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Forearm Compartment Syndrome after Diazepam Administration

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Intravenous diazepam is one of the most widely used agents for establishing sedation during ambulatory operative procedures. Although generally safe, a variety of local complications can occur with its use; irritation and thrombophlebitis are the most common.[1,2] We present a case of a patient developing forearm compartment syndrome after administration of injectable diazepam *via* an antecubital fossa vein.

Though not previously reported, compartment syndrome is a potentially limb-threatening complication of parenterally administered diazepam.

Case Report

The patient was a 51-yr-old man, right-hand dominant, who received 10 mg (2 ml) diazepam by direct percutaneous injection into the right antecubital fossa, for sedation during cystoscopy. An intravenous catheter was not inserted, nor was fluid administered during the procedure. No monitoring devices, such as blood pressure cuff, were applied to either upper extremity.

Although the patient denied drug allergies, he reported that after previous administration of diazepam *via* a right upper extremity vein, he had experienced "burning" during injection, with subsequent development of phlebitis with a palpable cord. Uneventful resolution occurred in that case.

During the current procedure, the patient experienced sharp pain during and immediately after direct diazepam injection, necessitating needle withdrawal from the site, and administration of another 10-mg dose *via* direct injection into a left antecubital vein. After satisfactory sedation was obtained, the urologic procedure was completed, and the patient was discharged home. A small area of ecchymosis was noted at the right antecubital injection site.

Approximately 8 h after the procedure, the patient was awakened by new, severe pain in the right forearm and was directed to the hospital emergency department. Examination of the right upper extremity revealed pale, cool digits, diminished grip strength and sensation, mottling of the extremity with cyanosis of the volar skin, extensor weakness, and global radial, median and ulnar nerve dysfunction. Symmetrical palpable radial pulses and absence of ulnar artery pulses were noted bilaterally. Bilateral radial and ulnar artery flow was confirmed, however, by Doppler examination. Hand surgery evaluation was obtained, 24 h postinjury, for probable compartment syndrome. The volar forearm was tense and exquisitely tender; forearm circumference, measured 5 cm distal to the medial epicondyle, was 30.5 cm on the right and 26 cm on the left. The patient was taken to the operating room for emergency exploration of the brachial artery to rule out laceration or injection injury and for release of the forearm fascial compartments.

At surgery, there was no evidence of injury, spasm or thrombosis of the brachial artery from the distal arm to its bifurcation in the forearm. An arterial puncture site was not identified, and there was no evidence of periarterial bleeding or adventitial hematoma. A tense anterior compartment was observed, however, which, when incised, produced bulging, pale, edematous forearm musculature. The wrist flexor and carpal ligaments were released. Forearm skin color and hand circulation improved gradually after release.

Postoperatively, however, progressive dry gangrene of all digits, particularly the ulnar digits, occurred. Subsequently, multiple reconstructive procedures have been performed, including skin grafts and flaps, release of flexion contractures, revision of fasciotomy sites, revision of amputation sites, and flexor lengthening. The patient has returned to work.

Discussion

Since its introduction in 1965, intravenous diazepam has become one of the most widely used agents during ambulatory surgical and endoscopic procedures. Previously reported local complications resulting from parenteral diazepam administration range from irritation and phlebitis after intravenous infusion[1,2] to limb loss after inadvertent intraarterial administration.[3]

Compartment syndrome is a symptom complex resulting when microcirculation and tissue function within a closed osseofascial space are compromised by increased tissue pressure within that space. The classic findings of compartment syndrome include pain, increased compartment pressure, pulse preservation, paresis, and paresthesia. The pain characteristically is persistent and progressive, unrelieved by immobilization, and exacerbated by passive muscle stretching. Distal pulses rarely are obliterated, even under conditions of profound nerve and muscle ischemia. Increased pressure, with a palpably tense compartment, is the pathognomonic sign of compartment syndrome.[4,5],§

The diagnosis is made clinically, based on findings consistent with pressure-induced muscle and nerve ischemia. If the diagnosis is in doubt or if clinical findings are equivocal, confirmation may be obtained by various modalities,

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§ Mubarak SJ, Owen CA, Hargens AR: Acute compartment syndromes: Diagnosis and treatment with the aid of the wick catheter. J Bone Joint Surg 60A:1091–1095, 1978.

including intracompartment pressure measurement and electromyography.[6,§]

As many as 62% of patients receiving intravenous diazepam develop phlebitis, as our patient had previously. The propylene glycol solvent used in production of injectable diazepam is an intravascular irritant.[1,2] Inadvertent intraarterial infusion can cause marked platelet aggregation, leading to thrombosis and even limb loss.[3]

Possible causes of compartment syndrome in this case may include: inadvertent intraarterial injection, with profound vasospasm and thrombosis; iatrogenic injury of the brachial artery, with subfascial bleeding; subcutaneous or subfascial administration of the drug; or an idiosyncratic or allergic reaction to the agent or the diluent.

In this case, intraarterial injection is quite unlikely since exploration and direct visual inspection of the brachial artery proximal and distal to the skin injection site did not reveal evidence of puncture or laceration. Furthermore, massive subcutaneous edema, adventitial hematoma, vessel thrombosis, or hematoma within the anterior compartment were not present. Lack of cannulation of the antecubital vein or infiltration after cannulation, with subfascial infusion or extravasation of diazepam, may have occurred during the initial injection, resulting in the pain reported by the patient.

Injectable diazepam solution is hypertonic.¶ Perhaps the hypertonicity of the solution induced fluid shifts, with net movement of fluid into the unyielding confines of the closed osseofascial forearm compartment, resulting in development of a compartment syndrome. Compartment syndrome, secondary to massive subcutaneous edema, has been reported after use of hypertonic saline in a local anesthetic solution used for regional intravenous anesthesia of the upper extremity; compartment syndrome in that case presumably was due to the osmotic effect of the hypertonic solution.[7] Platelet antibodies to diazepam have been reported,** and drug sensitization has been suggested as a cause of extensive intravascular thrombosis, necessitating above-elbow amputation.[3] Massive thrombosis was not evident, however, in the current case. Regardless of etiology, delay in diagnosis and treatment may result in irreversible ischemia and eventual tissue necrosis.

Local complications of parenteral diazepam administration may possibly be avoided by documenting intravenous cannulation, administering slowly, flushing with normal saline, and changing infusion sites immediately upon infiltration.[1] Direct injection should be avoided. Significant pain on infusion is abnormal and may indicate intraarterial or extravenous injection. Injection of diazepam within a closed subfascial space may result in gradual development of compartment syndrome due to osmotic pressure gradients, which if not recognized and promptly treated, may lead to Volkmann's ischemic contracture and/or frank tissue necrosis.

¶ Korttila K, Sothman A, Andersson P: Polethylene glycol as a solvent for diazepam: Bioavailability and clinical effects after intramuscular and rectal administration: Comparison of oral, intramuscular and rectal administration, and precipitation from intravenous solutions. Acta Pharmacol Toxicol 39:104–116, 1976.

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