Technology is not to blame for adverse perinatal outcomes in assisted conception

Singleton babies born after assisted fertilisation are at higher risk of low birth weight, preterm delivery, and perinatal death than spontaneously conceived ones. But a new study suggests that this is mainly the result of factors associated with infertility rather than the technology itself.

A Norwegian population based cohort study, which compared perinatal outcomes in more than 1200000 singletons born as a result of spontaneous conception and more than 8000 singletons born after assisted conception, found that those born after assisted conception were lighter at birth (difference 25 g, 95% CI 14 to 35), had shorter duration of gestation (2.0 days, 1.6 to 2.3), and had an increased risk of perinatal death (odds ratio 1.31, 1.05 to 1.65) and being small for gestational age (1.26, 1.10 to 1.44).

However, when the researchers compared babies born to 2546 women who, in consecutive pregnancies, gave birth to a singleton after assisted conception and after spontaneous conception, they found that outcomes differed little (difference in birth weight 9 g, −18 to 36; gestational age 0.6 days, −0.5 to 1.7; and odds ratio for small for gestational age 0.99, 0.62 to 1.57). Babies born after assisted conception even had a lower risk of perinatal death (0.36, 0.20 to 0.67).

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Para-aortic lymph node dissection doesn’t improve on standard surgery for stomach cancer

In Japan, gastrectomy with D2 lymphadenectomy—extensive removal of local lymph nodes—is the standard surgical treatment for curable gastric cancer. A trial randomised 523 people with T2b, T3, or T4 stage cancer, treated in 24 specialised hospitals, to receive standard surgery or standard surgery plus dissection of para-aortic lymph nodes. None of the patients received adjuvant treatment.

People whose para-aortic lymph nodes were removed during surgery had more operative complications than those who received standard surgical treatment (28.1% (73/260) vs 20.9% (55/263)), they lost more blood (a median difference of 230 ml), and their operations lasted longer (median difference 63 minutes). Complications classified as minor (pleurorrhoea, left pleural effusion, and severe diarrhoea) were significantly more common in the intervention group, but the groups did not differ in the occurrences of anastomotic leakage, pancreatic fistula, abdominal abscess, pneumonia, or all-cause death within 30 days of surgery.

Long term results showed no benefits with the tested intervention. After five and a half years, the groups were comparable in overall survival (about 70% in both groups) and recurrence free survival (about 62% in both groups). An editorial (p 448) discusses the epidemiology of gastric cancer in Japan, which has the highest prevalence of this disease in the world. In such a setting, trials that explore the best prevention strategies would be feasible and are much needed.


Ciclosporin reduces myocardial reperfusion injury

A pilot study tested a hypothesis that because ciclosporin inhibits the opening of the mitochondrial permeability transition pores, it might attenuate myocardial reperfusion injury, which in patients with myocardial infarction accounts for up to a half of the final size of the infarct. Fifty eight people with acute ST elevation myocardial infarction were randomised to an intravenousbolus of 2.5 mg of ciclosporin per kg of body weight, or saline, before undergoing percutaneous coronary intervention.

Ciclosporin significantly reduced the release of creatine kinase (P=0.04) and lowered troponin I, although not significantly (P=0.15). Also, in the 27 people who had magnetic resonance imaging five days after infarction, those who received ciclosporin had about 20% less damage to the heart muscle than people who had been randomised to saline (median mass of the infarcted area 37 g vs 46 g). We now need larger trials to determine whether reducing myocardial injury with ciclosporin affects clinical outcomes.

Although no adverse effects were recorded, the editorialists (p 518) call for research into more specific and safer inhibitors of the mitochondrial permeability transition pores. This new treatment strategy holds promise for better management not only for heart attack, but also for stroke, heart surgery, and organ transplantation.


Eradicate Helicobacter pylori after removal of early stomach cancer

Prophylactic eradication of Helicobacter pylori seems to be effective in the prevention of monochronous gastric cancer after

SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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CUMULATIVE INCIDENCE OF NEW CARCINOMA

Adapted from Lancet 2008;372:392-7

endoscopic removal of early stomach cancer. A Japanese trial looked at 544 people who had either undergone or were scheduled to undergo endoscopic removal of early gastric cancer and were thus at high risk of developing monochronous cancer. These patients were randomised to receive \textit{H pylori} eradication treatment (lansoprazole 30 mg twice daily, amoxicillin 750 mg twice daily, and clarithromycin 200 mg twice daily for a week) or usual care that did not include antibiotics.

