Efficacy of 30-day treatment of fidaxomicin for multiple recurrent Clostridium difficile infection

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INTRODUCTION

Recurrent Clostridium difficile (rCDI) infections pose major challenges to patients and to the healthcare system. rCDI is associated with multiple, prolonged hospitalizations and significantly higher costs. It can also lead to chronic, severe diarrhea, coloectomy or death. Fecal microbiota transplantation (FMT) is an effective treatment but its long-term safety remains unknown, and approximately 10% of patients do not respond to multiple FMTs. A 30-day course of fidaxomicin was evaluated for treatment of multiple rCDI, including those who did not respond to multiple FMTs. Fidaxomicin was chosen because it disrupts the fecal microbiome less than vancomycin.

METHODS

29 adult patients with at least 2 episodes of recurrent CDI were initiated on fidaxomicin 200mg when they experienced new episode of CDI (symptoms plus positive for CD toxin gene by polymerase chain reaction). These patients continued with fidaxomicin 200mg twice daily for 10 days, and 200mg once daily for 20 additional days in an open label clinical trial. The primary endpoints were a clinical response at the completion of 30-day course of fidaxomicin and a sustained clinical response at week 8 from the last dose of fidaxomicin. Patient health related quality of life was evaluated throughout the treatment using the RAND-36 Item Health Survey (copyright© the RAND Corporation).

RESULTS

24 of the 29 patients (83%) experienced clinical resolution of CDI-related symptoms at the completion of 30-day fidaxomicin treatment. 22 of the 29 patients had a sustained clinical response with the overall cure rate of 76% (22/29). Eleven of the 29 patients had multiple FMTs and were enrolled into this study as they failed FMTs. Eight of the 11 patients (73%) of these patients had a sustained clinical response. Statistically significant improvements (p<0.05) in multiple domains of quality of life according to the RAND-36 Item Health Survey were observed. Fidaxomicin did not disrupt the microbiota of the colon to the extent that vancomycin did as measured by the ratio of Bacteroides/Prevotella.

DISCUSSION AND CONCLUSION

Metagenomic studies show patients with rCDI lack diversity and richness of their colonic microbiota and remain in a state of chronic dysbiosis.

The efficacy of standard antibiotics for rCDI is limited as oral vancomycin and metronidazole suppress the growth of Bacteroides fragilis group which protect against the proliferation of C. difficile. In vitro study has shown that fidaxomicin has no activity against B. fragilis and may explain the reduction in C. difficile recurrences. The persistent disruption of healthy colonic flora may be the reason for recurrences. Rates of recurrence are greater than 50% for those over the age of 65. There are lack of published clinical trials examining the efficacy of any treatment for rCDI.

While promising Fecal Microbiota Transplantation (FMT) has limitation as majority of healthcare facilities do not have the infrastructure available to offer the treatment as it requires readily available donors and laboratories to screen donors and manufacture treatments in a timely manner.

An extended regimen of fidaxomicin is an effective treatment for adults with multiple rCDI and in restoring quality of life, including those who failed FMTs.

REFERENCES