ORIGINAL ARTICLE

Evaluation of an Oral Vancomycin Capsule for the Treatment of *Clostridioides difficile* Infections in an Academic Medical Center in Thailand

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Background: The oral capsule formulation of vancomycin (Vancin-S) recently became available in Thailand; therefore, information on its effectiveness and safety in treating *Clostridioides difficile* infection (CDI) has not been available.

Objective: To evaluate CDI outcomes and to access safety at the HRH Princess Maha Chakri Sirindhorn Medical Center (MSMC) following recommended oral vancomycin capsule treatment.

Materials and Methods: Retrospective review of MSMC patients prescribed oral vancomycin capsule between December 1, 2022 and August 31, 2023. Inclusion and exclusion criteria were applied, analyzing CDI outcomes post- oral vancomycin capsule treatment and within 90 days thereafter. Safety of oral vancomycin capsule usage was also assessed.

Results: Of the 41 patients prescribed oral vancomycin capsule, 13 met inclusion criteria and did not meet with exclusion criteria. There were eight definite and five probable CDI cases, with 12 initial treatments and one initial fulminant treatment. The incidence of CDI in the MSMC was 21.33 person-year. Clinical improvements were observed by the tenth day, with one patient experiencing residual symptoms, subsequently testing negative for CDI. All patients were cured. The oral vancomycin capsule treatments were well-tolerated without significant adverse effects. No CDI recurrence was detected among 12 cases followed up within 90 days post-treatment.

Conclusion: The oral vancomycin capsule demonstrates safety and potential efficacy for CDI treatment in Thailand.

Keywords: Oral vancomycin; *Clostridioides difficile* infection; Thailand

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Clostridioides difficile infection (CDI) stands as one of the most prevalent hospital-associated infections worldwide[1]. In Thailand, CDI remains a significant concern, with reported prevalence ranging from 4.8% to 52.2% depending on study parameters and population demographics[2,3].

The current guidelines for CDI treatment, as outlined by the Infectious Diseases Society of America (IDSA), the Society for Healthcare Epidemiology of America (SHEA)[1], and the American College of Gastroenterology (ACG)[4], emphasize fidaxomicin as the preferred treatment due to favorable outcomes observed in various studies[5-8]. However, in fidaxomicin-limited settings, vancomycin remains an acceptable alternative[1]. The current treatment recommendations are summarized in Table 1.

Notably, fidaxomicin is not currently available in Thailand. Antimicrobial susceptibility studies of *Clostridioides difficile* (CD) isolated in Thailand revealed no resistance to fidaxomicin or vancomycin among the strains studied[9]. While some resistances to vancomycin in Thailand were recently reported[10], vancomycin remains the primary stay for CDI treatment in Thailand.

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Table 1. The IDSA/SHEA 2021 treatment recommendations for *Clostridioides difficile* infection in adults focused on the medicines available in Thailand[1]

Category	Treatments	Comments
Initial episode	Oral vancomycin 125 mg 4 times daily for 10 days	Fidaxomicin is not available in Thailand
	Oral metronidazole 500 mg 3 times daily for 10-14 days	Alternative for non-severe *Clostridioides difficile* infection
First recurrence	Oral vancomycin in a tapered and pulsed regimen	Fidaxomicin and bezlotoxumab are not available in Thailand
	Oral vancomycin 125 mg 4 times daily for 10 days	If metronidazole was used in the first episode
Second or subsequent recurrence	Oral vancomycin in a tapered and pulsed regimen	Fidaxomicin, rifaximin and bezlotoxumab are not available in Thailand
Fulminant	Oral vancomycin 500 mg 4 times daily and should add intravenous metronidazole 500 mg every 8 hours together	Consider vancomycin enema if ileus is present

Previously, oral vancomycin was unavailable in Thailand, necessitating healthcare providers to prepare intravenous vancomycin solutions for oral administration. The recent introduction of Vancin-S, an oral vancomycin capsule, in Thailand in late 2022[11] marks a significant development. However, information regarding the effectiveness and safety of oral vancomycin capsule for CDI treatment remains unavailable.

