Bedside Tool May Predict *C. difficile* Outcomes

BY M. ALEXANDER OTTO

FROM THE ANNUAL MEETING OF THE INFECTIOUS DISEASES SOCIETY OF AMERICA

VANCOUVER, B.C. – A simple scoring of five bedside assessments when *Clostridium difficile* infection is first diagnosed correlates significantly with cure rate.

"The higher the score, the lower the cure rate," said Dr. Mark Miller, head of the division of infectious diseases and chief of the department of microbiology at SMBD–Jewish General Hospital, McGill University, Montreal, who presented the findings.

VITALS

Major Finding: A score based on age, temperature, leukocytosis, albumin, and systemic antibiotic use correlates with cure rates in *C. difficile* infection with a *P* value of less than .001.

Data Source: ATLAS was tested using patient data from a large North American trial comparing fidaxomicin to vancomycin for CDI. ATLAS scores for 516 patients with CDI were calculated at their time of diagnosis and matched against their cure rates following 10 days of study treatment.

Disclosures: Dr. Miller is a scientific adviser and grant investigator to several pharmaceutical companies, including Merck & Co., Novartis Pharmaceuticals, and Optimer Pharmaceuticals.

The five parameters are age, temperature, leukocytosis, albumin, and systemic concomitant antibiotic use, ATLAS for short. The first four are rated on a 0-2 scale; 2 is added to the score if the patient is on systemic antibiotics, 0 if not. ATLAS scores range from 0 to 10. (See box at right.)

The score also correlates with recurrence, but the correlation is not statistically significant.

Dr. Miller said there is a need to be able to categorize patients by *C. difficile* infection (CDI) severity to determine who should be treated aggressively, assign and assess outcomes in clinical studies, and communicate with other medical workers.

"If someone calls up and says 'I have a case of moderate CDI,' it's pretty much left up to the imagination about what they are talking about," at present, he said.

Although much work has been done previously to create a prognostic system for CDI, proposed systems have not been adequately validated, Dr. Miller said.

However, "if you look at all these publications, it's all the same risk factors," he added.

So Dr. Miller and his colleagues combined them. "What we came up with was a simple combination of the bedside risk factors that are easy to collect and, we feel, should be most associated with cure and recurrence."

C. difficile strain type was omitted because it's not usually known at the time of diagnosis; baseline serum creatinine isn't either, so its elevation above baseline also was excluded.

ATLAS Bedside Scoring System

Parameter	0 points	1 point	2 points
Age (years)	< 60	60-79	> 80
Temperature (°C)	≤ 37.5	37.6-38.5	≥ 38.6
Leukocytosis	< 16,000	16,000-25,000	> 25,000
Albumin (g/L)	> 35	26-35	< 25
Systemic concomitant antibiotics during CDI Rx (=1 day)	No	—	Yes

Source: Dr. Miller

ELSEVIER GLOBAL MEDICAL NEWS

ATLAS was tested using patient data from a large North American trial comparing fidaxomicin to vancomycin for CDI. The ATLAS scores of 516 patients were calculated at their time of diagnosis and matched against their cure rates following 10 days of study treatment.

There was "an excellent correlation with cure rate," Dr. Miller said. (R^2 0.88, *P* value less than .001).

Patients with an ATLAS score of 0 had a 98% cure rate; the rate dropped incrementally with higher scores. ATLAS scores of 7 corresponded to a 55% cure rate.

Dr. Miller and his colleagues then checked the 450 subjects cured after treatment to see who had gotten another *C. difficile* infection.

"With recurrence, the ATLAS score didn't fair quite so well," he said.

Recurrence rates climbed with higher scores; 11% of patients with a 0 score had a recurrence, 43% with a score of 6.

But the correlation was weak (R^2, 0.32) and insignificant (*P*, .14).

A subgroup analysis found that 229 patients assigned to the vancomycin arm threw the recurrence results off (R^2, 0.02, *P*, .762). ATLAS scores predicted recurrence better in 221 fidaxomicin subjects (R^2, 0.70, *P*, .009).

Recurrence rates in the vancomycin arm were much higher, not neatly distributed along a curve, which might have thrown off the results, Dr. Miller said.

Perhaps, there may also "be some additional refinement of the systemic antibiotics score that would improve" ATLAS's correlation with recurrence, he said.

A second study presented in Vancouver showed significant correlation between ATLAS scores and 30-day CDI mortality in 308 adults aged 60 years or older.

