Science Vision

An Infectious Blend

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Breakthrough in Ovarian Cancer Treatment

This study has received wide academic and media attention, as it reports one of the largest survival benefits ever observed for a new therapy in gynecologic oncology. Standard therapy for ovarian cancer involves surgical "debulking" of the tumor, followed by intravenous therapy with a platinum analogue and paclitaxel. To determine whether postsurgical intraperitoneal chemotherapy offers greater advantage, the NIH-sponsored Gynecologic Oncology Group conducted a trial among 415 patients with stage III epithelial ovarian or peritoneal carcinoma and no residual mass greater than 1 cm in diameter after surgery.

Patients were randomized to receive intravenous paclitaxel plus intravenous cisplatin or intravenous paclitaxel plus intraperitoneal cisplatin. Treatments were administered every 3 weeks for six cycles. Patients with complications in the intraperitoneal group received intravenous therapy for the remaining cycles, and those with toxicity to cisplatin in either group had intravenous carboplatin substituted.

A full 83% of patients in the intravenous group - but only 42% in the intraperitoneal group - completed all six cycles of their assigned therapy. Despite this difference, the intraperitoneal group still had a significantly longer median duration of progression-free survival (23.8 vs. 18.3 months) and overall survival (65.6 vs. 49.7 months) than did the intravenous group. Three to 6 weeks after therapy, quality of life was significantly worse in the intraperitoneal versus the intravenous group, but this difference disappeared within a year.

Further randomized trials should be aimed at refining such therapy to reduce toxicity.

1. Armstrong DK, Bundy B, Wenzel L. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. N Engl J Med 2006; 354:34-43.

Natural History of Incidental Pancreatic Cysts

To determine the predictive value of preoperative studies, and whether nonmucinous cysts (based on cyst-aspiration analysis) can be observed safely, researchers in Cleveland evaluated 221 consecutive patients with suspected pancreatic cystic neoplasms.

Eighty patients underwent surgery because of symptoms, cyst-aspirate evaluations consistent with mucinous neoplasms (moderate or large amounts of extracellular mucin or carcinoembryonic antigen [CEA] concentrations 200 ng/mL), radiographic features that raise suspicion for mucinous neoplasm, or endoscopic or radiographic identification of intraductal papillary mucinous neoplasms. Of the remaining 141 asymptomatic patients with indeterminate cysts, 98 underwent radiologic surveillance by computed tomography scanning and have been followed for at least 12 months (including 11 who refused surgery, despite positive mucin stain or cyst CEA levels 200 ng/mL). Cysts decreased in size or resolved completely in 20 patients (23%) and increased in size in 16 (19%). Four patients underwent resection: two for symptoms (one with a mucinous neoplasm and one with a serous cystadenoma), one for an increase in cyst size (lymphoepithelial cyst), and one for symptoms and an increase in size (pseudocyst). None of the surveillance patients developed malignancies. The authors conclude that initial follow-up evaluation indicates that asymptomatic patients without evidence of a mucinous neoplasm by cyst aspiration can be followed clinically and with interval imaging. Although these data provide some insight into the natural history of indeterminate cysts, much longer follow-up will be required.

1. Walsh RM, Vogt DP, Henderson JM. Natural history of indeterminate pancreatic cysts. Surgery 2005; 138:665-71.

Toxic Shock Syndrome after Medical Abortion

In July 2005, the FDA issued an alert regarding four reports of fatal sepsis in women following medical abortion. At that time, Clostridium sordellii had been identified as the infection-causing organism in two of the women. Now, researchers have confirmed that C. sordellii caused toxic shock syndrome in all four women.

The otherwise healthy women (age range, 18-34) underwent medical abortion at 43 to 53 days' gestation with 200 mg of oral mifepristone followed by 800 µg of vaginal misoprostol. They presented 4 to 5 days later with nonspecific complaints including abdominal pain, vomiting, and diarrhea. Presentations were marked by tachycardia, hypotension, and marked leukocytosis; absence of fever, myonecrosis, and gas production; and rapid progression to capillary leak syndrome, refractory hypotension, and death. Autopsy revealed local infection of the uterus. Clostridial antigens were identified by immunocytochemistry, and 16s ribosomal RNA gene sequences were consistent with C. sordellii infection.

