The role of anion-exchange resins in the treatment of antibiotic-associated pseudomembranous colitis

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Antibiotic-associated pseudomembranous colitis (AAPMC) has been shown to recur in 5% to 55% of cases.[1] The illness and cost associated with the treatment of relapses have presented a therapeutic dilemma for clinicians. Vancomycin and metronidazole have frequently been used in such cases but are occasionally unsuccessful. This dilemma has prompted clinicians to question the role of anion-exchange resins in the treatment of AAPMC.

Anion-exchange resins are thought to act by binding *Clostridium difficile* cytotoxin (toxin B) in the colon.[2] On a weight basis colestipol appears to be more effective than cholestyramine in binding cytotoxin; however, the clinical significance of this finding is unknown.[3] Anion-exchange resins have been reported to bind vancomycin when used in combination; however, there appears to be no immediate loss of vancomycin's antibacterial activity.[2] We are unaware of any published data describing an in-vitro interaction between the resins and metronidazole.

We found several reports of the use of anion-exchange resins for AAPMC (Table 1).[4-12] The only randomized controlled clinical trial, by Keighley,[9] unfortunately had three deficiencies: (a) there were only about 13 patients per treatment group, (b) there was no follow-up to assess relapses and (c) the relaxed entry criteria allowed the inclusion of some cases in which only postoperative diarrhea had been documented and *C. difficile* detected in stool samples (i.e., cytotoxin was not detected). Keighley found that vancomycin therapy was associated with rapid elimination of *C. difficile* and its cytotoxin, whereas neither colestipol nor placebo had any effect on the organism or its cytotoxin. However, such a response to vancomycin would be expected, especially after a short follow-up period. Assessment of the response only at the end of treatment provides an inadequate evaluation of outcome since many patients may subsequently suffer a relapse.

Evidence of the possible benefit of combined anion-exchange resin and vancomycin therapy has been provided by Bartlett and associates,[8] Tedesco[10] and, most recently, Pruksananonda and Powell.[12]

In addition to the studies in Table 1 we have become aware of various anecdotal reports, personal opinions and unreferenced personal communications about the use of anion-exchange resins in the treatment of AAPMC. Recommendations have included the following: (a) resins should not be used in any circumstance, (b) they should be used in mild cases and (c) they should be given only in cases of multiple relapses with or without concomitant antibiotic therapy. These reports appeared to have little scientific merit.

The broad spectrum of anecdotal opinions and the lack of controlled trials and standardized treatment regimens succeed only in completely confusing clinicians. Prospective randomized trials are needed to delineate better the role of anion-exchange resins in the treatment of AAPMC. Until then the only rational use is in cases of multiple relapses after appropriate antimicrobial therapy. In such cases the resin should be given in combination with either vancomycin or metronidazole. However, until the

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clinical significance of the in-vitro binding of the resins with vancomycin is clarified the agents should be administered at separate times. We feel that anion-exchange resins have no role in the initial management of AAPMC, especially if the disease is mild.

References

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2. Taylor NS, Bartlett JG: Binding of *Clostridium difficile* cytotoxin and vancomycin by anion-exchange resins. *J Infect Dis* 1980; 141: 92–97

Table 1: Summary of clinical studies of anion-exchange resins in the treatment of antibiotic-associated pseudomembranous colitis

Study	Type of study	Type of management	No. of patients*	Regimen†	Duration of follow-up	No. of patients with favourable response‡
Burbige et al, 1975[4]	Case report	Initial	2	Cholestyramine, 4 g tid for 2 wk	–	2
Sinatra et al, 1976[5]	Pediatric case report	Initial	1	Cholestyramine, 0.5 g qid for 10 d	6 mo	1
Kreutzer et al, 1978[6]	Uncontrolled trial	Initial	12	Cholestyramine, 4 g tid (average dose) for mean of 9 d	"Several weeks"	12
Tedesco et al, 1979[7]	Retrospective review	Initial	7	Cholestyramine, 4 g tid for mean of 6 d	–	1
Bartlett et al, 1980[8]	Retrospective review	For relapse after vancomycin	2	Cholestyramine and vancomycin (dose and duration unknown)	–	2
Keighley, 1980[9]	Randomized controlled trial	Initial	7 (12)	Vancomycin, 125 mg qid for 5 d	To end of treatment	6
			5 (14)	Colestipol, 10 g qid for 5 d		0
			6 (14)	Placebo for 5 d		0
Tedesco, 1982[10]	Uncontrolled trial	For relapse after vancomycin, 125 mg qid	11	Colestipol, 5 g bid for up to 28 d, and vancomycin, 125 mg bid for 5–7 d then 125 mg/d for 5–7 d	≥ 6 wk	11
Kunimoto et al, 1986[11]	Case report	For relapse after vancomycin, metronidazole and bacitracin	1	Cholestyramine, 4 g tid for 12 mo	6 and 15 mo	1
Pruksananonda et al, 1989[12]	Pediatric case report	For relapse after vancomycin and metronidazole	1	Cholestyramine, 120 mg/kg tid for 4 wk, then dose tapered over 3 wk	7 mo	1
			1	Vancomycin, 40 mg/kg daily for 14 d; at 10 d cholestyramine, 120 mg/kg qid for 4 wk, added, then dose tapered over 3 wk	3 mo	1

