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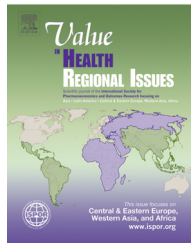

Cost-Effectiveness Comparison of Fidaxomicin and Vancomycin for Treatment of *Clostridium difficile* Infection: A Markov Model Based on Data from a South West Balkan Country in Socioeconomic Transition

Veroljub Marković, PhD, Marina Kostić, MSc, Ivana Ilićković, PhD, Slobodan M. Janković, DSc*

Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

ABSTRACT

Background: Recent studies have shown that fidaxomicin, a novel antibiotic, can reduce the rate of complications and mortality in patients with colitis induced by *Clostridium difficile*. Introduction of fidaxomicin in clinical practice is limited by its high costs. **Objectives:** The purpose of this study was to estimate the cost effectiveness of using fidaxomicin versus vancomycin in patients with colitis induced by *C. difficile* who did not respond to oral metronidazole. **Methods:** We constructed a Markov model that was than simulated by Monte-Carlo simulation using 1000 virtual patients with colitis induced by *C. difficile*. The perspective in our model was institutional. The time horizon was 3 months. Values of transition probabilities and therapy outcomes were estimated from the available literature, the prices of health services were obtained from the Republic Institute for Health Insurance Tariff Book, and the price of fidaxomicin was derived from data gained from the drug manufacturer. **Results:** The total costs of treating one statistical patient for 3 months with fidaxomicin were higher (48,106.19 ± 118.07 Republic of Serbia dinars [RSD]; 95% confidence interval 47,988.12–48,224.27) than the total costs of treating with vancomycin (25,872.85 ± 41.44 RSD; 95% confidence interval 25,831.41–25,914.29). Our results showed that the treatment of infections induced by *C. difficile* with fidaxomicin correlated with a lower rate of mortality and with a smaller number of colectomies. The incremental cost-effectiveness ratio of fidaxomicin versus vancomycin for colitis induced by *C. difficile* per saved life was estimated at 2.97 million RSD and for one avoided colectomy at 10.07 million RSD. **Conclusions:** Results of our model indicate that fidaxomicin is a cost-effective therapy compared with vancomycin in patients with colitis induced by *C. difficile* if the outcome is life-year saved. However, if the outcome is the number of avoided colectomies, then fidaxomycin is not a cost-effective option compared with vancomycin.

Keywords: colitis induced by *C. difficile*, cost-effectiveness, fidaxomicin.

Introduction

Clostridium difficile–induced colitis is a serious consequence of overzealous utilization of broad-spectrum antibiotics, with a rising rate of mortality [1]. *C. difficile* is a Gram-positive spore-forming bacillus, and the NAP1/BI/027 strain of this bacterium is characterized with an extremely high virulence [2,3]. Diarrhea and abdominal infections caused by *C. difficile* correlate with longer hospitalization, higher costs of treatment, and increased rate of morbidity and mortality in these patients [4,5].

Antibiotics, especially clindamycin, semi-synthetic penicillins, cephalosporins, and fluoroquinolones, are among the most frequent causes of colitis and other forms of abdominal infections caused by *C. difficile*. Gastrointestinal or other type of surgery, prolonged hospitalization, compromised immune status of a patient or any kind of serious comorbidity, advanced age, parturition, and heart transplantation are well known risk factors for *C. difficile*–induced abdominal infections [6]. The *C. difficile* infection is commonly presented as diarrhea with varying degrees of intensity, caused by *C. difficile* toxins, especially by toxin A.[4] Because of the intense inflammatory potential of toxin A, and cytotoxic effects of toxin B, the integrity of mucous membranes is harmed with ulcers and covered with white-gray fibrin's layers, which are known as pseudomembranes [7].

The therapeutic approach to *C. difficile*–induced disease includes withdrawal of suspicious precipitating antibiotics, maintenance of electrolyte balance, and adequate fluid replacement. This kind of treatment is effective in 25% of the patients [8]. However, for progressive form of *C. difficile*–induced disease or in the case of nonresponse to standard therapy, treatment with specific antibiotics is required [7]. Oral metronidazole is the first-line antibiotic in less severe forms of *C. difficile* infections, while for severe forms and in critically ill patients, oral vancomycin is the drug of choice [8]. Despite adequate response on oral

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* *Address correspondence to:* Marina Kostić, Faculty of Medical Sciences, Department of Pharmacology and Toxicology, University of Kragujevac, Svetozara Markovica 69, 34000 Kragujevac, Serbia.