Objective

The primary objectives were to evaluate the outcomes of CDI cases at the HRH Princess Maha Chakri Sirindhorn Medical Center (MSMC) following recommended oral vancomycin capsule treatment and to assess the safety profile of oral vancomycin capsule use.

The secondary objective was to analyze CDI outcomes within 90 days of post-treatment completion.

Materials and Methods

All the CDI patients at the MSMC who were prescribed oral vancomycin capsule between December 1, 2022 and August 31, 2023 were retrospectively reviewed for the study. The patients who met the inclusion criteria and did not meet with exclusion criteria were analyzed for the outcomes of their CDIs after oral vancomycin capsule treatment and within 90 days after the completion of the treatment. All oral vancomycin capsule usage cases were reviewed for any documentation of adverse events related to the oral vancomycin capsule to determine any safety issues. Oral vancomycin capsules were donated by the Siam Pharmaceutical Co., Ltd. from December 2022 until the official availability at the MSMC.

The CD toxins and the glutamate dehydrogenase (GDH) testing assays were done by the MSMC laboratory using Operon® Simple GDH-Toxins test. The CD polymerase chain reaction (PCR) tests were done by the outside laboratory using Certest™ VIASURE *Clostridium difficile* Toxins A+B real time PCR Detection kit.

Inclusion criteria

The inclusion criteria consisted of adult patients of the MSMC with at least a positive test with either of the CD toxins or the GDH testing assay or the CD PCR test and diarrhea (loose or watery stools three or more times a day) or evidence of colitis.

Exclusion criteria

The exclusion criteria included either no confirmation for the CDI from a positive for GDH but negative for the CD toxins and the CD PCR test, the incomplete treatment regimen (less than 10 days of oral vancomycin capsule treatment) or the inappropriate treatment (not according to the current treatment guidelines).

Definitions

Definite CDI cases were cases who met the inclusion criteria and had a positive test for the CD toxin(s) or positive test for the GDH assay and confirmed with the positive CD PCR test later[4].

Probable CDI cases were cases who met the inclusion criteria and had a positive test for the GDH assay but negative test for the CD toxins and no availability of the CD PCR test.

Ethics approval

The present study received approval from the Srinakharinwirot University Ethics Committee on September 10, 2023, protocol code SWUEC-663003.

Results

Forty-one cases were prescribed oral vancomycin capsule within the study period. Eleven cases were not included in the present study because they were

empirically treated with oral vancomycin capsule without the positive CD tests as ten cases had the negative CD tests, and one case was without the CD test. Fourteen cases were excluded because they had positive tests for the GDH assay but negative tests for the CD toxins and the CD PCR tests later. These 14 cases had the confirmation of negative CD PCR tests from day-1 to day-5 after the initiation of oral vancomycin capsule treatment. Three more cases were excluded from the study as one case had treatment less than 10 days and two cases had treatments not according to the current treatment guidelines. Therefore, 13 CDI cases including eight definite CDI cases and five probable CDI cases were reviewed for their CDI outcomes, which were 12 initial CDI treatments and one initial fulminant treatment for the patient with hypotension and ileus. The present study flowsheet is summarized in Figure 1.

There were 16 CDI cases at the MSMC that included 13 CDI study cases and three excluded cases throughout the 9-month study period, with nine definite CDI cases and seven probable cases diagnosed. The incidence of CDI was 21.33 person-year.

The 13 CDI cases achieved clinical improvements on the tenth day of the oral vancomycin capsule treatment course but one case, which is case 4 from Table 2, still had loose stool, so the patient was tested for CD tests to evaluate the outcome after the treatment. His CD tests were negative for the CD toxins, the GDH assay, and the CD PCR test. All were cured after the 10-day course of oral vancomycin capsule treatment. The outcomes of the definite CDI cases and the probable CDI cases after the treatment are summarized in Table 2 and 3.