*No. of cytotoxin-positive patients who met our inclusion criteria.
†All drugs were given orally.
‡Eradication of cytotoxin from stool samples.

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5. Sinatra F, Buntain WL, Mitchell CH et al: Cholestyramine treatment of pseudomembranous colitis. *J Pediatr* 1976; 88: 304-306
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11. Kunimoto D, Thomson ABR: Recurrent *Clostridium difficile*-associated colitis responding to cholestyramine. *Digestion* 1986; 33: 225-228
12. Pruksananonda P, Powell KR: Multiple relapses of *Clostridium difficile*-associated diarrhea responding to an extended course of cholestyramine. *Pediatr Infect Dis J* 1989; 8: 175-178

Conferences

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June 24-27, 1990: 3rd Symposium on Violence and Aggression
Sheraton-Cavalier, Saskatoon
Division of Extension and Community Relations, Rm. 105, Kirk Hall, University of Saskatchewan, Saskatoon, Sask. S7N 0W0; (306) 966-5539

June 24-29, 1990: International Society of Hypertension 13th Scientific Meeting
Montreal Convention Centre
Secretariat, 609-1410 Stanley, Montreal, PQ H3A 1P8; (514) 287-1070, FAX (514) 287-1248

June 24-29, 1990: 3rd International Conference on Emergency Medicine (hosted by the Canadian Association of Emergency Physicians, in association with the American College of Emergency Physicians, the Australian College for Emergency Medicine and the Casualty Surgeons Association of Great Britain)
Royal York Hotel, Toronto
Continuing Education, Faculty of Medicine, University of Toronto, Medical Sciences Building, Toronto, Ont. M5S 1A8; (416) 978-2718

June 25, 1990: Canadian Conference on Health Services Research
Westin Harbour Hotel, Toronto
Dr. Jorge Segovia, Chair Planning Committee, Division of Community Medicine and Behavioural Sciences, Faculty of Medicine, Health Sciences Centre, Memorial University of Newfoundland, St. John's, Nfld. A1B 3V6; (709) 737-6693; FAX (709)737-6400

June 25-28, 1990: Conference on Molecular and Cellular Mechanisms of Alcohol and Anesthetics
Calgary
New York Academy of Sciences, 2 E 63rd St., New York, NY 10021

June 25-29, 1990: Canadian Public Health Association 81st Annual Conference
Harbour Castle Westin, Toronto
Canadian Public Health Association, 400-1565 Carling Ave., Ottawa, Ont. K1Z 8R1, (613) 725-3769, FAX (613) 725-9826; or Ontario Public Health Association, 202-468 Queen St. E, Toronto, Ont. M5A 1T7, (416) 367-3313, FAX (416) 367-2844

June 28-30, 1990: 25th Meeting of the Canadian Congress of Neurological Sciences
Banff Springs Hotel, Banff, Alta.
Permanent Secretariat, Canadian Congress of Neurological Sciences, PO Box 4220, St. C, Calgary, Alta. T2T 5N1; (403) 229-9544

July 18-21, 1990: Genetics Society of America 59th Annual Meeting (cohosted by the Genetics Society of Canada)
San Francisco Hilton
Administrative Office, Genetics Society of America, 9650 Rockville Pike, Bethesda, MD 20814; (301) 571-1825

Aug. 10-13, 1990: 6th International Conference on Pharmacoepidemiology
Anaheim Marriott Hotel, Anaheim, Calif.
Dr. Stanley A. Edlavitch, Department of Epidemiology and Biostatistics, McGill University, 1020 Pine Ave. W, Montreal, PQ H3A 1A2; (514) 398-8983, FAX (514) 398-4503

Aug. 27-29, 1990: Canadian Health Economics Research Association 4th Conference: Restructuring the Health Services System — How Do We Get There from Here?
University of Toronto
Gail Thompson, conference coordinator, Institute of Health Management, University of Toronto, 12 Queen's Park Cres. W, Toronto, Ont. M5S 1A8, (416) 978-8384, FAX (416) 978-7350; or Dr. Raisa Deber, conference chair, Department of Health Administration, University of Toronto, (416) 978-8366

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