As human C. sordellii infections are very uncommon, those described likely were related to the abortion procedure. FDA investigation found that the mifepristone and misoprostol were not contaminated with C. sordellii. Of note, the etiologic agent was identified only at autopsy using molecular amplification.

C. sordellii toxic shock after medical abortion is rare, given that mifepristone and misoprostol have been used in about 460,000 abortions in the U.S. since the FDA approved mifepristone. Nonetheless, when women who have undergone medical abortion present with the symptoms described above, clinicians should consider the possibility of toxic shock, and immediate antibiotic treatment including anaerobic coverage may be warranted.

1. Fischer M, Bhatnagar J, Guarner J. Fatal toxic shock syndrome associated with Clostridium sordellii after medical abortion. N Engl J Med 2005; 353:2352-60

Rotavirus Vaccines are Coming Soon

Rotavirus disease kills nearly half a million children annually in developing countries, and it is a leading cause of hospitalization among infants and children in the U.S. In 1999, the first licensed rotavirus vaccine was withdrawn from the market because it was associated with intussusception (estimated rate, 1/10,000 recipients). Now, results are available from two industry-supported, randomized, placebo-controlled clinical trials of new rotavirus vaccines.

Rotarix, a monovalent vaccine derived from the most common rotavirus strain, was tested in 63,225 infants in Latin America and Finland. Compared with placebo, two active oral doses given at ages 2 months and 4 months reduced severe rotavirus gastroenteritis and rotavirus-associated hospitalization by 85%. Numbers of intussusception cases within 100 days after the first dose were similar in the two groups (9 in the vaccine group and 16 in the placebo group).

Rotateq, a pentavalent human-bovine reassortant vaccine, was tested in 68,038 infants in the U.S., Europe, Latin America, and Taiwan. Compared with placebo, three active oral doses, given 4 to 10 weeks apart, beginning between 6 and 12 weeks after birth, were highly efficacious

reducing rotavirus-associated gastroenteritis and hospitalization or emergency department visits by 95% at 14 or more days after the third dose. Efficacy against rotavirus-associated gastroenteritis covered by the vaccine (through the first full rotavirus season after vaccination) was 74%. Again, rates of intussusception were similar in the vaccine and placebo groups.

These are very promising results, given that rotavirus vaccines could substantially reduce childhood mortality in developing countries and health care use in the U.S.

1. Ruiz-Palacios GM, Perez-Schael I, Velazquez FR. Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. N Engl J Med 2006; 354:11-22.

New AHA Guidelines for CPR and Emergency Cardiovascular Care

The science of resuscitation has advanced since CPR and ECC guidelines were last published in 2000. The 2005 guidelines include several critical changes in approach, all geared toward improving patients' chances of survival. The key points are summarized below:

1. The importance of effective chest compressions to produce blood flow is a major area of emphasis. The guidelines now encourage rescuers to "push hard and fast" at a rate of about 100 compressions per minute, with about equal time for compression and relaxation and as few interruptions in compressions as possible.

2. The guidelines have set a new compression-to-ventilation ratio for lone rescuers of 30:2 for all victims from infants (excluding newborns) through adults. This is a change from the previous recommendation of 15:2 for adults and 5:1 for infants and children. The new approach should ensure that rescuers deliver a longer series of uninterrupted chest compressions.

3. The guidelines now recommend that rescue breaths last 1 second and cause the chest to rise. Previously, the duration standard was not precise and mentioned durations of 1 to 2 seconds, now deemed too long.

4. For defibrillation, the new guidelines recommend 1 shock followed by immediate CPR with chest compressions. (Previously, the rule was 3 shocks without CPR between them, which resulted in potentially harmful interruptions in compressions.) The new system increases the chances that the heart can create blood flow after the shock.

5. Basic life support is now emphasized over pulse checks and drug administration. Rescuers should not sacrifice chest compressions right after a shock to do pulse checks or administer drugs, although neither of these practices was eliminated from the guidelines.

6. The new guidelines recommend the use of automated external defibrillators for all children age 1 year or older.

7. There is a new recommendation that unconscious adults with return of spontaneous circulation after out-of-hospital cardiac arrest be cooled to 32° to 34° Celsius for 12 to 24 hours when the initial rhythm was ventricular fibrillation.

1. ECC Committee, Subcommittees and Task Forces of the American Heart Association. 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2005; 112:Suppl:IV-1-IV-211.