16:297-304.
- Hall RG 2nd, Cole TJ, Shaw C, Alvarez CA. The risk of clostridioides 7. difficile recurrence after initial treatment with vancomvcin or fidaxomicin utilizing cerner health facts. Antibiotics. 2022;11:295
- 8 Gouveia M. Costa J. Alarcão J. Borges M. Avaliação económica de fidaxomicina no tratamento de infeções por clostridium difficile graves ou recorrentes. Rev Port Farmacoter. 2013;5:264-73.