PERIOPERATIVE NEUROPROTECTION/GLUCOSE MANAGEMENT

From the 25th Annual Conference Challenges for Clinicians, presented by the University of Chicago Pritzker School of Medicine, Department of Anesthesia and Critical Care

Audio-Digest® ANESTHESIOLOGY


Perioperative Neuroprotection: An Enduring Fantasy

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Background: interventions already tried or proposed based on contemporaneous understanding of neurophysiology or of various insults; laboratory studies analyze intermediate variables; few have examined long-term functional outcomes; numerous pharmacologic agents tested as preventive or therapeutic agents; none has shown benefit

Effective interventions: hypothermia after witnessed cardiac arrest due to ventricular fibrillation, witnessed neonatal asphyxia (probably), and thrombolysis after stroke (applications limited; can be used only in patients without hemorrhage; ineffective if not administered within 3 to 6 hr after onset of symptoms)

Well studied but ineffectiv interventions

Hypothermic treatment of head trauma: oldest purported protective neurologic intervention; in 1997, Marion and colleagues reported good outcomes in short-term single-center study of 82 patients with severe closed head injuries; in 2001, Clifton and colleagues showed in multicenter study that patients exposed to hypothermia showed no benefit 6 mo later and had higher incidence of complications (mostly pneumonia); Cochrane analysis later concluded hypothermia not beneficial for treatment of head injury

Hypothermia for intraoperative protection during surgery for aneurysm: investigated due to high rate (25%–40%) of postoperative deficits associated with such procedures; speaker and colleagues conducted prospective trial of patients undergoing surgery for acute aneurysmal subarachnoid hemorrhage; compared use of intraoperative hypothermia to maintenance of normothermia; involved 1000 patients at 30 centers; primary measure score on Glasgow Outcomes Scale at 3 mo; authors observed no significant improvement in outcomes in patients treated with hypothermia

Barbiturates during cardiac surgery: early research suggesting protective effect of thiopental now considered flawed due to poor design; later research showed no evidence of protective effect associated with thiopental or propofol

Barbiturates during neurovascular surgery: never studied in formal trial; in retrospective nonrandomized study that compared patients undergoing temporary clipping during cerebral aneurysm surgery, Hindman and colleagues observed no protective effect associated with barbiturates in hypothermic or normothermic patients

Carotid endarterectomy: in General Anesthesia vs Local Anesthesia for Carotid Surgery trial, 3526 patients randomized to general vs local or regional anesthesia; primary outcome measures stroke, death, or myocardial infarction within 30 days of surgery; 70% of patients in general anesthesia group and 66% in local anesthesia group sustained neurologic deficits (difference statistically insignificant)

Conclusions: currently, no good data support use of intraoperative neuroprotection, except for deep hypothermia during circulatory arrest; “the concept that reducing brain metabolism will protect is almost certainly false”; effective treatments such as thrombolysis restore blood to ischemic tissue (may be harmful if done too late); mechanisms by which hypothermia produce benefit after cardiac arrest and asphyxia still unknown (may prevent fever); efficacy of intervention in one neurologic disorder does not necessarily translate to efficacy in another (biology and biochemistry of disorders such as stroke, subarachnoid hemorrhage, and head trauma differ substantially); no pharmacologic trials of neuroprotective agents currently ongoing; understanding of mechanisms behind neurologic injuries still incomplete; treatment based on inadequate knowledge may do more harm than good

Glucose Management

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Definition of diabetes mellitus: abnormal carbohydrate metabolism that results in hyperglycemia; involves relative or absolute insulin deficiency and various degrees of insulin resistance; most common endocrinopathy (estimated to affect >10% of North American population)

Type 1: associated with destruction of pancreatic β cells, which results in absolute insulin deficiency; primarily autoimmune in nature; subtypes include adult onset and idiopathic diabetes (no circulating antibodies seen)

Type 2: most common; seen in 90% of North American patients; characterized by varying degrees of insulin deficiency and resistance; subtypes include drug-induced and gestational diabetes

Diagnosis: 3 criteria established by American Diabetes Association (fasting glucose >126 mg/dL, random glucose >200 mg/

Educational Objectives

The goal of this program is to improve perioperative management by reviewing evidence on the effectiveness of perioperative neuroprotection and by improving perioperative glucose control. After hearing and assimilating this program, the clinician will be better able to:

1. Assess whether neuroprotective interventions are effective.
2. Identify and apply interventions that are known to be effective.
3. Diagnose diabetes according to the criteria established by the American Diabetes Association.
4. Manage glycemic complications of surgery and anesthesia.

