systemic vasodilation or other adverse effects. Studies in human volunteers have shown that inhaled NO reversed pulmonary hypertension caused by breathing a hypoxic gas mixture (12% oxygen). The effects of inhaled NO occurred within the first minute of inhalation, and there were no systemic effects.

Inhaled NO (40 ppm) has now been shown to be an effective, selective pulmonary vasodilator in the treatment of acute pulmonary hypertension. In contrast, epoprostenol (formerly prostacyclin) produces dose-related reductions in both pulmonary and systemic vascular resistance. The effects of inhaled NO are fully reversible within five minutes of discontinuation and can be reproduced with repeated administration. Inhaled NO has selectively decreased pulmonary arterial pressure and pulmonary vascular resistance in patients with congenital heart disease and after cardiac surgery. Inhaled NO improves oxygenation in newborns with persistent pulmonary hypertension, presumably by decreasing shunting across a patent foramen ovale or ductus arteriosus.

Inhaled NO has now become a therapeutic option in patients with severe adult respiratory distress syndrome (ARDS). Pulmonary hypertension and hypoxemia universally occur in patients with ARDS; the severity of each relates to mortality. Intravenous pulmonary vasodilator therapy with agents such as nitroglycerin sodium, nitroprusside, alprostadil (prostaglandin E), epoprostenol, and nifedipine results in small decreases in pulmonary arterial pressure but large decreases in systemic blood pressure and arterial oxygenation. The adverse effects on oxygenation occur because the decrease in pulmonary vascular resistance is primarily due to the reversal of hypoxic pulmonary vasoconstriction. In patients with ARDS, inhaled NO can decrease pulmonary vascular resistance and improve oxygenation. The improvement in oxygenation occurs because inhaled NO (as opposed to intravenous vasodilators) is distributed according to ventilation so that the associated vasodilation increases blood flow to well-ventilated alveoli. The magnitude of improvement in pulmonary hypertension and oxygenation is directly related to the degree of abnormality in each. Nitric oxide concentrations of 0.3 to 4.0 ppm are effective, and beneficial effects are sustained during administration periods as long as two months for patients on ventilators.

Although inhaled NO is clearly effective in improving pulmonary hemodynamics and oxygenation, the role of inhaled NO in patients with ARDS requires additional study. By ameliorating pulmonary hypertension and hypoxemia, inhaled NO may decrease the incidence of pulmonary edema, oxygen toxicity, and pulmonary barotrauma, thereby allowing the lungs to heal. The effects of nitric oxide and nitrogen dioxide on repair or fibrosis in injured lungs and on pulmonary host defenses are largely unknown, however. Survival with prolonged administration of inhaled NO was 86% in one major study, but only 14% in another major study. Inhaled NO is currently used by many centers on a "compassionate use" basis for patients with severe hypoxemia, but controlled clinical trials are needed to determine its value in most patients with ARDS.

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REFERENCES

Pearl RG: Inhaled nitric oxide—The past, the present, and the future. Anesthesiology 1993; 78:413-416

Rich GF, Murphy GD Jr, Roos CM, Johns RA: Inhaled nitric oxide—Selective pulmonary vasodilation in cardiac surgical patients. Anesthesiology 1993; 78:1028-1035

Rossaint R, Falke KJ, Lopez F, Slama K, Pison U, Zapol WM: Inhaled nitric oxide for the adult respiratory distress syndrome. N Engl J Med 1993; 328:399-405

Zapol WM, Rimar S, Gillis N, Marietta M, Bosken CH: Nitric oxide and the lung. Am J Respir Crit Care Med 1994; 149:1375-1380

Operative Hysteroscopy Intravascular Absorption Syndrome

ANESTHESIOLOGISTS ROUTINELY anticipate, recognize, and treat volume and electrolyte disturbances during transurethral resection of the prostate (TURP syndrome), but it is now established that operative hysteroscopy has the same potential for these serious pathophysiologic changes. The absorbed volume of fluids employed for uterine distention depends on the extent of intrauterine transection of vascular beds, the intrauterine distention pressures, the volume of media used, and the duration of the procedure. The biochemical composition of the instilled fluids determines the physiologic alterations.

Menstruant women have been shown to be at high risk for death or brain damage from even modest hyponatremia and, perhaps even more important, hypoosmolemia. The earliest signs of this syndrome are confusion and bradycardia with systolic and diastolic hypertension. As with the TURP syndrome, it may be advantageous to use regional anesthesia because awake patients are likely to display precursor symptoms that portend impending brain or cardiac dysfunction and injury. For patients subjected to general anesthesia, delayed diagnosis of the syndrome of operative hysteroscopy intravascular absorption (OHIA) can be mitigated against by adhering to a predetermined schedule for sampling patient blood for rapidly measuring the serum sodium concentration. An instillate solution that contains ethanol 1% as a biologic marker can be used to estimate fluid absorption by measuring the end-tidal ethanol content.

Dextran 70 32% in a 10% solution of glucose (Hyskon) is a hyperosmolar, viscous fluid (molecular weight 70,000) that is immiscible in blood and slowly metabolized over several days. It increases plasma oncotic pressure to the extent that it expands blood volume by ten times its absorbed volume. When substantial volumes (> 500 ml) are absorbed, hypervolemic pulmonary edema is to be expected; serum osmolarity and sodium changes are less prominent. Therefore, the use of Hyskon demands meticulous measurement of the instilled volume and a preoperative agreement with the surgeon as to the maximal acceptable volume instilled before the hysteroscopy is stopped. A prominent sign of intravascular overload is decreasing arterial oxygen saturation. Moreover, intravas-

cular overload may first become manifest during emergence from anesthesia when the vasodilatory effects of anesthetic drugs and techniques are dissipated or positive pressure ventilation is discontinued. Hyskon may directly cause a coagulopathy.

