Tigecycline for Severe Clostridium difficile Infection

Ashley Thomas, MD; Farhan Khan, MD; Mark R. Wallace, MD
Orlando Regional Medical Center, Orlando, FL

SUMMARY

Clostridium difficile is the most common infectious etiology of nosocomial diarrhea. Newer agents have been developed for treatment of mild to moderate disease but few agents are available for severe and severe complicated cases, which are characterized by hypotension/shock, ileus or megacolon.

Oral vancomycin is currently the recommended anti-infective agent for severe Clostridium difficile infection, but intravenous tigecycline has been suggested as adjunctive or even alternative therapy.

Our retrospective analysis reviews outcomes of patients at our institution with severe Clostridium difficile infection receiving intravenous, tigecycline as an adjunct to standard therapy.

We also conducted an unmatched retrospective case-control analysis to compare outcomes between patients who did and did not receive intravenous tigecycline.

A total of 44 cases of severe complicated Clostridium difficile infection were identified, 18 of which had received intravenous tigecycline.

In our analysis no statistically significant differences were found in rates of death, colectomy, recurrence or cure.

INTRODUCTION

The incidence and severity of Clostridium difficile infections (CDI) have increased over the past decade. Despite the availability of efficacious therapies (vancomycin, metronidazole, fidaxomycin), severe cases occur and often cause severe morbidity or mortality.

Oral vancomycin has been the mainstay of current treatment of severe disease, but there are significant limitations to its use in patients with ileus, megacolon or critical illness.

Hepers et al. suggested that IV tigecycline, an agent with in vitro activity against C. difficile, might be useful in severe C. difficile infections. In their report, it appeared efficacious in 4 patients.

Some of our ID clinicians have been using IV tigecycline in selected cases of Clostridium difficile - we review the outcomes.

MATERIALS AND METHODS

All patients admitted to our 808-bed medical center during 2011 with the diagnosis of Clostridium difficile infection were reviewed. A total of 473 inpatient case records of Clostridium difficile infections were examined and stratified according to published severity criteria by Zar et al. Diagnosis of CDI was established by positive C. difficile toxin B stool PCR (Cepheid GeneXpert®) and compatible clinical syndrome. CDI cases were included if they had received IV tigecycline >48 hours as part of their regimen. Observed outcomes included overall survival, rate of colectomy, recurrence, reported drug adverse effects, and time to resolution of diarrhea. Patients receiving IV tigecycline were further compared to the patient group receiving standard therapy in a retrospective case-control analysis.

RESULTS

Eighteen patients received tigecycline >48 hours in addition to both oral vancomycin and IV metronidazole. Median age was 55 years; all fulfilled the highest severity criteria, i.e. severe complicated CDI per IDSA guidelines (hypotension, shock, ileus or megacolon). 14 out of 18 patients survived (78%); 4 died of multi-organ failure and septic shock. 12 of 14 survivors were cured without colectomy. Median WBC at the time of diagnosis was 15’000/µl. at the initiation of tigecycline with a 24% decrease by day 3. Median duration till resolution of diarrhea was 4 days. In 2 out of 18 cases (11%) tigecycline had to be stopped due to nausea and vomiting. 2 out of 14 surviving patients (14%) developed recurrent CDI within 5 months.

The control group of 26 patients had a median age of 63 years and median WBC at time of diagnosis of 15’500/µl. Their WBC increased during the first 3 days of standard treatment by 5%. 3 out of 21 surviving patients (14%) developed recurrent CDI.

CONCLUSIONS

Both tigecycline treatment group and the control group showed similar outcomes. No statistically significant difference was found between the two groups. Average time to resolution of diarrhea and temperature were also not significantly different.

Possible interpretations:

1. Tigecycline provides no additional benefit to reduce mortality, recurrence or colectomy.

2. Tigecycline was used ‘too late’ in the disease course for any detectable effect to manifest.

3. Tigecycline may be a useful adjunct, however the sample size was too small.

Despite demonstrated in vitro activity of tigecycline against Clostridium difficile as well as non-induction of toxin production, the current study does not support the use of IV tigecycline for severe Clostridium difficile infection.

REFERENCES