"ATLAS score appears to … predict severity in CDI in our patient population," according to the abstract, of which Dr. Miller was a coauthor. ■

Fecal Transplantation an Option for Recurrent *C. difficile*

BY M. ALEXANDER OTTO

EXPERT ANALYSIS FROM THE ANNUAL MEETING OF THE INFECTIOUS DISEASES SOCIETY OF AMERICA

VANCOUVER, B.C. – A decades-old technique – fecal transplantation – cures more than 90% of *C. difficile* patients who relapse after antibiotic therapy, as up to a third do, according to Dr. Johan Bakken.

In fecal transplantation, donor stool is delivered from below through a colonoscope or retention enema, or from above through a nasogastric or nasoduodenal tube, to replace colonic flora wiped out by antibiotics, reestablishing the patient's resistance to colonization by *C. difficile*.

To date, at least 159 cases have been reported in the literature, dating back to 1958. Cure rates in case series range from 50% to 100%, with most toward the higher end of the scale, and an overall success rate of 91% (Euro. Surveill. 2009;14:19316).

"Why do it? Because it works," said Dr. Bakken, an infectious disease specialist at St. Luke's Hospital in Duluth, Minn.

"It's a simple and logical replacement therapy that works when antibiotic therapy fails, with a greater than 90% success rate. It's safe, inexpensive, reimbursable, quick, and easy to perform. The first bowel movement afterward is normal within 24 hours," he said.

In one case series, patients reported rapid resolution of abdominal pain, normalization of stool frequency and consistency, and an increased sense of well-being within 24-48 hours (Clin. Infect. Dis. 2003;36:580-5).

A randomized trial is currently underway in the Netherlands pitting vancomycin therapy against nasoduodenal tube fecal transplantation for recurrent *C. difficile* infections (Euro. Surveill. 2009;14:19316).

Dr. Bakken made his comments during a debate about fecal transplantation's merits with Dr. Dale N. Gerding, professor of medicine at Loyola University, Chicago.

Tapered, pulsed, and intermittent vancomycin are other options, though success varies, Dr. Gerding said.

Researchers are also working on antibiotics less punishing to healthy gut flora than vancomycin, synthetic stool preparations to avoid the use of donor stool, nontoxigenic *C. difficile* to outcolonize toxic strains, and vaccines and antibodies to bolster immune responses to the pathogen.

"This is 2010, not 1910. We can do better than fecal transplantation," Dr. Gerding said.

Even so, there is "no question that [fecal transplantation] results are impressive even without controlled, randomized, and blinded trials," he said.

"The cost of goods is low, unlikely to be in short supply, and unlikely to be addictive. It is obvious that feces have the right stuff," Dr. Gerding said.

Dr. Bakken recently published a review of the fecal transplantation literature and described his technique for the procedure (Anaerobe 2009;15:285-9). His medical group in Duluth has performed transplants in more than 80 patients, he said.

Although donor stool was delivered through a colonoscope or retention enema in about three-quarters of published cases, Dr. Bakken prefers the nasogastric tube for instillation.

It's less messy and guarantees delivery of bacteria to the entire gut, and one instillation is usually enough. Far less donor stool is needed, as well; up to 200 g of donor stool must be delivered from below, and often more than once.

A 4-day course of vancomycin is usually given before instillation to reduce the burden of vegetative *C. difficile* colonies; 20 mg of oral omeprazole are given the evening before and the morning of the procedure to cut stomach acid and create a receptive environment for instilled bacteria.

Although there have been no reports of contagions passed through donor stool, donors are screened for hepatitis A, B, and C viruses, as well as HIV, cytomegalovirus, Epstein-Barr virus, human T-lymphotropic virus, and syphilis. Dr. Bakken said he also screens donor stool for *C. difficile* toxin, ova, and parasites, and cultures it for enteric bacterial pathogens.

As an added precaution, a spouse donor is preferred; daily contact means spouses likely already share gut flora with patients. "Severe [*C. difficile* infection] represents the single situation when you should be willing to take crap from your spouse," Dr. Bakken joked.

Dr. Bakken disclosed he is a nonsalaried consultant to Cobax Biopharma, which is developing a synthetic stool product. Dr. Gerding disclosed he holds patents for the treatment and prevention of *C. difficile* infection licensed to ViroPharma, and is a consultant for the company, as well as several others, including Astellas, Cubist, Merck & Co., Pfizer, and Schering-Plough. He also holds research grants from Eurofins Medinet, GOJO, Merck, Optimer, Sanofi Pasteur, and ViroPharma. ■

Pages 28a—28b