Both 1.5% glycine and a premixture of 2.7% sorbitol and 0.54% mannitol are low-viscosity, hypo-osmolar (200 and 178 mOsm per liter, respectively), rapidly metabolized instilling fluids. Excessive absorption can result in substantial hyponatremia and hypo-osmolemia.

A solution of 5% mannitol may have a wider margin of safety compared with the other instilling fluids because it is iso-osmolar (278 mOsm per liter). In fact, mannitol is commonly administered intravenously during neuroanesthesia, often in volumes and concentrations greater than those encountered in operative hysteroscopy and without pathophysiologic sequelae. Excessive intravascular absorption of instilled 5% mannitol solution will cause hyponatremia, but serum osmolarity will not change. Furthermore, mannitol initiates a diuresis that self-corrects volume overload.

Although treatment regimens for hyponatremia, hypo-osmolemia, and circulatory overload are well established, anesthetic management of these otherwise healthy women should emphasize the prevention of the OHIA syndrome and its attendant morbidity and possible mortality.

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REFERENCES

Arieff AI, Ayus JC: Endometrial ablation complicated by fatal hyponatremic encephalopathy. JAMA 1993; 270:1230-1232

Baggish MS, Brill AI, Rosenzweig B, Barbot JE, Indman PD: Fatal acute glycine and sorbitol toxicity during operative hysteroscopy. J Gynecol Surg 1993; 9:137-143

Witz CA, Silverberg KM, Burns WN, Schenken RS, Olive DL: Complications associated with the absorption of hysteroscopic fluid media. Fertil Steril 1993; 60:745-766

Desflurane—A New Inhalation Anesthetic

BEFORE 1993, three volatile inhalation anesthetics were in routine use. These inhalation anesthetics—halothane, enflurane, and isoflurane—have many desirable qualities. As the number of outpatient procedures continues to increase, recent emphasis in anesthetic practice has been toward the development of agents that provide more rapid recovery. A new inhalation anesthetic, desflurane, provides more precise control during delivery and more rapid recovery than preexisting inhalation anesthetics. These improved properties result from its low blood-gas solubility coefficient, which promotes more rapid induction and emergence from anesthesia. This blood-gas solubility coefficient is 0.45, which is similar to cyclopropane (0.42) and nitrous oxide (0.47) and less than half that of isoflurane (1.4). Sevoflurane is another new inhalational agent that has a low solubility coefficient (0.60), but it is still undergoing clinical trials for approval by the Food and Drug Administration.

Desflurane was recently released for clinical use in the United States. Because its high vapor pressure at 20°C is 669 mm of mercury, desflurane is near its boiling point at room temperature. Accurate delivery must be accomplished by using a heated vaporizer that maintains its near-constant temperature, converting desflurane to a gas and then blending this gas with fresh gas flow. In addition to its lower blood-gas solubility, another of desflurane's attractive properties is its low level of biotransformation in the body. Many of the toxicities attributed to earlier inhalation anesthetics are caused by metabolites from hepatic biotransformation. Desflurane is biotransformed at less than an eighth the rate of isoflurane, which previously had been the least biotransformed inhalation agent. In addition, it has excellent physical stability. Its effect on vital organ systems, when higher concentrations are used, is similar to that of existing inhalation agents. It depresses ventilation, lowers mean arterial pressure, and causes some cerebral vasodilation.

Desflurane differs from sevoflurane in several ways: it is stable in carbon dioxide absorbents where sevoflurane has some instability, it undergoes much less hepatic biotransformation than sevoflurane, it may produce a tachycardia at higher concentrations, and its pungency produces airway irritation that precludes its use for inhalation inductions in children.

Desflurane should not produce hepatotoxicity of the form observed with halothane. Although it is not perfect, it does appear to offer specific advantages over previous agents. Cost-benefit comparisons with existing inhalational agents will be another important consideration.

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REFERENCES

Eger EI II: Desflurane: An overview of its properties. Anesthesiol Rev 1993; 20:87-92

Tsai S, Lee C, Kwan WF, Chen BJ: Recovery of cognitive functions after anaesthesia with desflurane or isoflurane and nitrous oxide. Br J Anaesth 1992; 69:255-258

Intraspinal Narcotics for Obstetric Analgesia

THE USE OF intraspinal narcotics has found widespread acceptance in obstetric analgesia, but has generally been confined to epidural administration. A better understanding of the pharmacology of narcotics and advances in the equipment available have led to the increasing use of intrathecal narcotics in labor. This technique is now a reasonable alternative for women in early labor, in particular, and perhaps a cost-effective alternative in obstetric centers without full-time "in-house" obstetric anesthesia services.

The early use of intrathecal morphine sulfate for labor was effective, but the side effects of pruritus, nausea, and vomiting and the limitations of a single injection (that is, no easy route for further intervention) and its slow onset (30 to 90 minutes) led to its near abandonment. The technique was recently "reinvented," however. The problem of a slow onset was solved by adding one of the lipid-