E-mail: marrina2006kg@yahoo.com.

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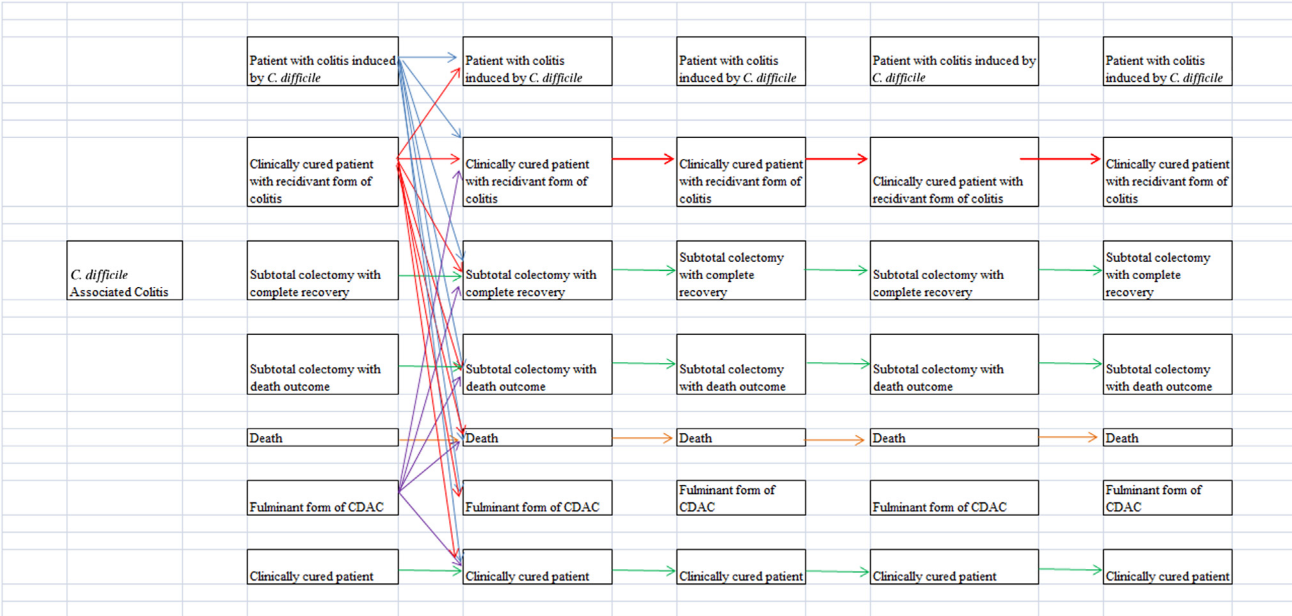

Fig. 1 – Markov model for fidaxomicin treatment versus vancomycin in patients with *Clostridium difficile*–associated colitis. CDAC, *Clostridium difficile*–associated colitis.

metronidazol or oral vancomycin, therapeutic benefit is diminished by a high rate of recurrence [1].

Fidaxomicin is a novel macrocyclic antibiotic characterized by low absorption, excellent efficacy, and higher activity in vitro and in vivo against the NAP1/BI/027 strain of *C. difficile* than does vancomycin [9]. The rate of recurrence of *C. difficile*–induced disease after treatment with fidaxomicin is 15.4%, which is lower than after treatment with vancomycin, 25% [1]. The results of

Table 1 – Transition matrix for a patient treated with fidaxomicin.

B

A	Transition matrix (from A to B)	Patient with CDAC	Clinically cured patient with recidivant form of colitis	Subtotal colectomy with complete recovery	Subtotal colectomy with death outcome	Death	Fulminant form of CDAC	Clinically cured patient
	Patient with CDAC	0.07	0.13	0.00712	0.003996	0.027	0.018884	0.741522
	Clinically cured patient with recidivant form of colitis	0.07	0.119931	0.00712	0.003996	0.027	0.018884	0.753069
	Subtotal colectomy with complete recovery	0	0	1	0	0	0	0
	Subtotal colectomy with death outcome	0	0	0	1	0	0	0
	Death	0	0	0	0	1	0	0
	Fulminant form of CDAC	0	0.03325	0.25	0.25	0.25	0	0.21657
	Clinically cured patient	0	0	0	0	0	0	1

CDAC, *Clostridium difficile*–associated colitis.