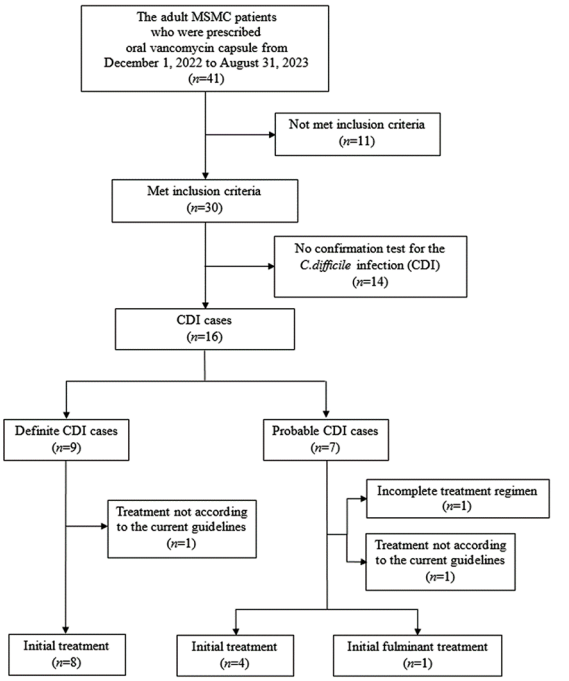

Figure 1. The study flowsheet.

The oral vancomycin capsule treatments were well tolerated and did not show any significant adverse effects after the treatment in these 13 CDI cases and in the other 28 cases who had oral

Table 2. The outcomes of the definite CDI cases after the treatment and within 90 days after the completion of the treatment

No.	Age (years)	Initial CD tests			Dosage of vancomycin	Route of administration	End of treatment				Within 90 days after treatment			
		Toxin A/B	GDH	PCR			Toxin A/B	GDH	PCR	Outcome	Toxin A/B	GDH	PCR	Outcome
1	71	+	+	N/A	125 mg 4 times daily for 10 days	Mouth	N/A	N/A	N/A	Cure	N/A	N/A	N/A	No recurrence
2	79	–	+	+	125 mg 4 times daily for 10 days	Mouth	N/A	N/A	N/A	Cure	N/A	N/A	N/A	No recurrence
3	47	+	+	N/A	125 mg 4 times daily for 10 days	Mouth	N/A	N/A	N/A	Cure	N/A	N/A	N/A	No recurrence
4	46	–	+	+	125 mg 4 times daily for 10 days	NG tube	–	–	–	Cure	–	+	–	No recurrence
5	70	+ (B)	–	N/A	125 mg 4 times daily for 10 days	Mouth	N/A	N/A	N/A	Cure	N/A	N/A	N/A	No recurrence
6	64	+	+	N/A	125 mg 4 times daily for 10 days	NG tube	N/A	N/A	N/A	Cure	N/A	N/A	N/A	No recurrence
7	62	+ (B)	+	N/A	125 mg 4 times daily for 10 days	Mouth	N/A	N/A	N/A	Cure	N/A	N/A	N/A	No recurrence
8	66	–	+	+	125 mg 4 times daily for 10 days	Mouth	N/A	N/A	N/A	Cure	LFU	LFU	LFU	LFU

CD=*Clostridioides difficile*; GDH=glutamate dehydrogenase; LFU=loss to follow-up; N/A=not available; NG tube=nasogastric tube; PCR=polymerase chain reaction

Table 3. The outcomes of the probable CDI cases after the treatment and within 90 days after the completion of the treatment

No.	Age (years)	Initial CD tests			Dosage of vancomycin	Route of administration	End of treatment				Within 90 days after treatment			
		Toxin A/B	GDH	PCR			Toxin A/B	GDH	PCR	Outcome	Toxin A/B	GDH	PCR	Outcome
1	51	–	+	N/A	125 mg 4 times daily for 10 days	Mouth	N/A	N/A	N/A	Cure	N/A	N/A	N/A	No recurrence
2	85	–	+	N/A	125 mg 4 times daily for 10 days	NG tube	N/A	N/A	N/A	Cure	N/A	N/A	N/A	No recurrence
3	25	–	+	N/A	500 mg 4 times daily for 10 days (and metronidazole IV every 8 hours)	Mouth	N/A	N/A	N/A	Cure	N/A	N/A	N/A	No recurrence
4	65	–	+	N/A	125 mg 4 times daily for 10 days	Mouth	N/A	N/A	N/A	Cure	N/A	N/A	N/A	No recurrence
5	78	–	+	N/A	125 mg 4 times daily for 10 days	Mouth	N/A	N/A	N/A	Cure	N/A	N/A	N/A	No recurrence

