A 61-year-old woman is admitted to the ICU with head trauma following an alcohol-induced fall down a flight of stairs. She is known to have moderately severe COPD, but is otherwise in relatively good health. Her admission CT scan of the head is normal. Five days after ICU admission, she has a Glasgow coma scale score of 10, with pupils 4 mm and reactive to light. She opens her eyes to voice, loud sounds, and pain, but makes only incomprehensible sounds. She localizes and withdraws purposefully to painful stimuli. No seizure activity has been observed, and an EEG shows only diffuse slow-wave activity. She is afebrile and remains extubated, and has a forceful spontaneous cough productive of mucoid phlegm. Her medications consist of occasional morphine for discomfort and nebulized albuterol and ipratropium bromide for COPD. While you are discussing her status and prognosis at the bedside with her husband, the nurse interrupts your conversation to tell you that the patient has a fixed and dilated pupil on the right side (Fig 1). You immediately examine the patient, but apart from the dilated pupil, her physical examination remains unchanged. An urgent CT scan of the head shows no changes. The patient’s husband, a retired neurologist, is alarmed and asks what will be done next. What is the best course of action at this point?

A. Reassure her husband that this is likely a transient medication side effect that should spontaneously resolve.
B. Administer 25 g of 20% mannitol IV over 30 min.
C. Intubate the patient and begin deliberate hyperventilation to reduce the PaCO₂ to 15 to 20 mm Hg.
D. Call for an emergency neurosurgery consult to arrange for an urgent craniotomy.
E. Advise the husband that only palliative measures are indicated, as a brainstem herniation is developing and she will soon die.

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Answer: A. Reassure her husband that this is likely a transient medication side effect that should spontaneously resolve

The only change in this patient’s clinical status is the development of a fixed and dilated pupil. Because the repeat CT scan of the head was unchanged and normal, and in the absence of other signs of cerebral deterioration, it is highly unlikely that she has had a new intracerebral catastrophe. Another explanation for her unilateral pupillary dilatation should thus be considered. Causes of a unilateral dilated pupil include brainstem herniation, mydriatic agents, third cranial nerve palsy, local eye trauma, and acute glaucoma. In this case, the most likely explanation is a drug effect (option A), specifically pupillary dilatation and the possible risk of acute angle glaucoma secondary to topical deposition on the eye of nebulized bronchodilators.

Pupillary dilatation increases the tightness of contact between the iris and the lens, which can impede the flow of aqueous humor out of the anterior chamber of the eye. In subjects predisposed to angle-closure glaucoma, this can provoke a rise in intraocular pressure and an acute attack. Any stimulus that causes pupillary dilatation can trigger an acute attack of angle-closure glaucoma, including instillation of mydriatic drops, dim lighting, emotional stress, and the use of anticholinergic or sympathomimetic medications. Although this effect has been reported with nebulized ipratropium bromide alone, several case reports suggest an additive effect of combined therapy with nebulized β2-adrenergic and anticholinergic bronchodilators. In a randomized controlled trial in 46 patients with COPD, 36 of whom had proven glaucoma, when both albuterol and ipratropium bromide were nebulized in combination, pupillary dilatation occurred, followed by a rise in intraocular pressure in patients with angle-closure glaucoma, but not in those with open-angle glaucoma or in control subjects. Intraocular pressures did not rise when either bronchodilator was nebulized separately, or when goggles were used to prevent topical deposition of the bronchodilators. Continuation of antiglaucoma therapy also appeared to be protective.

The incidence of glaucoma is estimated at 1.2% in people > 40 years of age; therefore, it is to be expected that acute glaucoma will occur from time to time in patients receiving nebulized bronchodilators by either face mask or even possibly by tracheostomy hood. Bronchodilators administered via an endotracheal tube would not be expected to lead to topical deposition on the eyes and acute glaucoma in patients at risk, unless associated with a significant breakdown in technique. While our patient had pupillary dilatation secondary to topical deposition of bronchodilators in the right eye, she showed no other signs or symptoms of acute glaucoma because she did not have acute angle-closure glaucoma as an underlying condition.

Because an intracerebral catastrophe is highly unlikely in our patient, options B, C, D, and E are incorrect. If it existed, elevation of raised intracranial pressure due to hyperemia might temporarily respond to acute hyperventilation, but the target PaCO2 of 15 to 20 mm Hg suggested in option C is too aggressive and might even cause harmful cerebral vasoconstriction. Similarly, infusing IV mannitol might also help treat intracranial hypertension if it existed (option B), but the dose of mannitol usually recommended would not be the 25 g suggested in option B, but rather 1.5 to 2 g/kg, which for the average adult would be 100 to 150 g.

Selected Readings

Kaltra L, Bone MF. The effect of nebulized bronchodilator therapy on intraocular pressures in persons with glaucoma. Chest 1988; 93:739–741