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## **Outcomes of Clostridium difficile-Associated Disease Treated With Metronidazole or Vancomycin Before and After the Emergence of NAP1/027.**

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**OBJECTIVE:** To reassess the comparative efficacy of vancomycin versus metronidazole in the treatment of Clostridium difficile-associated disease (CDAD) after the emergence in 2003 of the hypervirulent NAP1/027 strain. **METHODS:** A retrospective cohort study was conducted in a tertiary-care Canadian hospital among 1,616 patients treated initially with metronidazole (N = 1,360), vancomycin (N = 219), or both (N = 37), between 1991 and 2006, and followed for 60 days after diagnosis. Primary outcome was severe/complicated CDAD (SC-CDAD) defined as any of: (a) death within 30 days, (b) septic shock, (c) megacolon, (d) perforation, or (e) emergency colectomy. Adjusted odds ratios (AOR) and their 95% confidence intervals (CI) were calculated, stratifying into pre-epidemic (1991-2002) and epidemic (2003-2006) periods. Secondary outcome was recurrence within 60 days. **RESULTS:** Risk factors for SC-CDAD were the same in both periods: age  $\geq 65$  yr, male sex, immunosuppression, hospital acquisition, tube feeding, short duration of diarrhea, fever, elevated leukocytosis, or creatinine. Adjusting for confounders and using metronidazole therapy as baseline, vancomycin therapy was associated with a lower probability of developing SC-CDAD in 1991-2002 (AOR 0.21, 95% CI 0.05-0.99, P= 0.048) but not during 2003-2006 (AOR 0.90, 95% CI 0.53-1.55, P= 0.71). For both metronidazole and vancomycin, risk of recurrence increased in 2003-2004 but decreased in 2005-2006. **CONCLUSIONS:** Loss of superiority of vancomycin over metronidazole coincided with the emergence of NAP1/027. Toxin hyperproduction by NAP1/027 might be such that the disease follows its natural course. Novel therapeutic approaches are needed. The higher risk of recurrence in 2003-2004 probably reflected reinfections rather than relapses.

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