CD=*Clostridioides difficile*; GDH=glutamate dehydrogenase; IV=intravenous; N/A=not available; NG tube=nasogastric tube; PCR=polymerase chain reaction

vancomycin capsule use but were not included or were excluded from the present study. The authors reviewed all 41 medical records during the period of the oral vancomycin capsule use and did not find any documentation to point out any adverse events related to the oral vancomycin capsule.

There were twelve cases with follow-up data within 90 days after the completion of the treatment. One case was lost to follow-up after the treatment. One case, which was case 4 from Table 2, had recurrent diarrhea in the sixth week after the completion of the treatment. Again, the patient was tested for CD tests to determine the possibility of CDI recurrence. The results of the CD tests were positive GDH assay but negative CD toxins and CD PCR test. The CDI recurrence was excluded. The other eleven cases were without diarrhea within 90 days after the completion of the study treatment so there was no CDI recurrence. The outcomes of the definite CDI cases and the probable CDI cases within 90 days after the completion of the treatment are also summarized in Table 2 and 3.

Discussion

CDI remained prevalent at the MSMC throughout the 9-month study period. The incidence of CDI was 21.33 person-year. It is likely that more cases occurred than those detected in the present study, as alternative CDI treatment regimens such as vancomycin solution or metronidazole, were available at the MSMC during this period.

Diagnostic practices at the MSMC involved screening for both CD toxins and the GDH assay in suspected cases. Positive CD toxins confirmed CDI, while negative CD toxins and positive GDH assay prompted CD PCR testing for confirmation. However, the CD PCR test, conducted by an outside laboratory, faced delays, particularly during extended holiday periods, with turnaround times sometimes lasting five to seven days.

Despite CD PCR test delays, CDI confirmation may not have been significantly impacted. Research by Saha et al. indicated a median time to negative PCR test of nine days from treatment initiation[12]. In the present study, CD PCR confirmation delays ranged from one to five days.

The oral vancomycin capsule demonstrated greater convenience compared to vancomycin solution. It eliminated the need for healthcare personnel or patients to dissolve vancomycin powder, and dosage adjustment was unnecessary. Additionally, it could be easily administered via a nasogastric tube when required.

The safety of oral vancomycin capsule treatment was evident, with all 41 cases tolerating the medication well without significant adverse effects or premature termination. Discontinuation of oral vancomycin capsule occurred only upon completion of CDI treatment or negative CD PCR test results. Furthermore, evidence suggests that orally administered vancomycin at 125 mg four times daily is not absorbed from the gastrointestinal tract[13]. However, concerns remain regarding absorption in patients with significant renal impairment and bowel injury[14].

All definite and probable CDI patients were cured with a 10-day course of oral vancomycin capsule treatment, with no CDI recurrence within 90 days post-treatment completion. These findings support the safety and effectiveness of oral vancomycin capsule for CDI treatment at the MSMC.

While data suggest the safety and efficacy of

oral vancomycin capsule for CDI treatment, the study had limitations, including a small number of definite CDI cases. Nonetheless, given the low incidence of vancomycin-resistant CD strains in Thailand[9,10] and the necessity for improved symptomatic CDI treatment[15,16], further studies with larger case cohorts would validate the efficacy of this oral vancomycin capsule.

Conclusion

The oral vancomycin capsule demonstrates safety and potential efficacy for CDI treatment in Thailand.

What is already known on this topic?

Vancomycin is an alternative for the treatment of CDI. In Thailand, oral vancomycin was prepared by dissolving intravenous vancomycin solutions for oral administration.

What does this study add?

The oral vancomycin capsule was recently available in Thailand. The oral vancomycin capsule demonstrates safety and potential efficacy for CDI treatment in Thailand.

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Conflicts of interest

The authors declare no conflicts of interest.

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