5. Develop an appropriate treatment plan for a patient with perioperative hyperglycemia.

Faculty Disclosure

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Acute glycemic complications: Treatment: Impact of end-organ pathology on anesthetic practice

Preoperative management: eg, Cardiovascular: diabetes is intermediate predictor of coronary artery disease; increases risk for virtually every cardiovascular complication; \( \beta \)-blockers not contraindicated for people with diabetes (do not interfere with glycemic control)

Renal: diabetes is leading cause of renal failure requiring renal replacement therapy in North America; diabetic patients may have impaired creatinine clearance (choose drugs and doses accordingly)

Other, peripheral and autonomic neuropathy — consider when positioning patient; altered hemodynamic responses — patient may be unable to mount tachycardic response to hypotension; gastroparesis — patient should not be at increased risk for aspiration with appropriate preoperative fast (but gastroparesis may occur); abnormal collagen cross-linking — may decrease joint mobility; obesity — may contribute to challenges in airway management; also consider associated pathologies

Acute glycemic complications: surgery or reason for surgery may disrupt glycemic control; anesthesia and surgery cause relative insulin hyosecretion and resistance; infection and stress also affect glycemic control; greatest challenges hyperglycemia and hypoglycemia; hyperglycemia associated with diabetic ketoacidosis (DKA) and nonketotic hyperosmolar states (NKHS; conditions may coexist)

DKA: associated with relatively significant risk for mortality; patients hyperglycemic, dehydrated, hyperosmolar, and have increased anion gap; develop deep Kussmaul breathing in effort to blow off carbon dioxide; associated with characteristic fruity-smelling breath; nausea and vomiting may exacerbate dehydration; hyperkalemia frequently present; patients often have deficits of other electrolytes; severe hyperglycemia may cause false depression in sodium, which leads to spurious hyponatremia; for every 100 mg/dL above 100 mg/dL of blood glucose, add 1.5 to 2 mEq to measured sodium; management — in addition to routine monitoring, place arterial access (for frequent blood draws) and central venous access (for volume and electrolyte administration); start intravenous insulin and crystalloid; start dextrose when blood glucose approaches 200 mg/dL; continue insulin until ketones cleared and acidosis resolved

NKHS: occurs in patients with type 2 diabetes; patients typically more dehydrated, hyperosmolar, and hyperglycemic than those with DKA; neurologic manifestations, which range from stupor to focal neurologic deficit, common; ketone production lacking, but lactacidosis may be present secondary to thrombotic events caused by dehydration; management — insulin therapy and volume resuscitation with crystalloid; correct hypovolemia more gradually than in DKA, due to concerns about cerebral edema; monitor neurologic status closely

Hypoglycemia: usually defined as blood glucose <50 mg/dL; causes include residual drug effects, overaggressive treatment for hyperglycemia, and decreased caloric intake; correct as quickly as possible

Goals of perioperative glucose management: diabetes associated with increased rate of hospitalization and length of stay; hyperglycemia associated with increased risk for infection and impaired wound healing; risk for osmotic diuresis also increased, with associated abnormalities in electrolytes and acid-base balance; in 2001 study of diabetic patients undergoing coronary artery bypass grafting (CABG), diabetes and postoperative hyperglycemia independently associated with development of surgical site infections; in retrospective study of >2000 consecutive hospital patients, 38% hyperglycemic on admission; one-third of hyperglycemic patients had no history of diabetes; newly discovered hyperglycemia associated with mortality rate of 16%, compared to 3% among known diabetics and 1.7% among patients with normoglycemia; impact on anesthesia practice — patients with preoperative fasting hyperglycemia have poorest outcomes; consider evaluating such patients in manner appropriate for known diabetic

Hypoglycemia and stroke: in systematic review of 26 studies, glucose of >144 mg/dL at admission associated with increased risk for in-hospital and 30-day mortality and poorer functional status among survivors; similar relationship observed between hyperglycemia and MI; intensive insulin therapy reduced long-term mortality among patients with MI

