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Case report

Prognosis with Proton Pump Inhibitor Versus H_2 Blocker Therapy in *Clostridium Difficile* Infection

Istvan Varkonyi[1*], Olena Misak[1], Laszlo Kardos[1], Erzsebet Komaromi[1], Zoltan Szilvassy[2] and Eva Rakoczi[1]

[1]*Kenezy Gyula Hospital and Outpatient Facility, Debrecen, Hungary*

[2]*University of Debrecen Medical and Health Science Center, Debrecen, Hungary*

Abstract

An 83-year-old female patient recovered from her primary *Clostridium difficile*-associated colitis upon antibiotic treatment and the suspension of her regular proton pump inhibitor (PPI) therapy, and had a recurrence of the infection once PPI was restarted. After the treatment of the recurrent episode, the PPI was replaced with a histamine H_2 receptor blocker, and she developed no more relapses. The switch from PPI to a H_2 blocker may have been a recovery factor. More research is encouraged to clarify the extent of the suggested effect.

Keywords: *Clostridium difficile*; prognosis; proton pump inhibitors; histamine H_2 receptor antagonists.

Introduction

The increase in *Clostridium difficile* associated colitis (CDAC) cases and the associated high mortality are unsolved global problems. Main risk factors include age above 65, and recent history of antibiotic treatment and proton pump inhibitor (PPI) therapy [1].

This case report describes an episode of CDAC in an 83-year-old female patient, who recovered from her primary infection after the suspension of her regular PPI therapy, and had a recurrent infection once PPI was restarted. After the treatment of the recurrence, the PPI was replaced with a histamine H_2 receptor blocker; she developed no more relapses.

Case report

The patient's medical history included hypertension, cholelithiasis, and dementia; her medication comprised acetylsalicylic acid and long term PPI therapy. During a 5-week inpatient period at a psychiatric ward, she received beta-lactam treatment for a febrile state. Three weeks after discharge, she was re-admitted for diarrhoea; her stool tests were positive for CD toxin and antigen.

Upon admission, metronidazole for her colitis was accompanied by the suspension of PPI therapy; after six days, she was discharged with improved stool consistency. PPI therapy was immediately restarted at home, and ten days later, she was re-admitted due to diarrhoea. On admission, she was afebrile, hemodynamically stable, with increased C-reactive protein (168 mg/L) and white blood cell count (10.9 G/L); liver, kidney function tests, and ion levels were normal. The admitting physician prescribed 4×250 mg daily of vancomycin. The patient also received PPI therapy, and after 10 days, she was discharged with no symptoms. Her general practitioner switched the PPI to a H_2 blocker, which she continues to receive today. Fourteen months after the relapse, she was placed in an elderly home; her condition is satisfactory, and there has been no recurrence of her diarrhoea.

Discussion

A meta-analysis published in 2012 by Janarthanan [1] demonstrated on observations from 300,000 patients that the proportion of CDAC cases amongst PPI users was as high as 65%. No comparison with H_2 blockers was undertaken. Another meta-analysis by Garey et al [2] investigated the risk factors for CDAC relapse, including acidity neutralizers. The study confirmed the risk increase associated with concomitant use of acidity neutralizers and antibiotics in CDAC; however, two of the three studies had no subgroup differentiation, therefore no stratified effect estimation for acidity neutralizer subgroups was possible. A systematic multicentre meta-analysis by Tleyjeh et al [3] used the data of nearly 202,000 patients to estimate the risks associated with H_2 blockers in CDAC, primarily in a hospital setting, with concurrent antibiotic treatment. The analysis did not address the effect of H_2 blockers on CDAC outcomes.

To date, there is only one population-based analysis addressing the effects on outcomes of PPIs and H_2 blockers in CDAC [4]. The effect of the two medication types was evaluated in a pooled fashion; multiple regression adjusted for age and co-morbidities revealed no relationship between acidity neutralizer treatment and infection severity.

***Corresponding author:** Istvan Varkonyi, Kenezy Gyula Korhaz, Infektologiai Intezet, Debrecen, Tel: +36 52 511 853; Fax: +36 52 511 857; E-mail: i.varkonyi@clintrial-audit.hu & Laszlo Kardos, Kenezy Gyula Korhaz, Infektologiai Intezet, Debrecen, Tel: +36 20 328 8934; Fax: +36 52 511 857; E-mail: l.kardos@orvosbiostat.hu

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In our presented case, the patient relapsed after being restarted on a PPI; however, upon a switch to a H_2 blocker, she developed no additional relapses in 14 months of follow-up.

It is presumable that the switch from PPI to a H_2 blocker was a recovery factor, which could be explained by effect mechanism differences: PPIs are multi-target acidity regulators, as opposed to single-target receptor inhibition by H_2 blockers. The pharmacological effects of PPIs have long been known; however, epidemiological studies into H_2 blocker and PPI treatment have not yet demonstrated the existence of differences between the two that are relevant for therapeutic outcomes [5]. In relation to CDAC infection, the pharmacodynamic differences described here have not been published so far.

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