Practice Tips

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Subcutaneous midazolam for acute hemorrhage in patients with advanced cancer

Although the incidence of massive or catastrophic bleeding in advanced cancer patients is infrequent (estimated at about 10%[1]), when it does occur, it can be distressing for patients, their families, and often their health care providers. Tumours prone to massive bleeding include chest wall masses with breast carcinoma, advanced cervical carcinoma, and large intra-abdominal tumours, such as sarcomas.[2]

Infiltration of large vessels or vascular structures also can result in catastrophic bleeding, as with cancers of the head and neck. Other causes of massive bleeding include hemostatic disorders resulting from bone marrow failure, diffuse intravascular coagulopathy, liver failure with clotting dysfunction, and thrombocytopenia secondary to malignancy or its treatment.[3] Medications, such as nonsteroidal anti-inflammatory drugs, acetylsalicylic acid, and anticoagulants, also can exacerbate bleeding.

Indications

In some cases of massive bleeding, death occurs rapidly. Other times the event is more prolonged, and this exacerbates an already emotionally distressing situation. In some cases, a patient might need to be sedated in order to alleviate his or her distress. We, the Palliative Care Program in Edmonton, have found the benzodiazepine, midazolam (Versed), to be an ideal medication for these situations.

The properties of midazolam that make it so appealing include its rapid onset of action, usually from within seconds to a few minutes[4]; its lack of need for refrigeration; and the fact that it can be administered subcutaneously.[5] A standard starting dose of 5 mg subcutaneously can be repeated every 10 to 15 minutes until the patient is adequately sedated.

Procedure

To establish a subcutaneous line, select an area of the body that is free of infection and lymphedema. Common sites of insertion are the anterior torso and the proximal humerus. Clean the site with isopropyl alcohol. Insert a 23- or 25-gauge butterfly needle with attached short tubing (eg, an E-Z set) at about a 45° angle into the subcutaneous tissue. Ensure a lock for injecting medications is attached to the end of the tubing. Appropriately secure the butterfly needle and tubing with tape or adhesive dressing. Flushing of the line with water or heparin is not required to maintain patency. Observe the site every 3 days to monitor for redness or swelling that would necessitate needle removal and change of site. Midazolam can be injected from a syringe into the line as required.

Discussion

One advantage to midazolam is that it can be stored in prefilled syringes at room temperature; lorazepam (eg, Ativan), on the other hand, requires refrigeration. If midazolam is kept in a prefilled syringe, however, it does exhibit some instability and, for this reason, it is suggested that syringes be refilled at least every 4 to 7 days.[5]

One side effect of midazolam is respiratory depression, which is more likely to occur when large or closely spaced repetitive doses are administered. Respiratory depression from midazolam administered for acute hemorrhage in advanced cancer patients is less of a concern, given that the ➢

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CLINICAL CHALLENGE

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hemorrhage is almost always the terminal event.

Midazolam can be used in acute palliative care units or hospices, but also can be used by family members or home health care workers, providing they feel comfortable and have been instructed on appropriate dosing and administration, for patients at home. ✱

References

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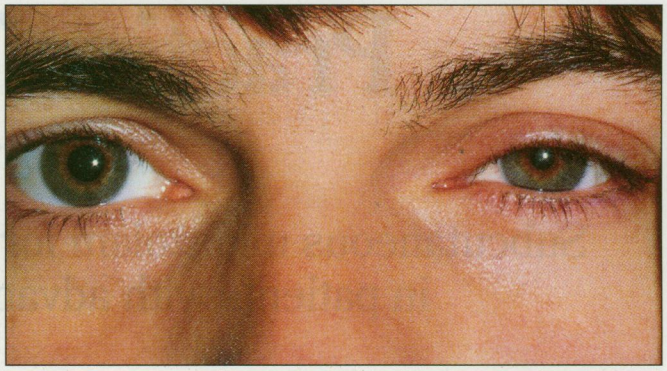
Figure 1. Left eye demonstrates Horner's syndrome: *Ptosis and miosis (small pupil) are evident.*



Answer to Ophthaproblem

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2. Horner's syndrome (left eye)

The size of the pupil is controlled both sympathetically and parasympathetically. When catecholamines are released, pupillary dilators are stimulated, and the pupil diameter increases. When the parasympathetic system is stimulated, pupillary constrictors are stimulated, and the pupil becomes smaller.

Parasympathetic nerve fibres arise from the Edinger-Westphal nucleus (one of the subnuclei of the third cranial nerve), and travel in the outer fascicles of the third cranial nerve through the subarachnoid space, the cavernous sinus, and the orbit before entering the eye. Disruption of these fibres causes the pupil to enlarge (mydriasis). Third-nerve palsies are classified as pupil-involving or pupil-sparing. Common causes of third-nerve palsies include diabetes, hypertension, neoplasms, and aneurysms. Posterior communicating aneurysms should be ruled out in patients with pupil-involving third-nerve palsy.

The sympathetic fibres innervating the eye consist of a three-neuron system. Cell bodies of first-order neurons arise from the posterolateral hypothalamus and synapse at Budge's centre (C-8 to T-2 level). Second-order neurons exit the spinal cord at the T-1 level in the ventral root and travel near the apex of the lung and synapse at the superior cervical ganglion. Third-order neurons travel with the internal carotid artery through the cavernous sinus and enter the orbit with the third cranial nerve.

Disruption of the sympathetic fibres anywhere along this three-neuron pathway results in the classic features of Horner's syndrome: miosis (disruption of the pupillodilator fibres), ptosis (sympathetic fibres stimulate Müller's muscle to work in conjunction with the levator muscle to open the eyelid), and anhidrosis (loss of ability to sweat on the affected side).

The causes of Horner's syndrome can be considered in terms of which neuron is affected: first-order neuron dysfunction (stroke or tumour), second-order neuron dysfunction (tumour—lung carcinoma, metastasis, thyroid adenoma, or neurofibroma), third-order neuron dysfunction (headache syndrome—cluster, migraine or Raeder's paratrigeminal syndrome neuralgia, otitis media, or Tolosa-Hunt syndrome).[1] Maloney and colleagues reviewed 450 cases of Horner's syndrome and noted that malignant neoplasms caused 8% of cases.[2] Most of these patients also had concomitant sensations in their arms suggestive of a Pancoast tumour.[2] Horner's syndrome can be classified clinically as preganglionic (first- or second-order neuropathy) or postganglionic (third-order neuron) and confirmed pharmacologically.[3,4] Patients with preganglionic Horner's syndrome should

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