After three years, metachronous gastric cancer developed in nine people randomised to the eradication group and in 24 people who received usual care (odds ratio 0.35, 95% CI 0.16 to 0.78). The only notable adverse events seen in the eradication group were soft stools (12% (32/255)) and diarrhoea (7% (19/255)).

A commentator (p 350) argues that, in the absence of large trials of primary prevention, the implications of these findings should extend beyond high risk patients, and that eradication of \textit{H pylori} to prevent stomach cancer should become a priority in regions with high incidence. Colorectal cancer kills fewer people, says the commentator, yet screening by colonoscopy is widely accepted, despite the lack of direct evidence of benefits and the risks of such a strategy.

\textit{Lancet} 2008;372:392-7

Empirical fluconazole doesn’t prevent invasive candidiasis in the ICU

Patients in the intensive care unit (ICU) are at risk of infection with \textit{Candida} spp, and the risk of associated mortality and morbidity is high. Empirical antifungal treatment has proved helpful for other high risk groups, such as cancer patients with febrile neutropenia, and several studies have postulated that such strategies could work in the intensive care unit, with mixed results.

Now a randomised trial from the US seems to have laid the matter to rest. Of 270 critically ill patients with a fever—despite being given broad spectrum antibiotics—those who received 800 mg of fluconazole daily for two weeks were no more likely to reach the composite outcome, defined as success in four end points that included fever resolution and absence of invasive fungal infection, than those who received placebo (36% (44/122) vs 38% (48/127), relative risk 0.95, 95% CI 0.69 to 1.32).

The authors acknowledge that the composite outcome leaves their results open to criticism, but an accompanying editorial (p 140) notes that the intervention had little effect on invasive candidiasis—a single hard outcome (5% for fluconazole vs 9% for placebo, 0.57, 95% CI 0.22 to 1.49). It suggests attempts at tackling \textit{Candida} infections should be directed at better infection control and earlier diagnosis, and that the “blunt tool” of antifungal prophylaxis should be dropped for good.

\textit{Ann Intern Med} 2008;149:83-90

Cellulose sulphate vaginal gel doesn’t protect against transmission of HIV

A randomised double blind placebo controlled trial enrolled nearly 1400 women from Africa and India who were at high risk of infection with HIV. To be eligible, women had to report having at least three vaginal intercourses each week and to having had at least three different partners in the preceding three months.

The trial was stopped early after an interim analysis showed that the rate of newly acquired infection with HIV in the sulphate gel group was more than double that seen in the placebo group. By the time the trial was stopped, another six infections had been acquired, and the results were no longer statistically significant (25 new HIV infections in the intervention group vs 16 in the placebo group, hazard ratio 1.61, 95% CI 0.86 to 3.01). Compared with placebo, cellulose sulphate also did not reduce new infections with gonorrhoea or \textit{Chlamydia trachomatis}.

Overall, women reported using condoms in just over 95% of vaginal intercourses and vaginal gel in nearly 90%. However, during high risk intercourses—when condoms were not used—they reported that use of the gel fell to below 50%.

The authors say that despite these disappointing results, and other unsuccessful attempts to find effective strategies to reduce transmission of HIV, the search for preventive methods that can be used by women must continue.


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Fewer acute coronary syndromes after Scotland’s smoking ban

Many studies indicate that laws against smoking in public places can be followed quickly by a reduction in admissions for acute coronary syndrome. It is unclear how this occurs though, because small population sizes, retrospective data, and a lack of information on smoke exposure have all muddied the picture.

Scotland prohibited smoking in enclosed public spaces from the end of March 2006. A prospective study of all admissions for acute coronary syndrome in nine Scottish hospitals serving more than three million people has shown that such admissions fell by 17% (95% CI 16% to 18%) between the 10 months before the ban (3235 admissions) and the same period in the next year (2684 admissions). This was more than the 3% mean annual drop in admissions over the previous 10 years, and the maximum drop of 9% recorded in 2000. Admissions in England, which did not have a ban at the time, fell by 4% during a similar period. Out of hospital deaths from acute coronary syndromes also decreased, by 6%.

Non-smokers were responsible for two thirds of the reduction. The fall in admissions was greatest for those who had never smoked and for women. Questionnaires showed that exposure to second hand smoke was lower in non-smokers after the ban, a finding that was backed up by lower serum cotinine concentrations, especially in women.