Intensive insulin therapy: continuous intravenous insulin infusion associated with reduced mortality among critically ill patients, most of whom postsurgical (60% of these had cardiac procedures); greatest decline seen in patients spending >5 days in intensive care unit (ICU); later research showed mortality increases in relation to mean blood glucose levels in patients of all ages; observational studies in anesthesiology literature reported association between poor glycemic control and severe morbidity; in prospective study of 400 patients undergoing cardiac surgery, intensive intraoperative insulin therapy associated with increased incidence of stroke and death, compared to conventional glycemic control; later studies found intensive insulin therapy to be associated with unacceptably high risk of hypoglycemic events; in Normoglycemia in Intensive Care Evaluation and Survival Using Glucose Algorithm Regulation (NICE-SUGAR) study, patients with anticipated length of stay >48 hr randomized to intensive (81-108 mg/dL) or conventional (<180 mg/dL) glycemic control; intensive treatment associated with increased mortality; mounting data suggest culprit may be hypoglycemia associated with increased risk; some observers believe fluctuating glucose levels associated with tight control represent significant independent risk factor for mortality
Conclusions: several quality-control guidelines call for maintenance of postoperative glucose among patients undergoing cardiac surgery (hospitals required to report glucose levels drawn at 6 AM on postoperative days 1 and 2; should be <200 mg/dL).

Sample case: obese hypertensive patient scheduled for carotid endarterectomy; has no inducible cardiac ischemia; serum creatinine 1.3 mg/dL; preoperative glucose level 162 mg/dL; immediate preoperative glucose 160 mg/dL; insulin infusion not indicated; speaker would obtain hemoglobin A1c level to allow assessment of long-term glucose levels; blood glucose measured during case 185 mg/dL. (insulin infusion now indicated, if resources available)

Summary: available data suggest adverse outcomes associated with hyperglycemia, hypoglycemia, and glucose variability; care plan must balance risks and effects; current data suggest ideal perioperative glucose 130 to 160 mg/dL.

Acknowledgements

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Suggested Reading


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Estimated time to complete the educational process:

- Review Educational Objectives on page 1: 5 minutes
- Take pretest: 10 minutes
- Listen to audio program: 60 minutes
- Review written summary and suggested readings: 35 minutes
- Take posttest: 10 minutes
1. In which of the following situations is hypothermia an effective form of neuroprotection?
   (A) After witnessed ventricular fibrillation
   (B) After head trauma
   (C) Intraoperatively during surgery for aneurysm
   (D) All the above

2. A study assessing the neuroprotective effects of barbiturates in patients undergoing temporary clipping during cerebral aneurysm surgery found:
   (A) Efficacy in hypothermic patients
   (B) Efficacy in normothermic patients
   (C) A and B
   (D) Neither A nor B

3. Which of the following statements best summarizes the incidence of neurologic deficits among patients undergoing carotid endarterectomy with general vs local anesthesia?
   (A) Greater among patients who had general anesthesia
   (B) Greater among patients who had local anesthesia
   (C) Lower among patients who had local anesthesia supplemented with barbiturates
   (D) Similar among the general and local anesthesia groups

4. The diagnostic criteria for diabetes established by the American Diabetes Association include:
   1. History of ≥1 perioperative glucose reading ≥180 mg/dL
   2. Fasting glucose >126 mg/dL
   3. Random glucose >200 mg/dL associated with polydipsia or polyuria
   4. Glucose >200 mg/dL 2 hr after challenge with 75 g of glucose
      (A) 1,2,3,4
      (B) 2,3,4
      (C) 2,4
      (D) 3,4

5. Which of the following should be avoided by patients with renal or hepatic dysfunction?
   (A) Glyburide
   (B) Rosiglitazone
   (C) Long-acting insulin
   (D) Metformin

6. β-blockers are contraindicated for people with diabetes.
   (A) True
   (B) False

7. Which of these statements about nonketotic hyperosmolar states is accurate?
   (A) Occur exclusively in patients with type 1 diabetes
   (B) Symptoms usually milder than those associated with diabetic ketoacidosis
   (C) Often associated with neurologic manifestations
   (D) Not associated with lactacidosis

8. Perioperative hyperglycemia has been associated with:
   (A) Longer length of hospital stay
   (B) Higher rate of surgical site infections
   (C) Impaired wound healing
   (D) All the above

9. The current view of intensive intraoperative insulin therapy is that it:
   (A) Increases the risk for stroke and death
   (B) Is no better or worse than conventional insulin therapy
   (C) Improves outcomes only in patients with type 1 diabetes
   (D) Reduces the risk for perioperative hypoglycemic events

10. The ideal range of perioperative glucose for a diabetic patient is currently believed to be:
    (A) 100 to 130 mg/dL
    (B) 110 to 140 mg/dL
    (C) 120 to 150 mg/dL
    (D) 130 to 160 mg/dL

Answers to Audio-Digest Anesthesiology Volume 54, Issue 13: 1-D, 2-C, 3-B, 4-A, 5-D, 6-B, 7-C, 8-A, 9-C, 10-D