Quality of Care: Time to Make the Grade
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COMMENTARIES

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Fomepizole in the Treatment of Poisoning

Alcohol dehydrogenase. It is unique in clinical toxicology as the enzyme that changes relatively benign agents into dangerous, even lethal, toxicants. Without alcohol dehydrogenase, methanol is merely irritating and inebriating. With alcohol dehydrogenase, methanol becomes formaldehyde, then formic acid. These cause anion gap metabolic acidosis, blindness, seizures, coma, and death. Without alcohol dehydrogenase, ethylene glycol is a gastrointestinal irritant, and a more potent inebriant than ethanol. With alcohol dehydrogenase, ethylene glycol becomes glycoaldehyde then glycolic acid. Profound metabolic acidosis results; calcium oxalate precipitates in soft tissues, damaging the kidneys and the heart; hypocalcemia contributes to seizures, tetany, and dysrhythmia; coma and death can occur.

Alcohol dehydrogenase is an obvious target in the treatment of victims of methanol or ethylene glycol poisoning. Ethanol is a competitive inhibitor of alcohol dehydrogenase. Ethanol is a logical choice, as the preferred substrate for alcohol dehydrogenase, and it works: serum ethanol levels of ≥100 mg/dL block metabolism of ethylene glycol and methanol in their usual overdose concentrations.1

Unfortunately for patients, ethanol has its own toxicity. At therapeutic concentrations, ethanol is inebriating and may cause hypoglycemia. Unfortunately for clinicians, ethanol is difficult to use. Kinetics vary widely among individuals, and in the same individual over time. Published dosing schemes vary widely among sources. Oral absorption is erratic; intravenous preparations are rarely shelved2 in most hospitals, and some emergency departments obtain the antidote from the local liquor store. Even the math is challenging: ethanol concentrations may be reported with units of proof or percent; percent alcohol sometimes refers to mass:mass, mass:volume, or volume:volume, and even 100% solutions don’t have as much as one might guess, because the density of ethanol is <1. All of these problems add up to delays in acquiring, calculating, preparing, and administering the dose, and too many opportunities for error in the process. Ethanol dosing usually means drawing hourly ethanol and glucose levels from an intubated patient in the intensive care unit, with frequent changes in the ethanol dose.3

In 1986 fomepizole was introduced as a safer and more effective blocker of alcohol dehydrogenase.4 Administration is simple: a 15-mg/kg loading dose is given intravenously over 30 minutes, followed by 10 mg/kg every 12 hours for 4 doses, then 15 mg/kg every 12 hours. Treatment is continued until methanol or ethylene glycol levels are <20 mg/dL. Fomepizole is approved by the Food and Drug Administration for treatment of confirmed or suspected ethylene glycol poisoning in adults; it appears equally safe and effective in methanol poisoning,5 and in children.

Because it only blocks further conversion of methanol and ethylene glycol to toxic metabolites, fomepizole does not replace bicarbonate in acidic patients, nor dialysis in patients with acidosis, renal insufficiency, or massive overdose. Side effects seem to be minimal; seizures reported in 2 patients shortly after the fomepizole administration may have been attributable to the underlying ethylene glycol intoxication,6 and both patients received additional doses without problems. At $1000 per 1500-mg vial ($4000 per 4-vial pack, wholesale cost direct from manufacturer), drug acquisition cost is the major problem with this drug. Although fomepizole may lower other costs (by allowing less dialysis, intensive care unit admissions, blood ethanol and glucose measurements, and by eliminating the delays and risks of ethanol dosing), a formal pharmacoeconomic study is needed.7

Fomepizole improves the care of the methanol- or ethylene glycol-poisoned patient and makes the physician’s job easier, too.

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Quality of Care: Time to Make the Grade

When the Institute of Medicine (IOM) reported in December 1999 that as many as 98,000 persons die each year because of medical errors, the media and the public “got it” with respect to the problems in health care quality. Yet for clinicians and researchers, much of the information in the IOM report was already familiar. Errors of commission or omission are just one dimension of the quality challenge facing health care today. Decades of health services research have repeatedly demonstrated that the quality of health care often falls short of good, let alone ideal. In the past 5 years, this extensive literature has been used to inform and galvanize action in both the public and private sectors. Several important milestones have occurred. In 1998, a presidential commission called for a national commitment to quality improvement in health care. In October 1999, in his keynote address to the American Academy of Pediatrics (AAP), Dr Berwick challenged pediatricians to rise to the quality challenge and laid out a 5-point strategy. In the same year, the federal Agency for Health Care Policy and Research was renamed the Agency for Healthcare Research and Quality (AHRQ) and charged with providing the science base for measurable and improving quality of care. Also included in the legislation was a new call to focus on children. Finally, last spring, Dr Berman challenged all of us in stating that, “In order to succeed, we need to reject the status quo and begin to inherently value change. We must be willing to recognize that the current standard of pediatric care, although good, is not good enough, and there are ample opportunities for improvement.”

The article by Ferris et al in this issue provides a much-needed baseline for our improvement efforts. This review of the state of quality improvement (QI) research in child health presents us with several important conclusions. First, substantial improvement is possible in the quality of care for children. Second, certain interventions have been well-demonstrated to be effective and are ready for widespread diffusion into pediatric practice. For example, reminder systems show improvements in physician immunization, screening, and counseling practices to a degree greater than all other interventions studied. Third, quality improvement for children appears from the research to be similar to adult QI despite the perception by experts in the field that it is more difficult. Finally, the number of studies being published has grown tremendously in the past few years, which bodes well for our future ability to respond to the challenges laid out by Drs Berwick and Berman.

However, this review also highlights a number of gaps in our research base. A majority of the studies reviewed were directed at children <5 years old and were located in a small number of cities. In most of the QI intervention categories assessed the authors found insufficient evidence to adequately inform clinicians and administrators. Fully 90% of studies of chronically ill children examined asthma and few included child health outcomes. All of these limitations reflect the emerging, but still inadequate, capacity for child and adolescent health services research in academic and office based settings. AHRQ’s priorities for continued and expanded support for child health services research, training of new investigators, and the development of research networks, combined with the AAP’s clinical leadership, should help to expand and implement the science base for public and private efforts to make the grade for quality for children.

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