An adverse reaction with hydralazine: A case study

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The authors discuss a case in which bradycardia occurred following the administration of hydralazine. They caution anesthetists to be aware of such potential adverse reactions when using this agent.

The mechanism of antihypertensive action of hydralazine (Apresoline®) is primarily direct relaxation of vascular smooth muscle. It produces a greater drop in the diastolic pressure than in systolic pressure because of the marked relaxant effect on arterioles over venules, decreasing systemic resistance. This preferential effect on arterioles increases cardiac output, heart rate, stroke volume and minimizes postural hypotension.¹

Hydralazine-produced peripheral vasodilatation occurs throughout the body, but without uniformity. Unless the blood pressure falls precipitously, blood flow is increased to the splanchnic, coronary, cerebral and renal areas of the body. Tachycardia is seen in even small doses of hydralazine and is believed attributable to a reflex response to decreased blood pressure.¹

The normal action of hydralazine is to decrease blood pressure, primarily diastolic, and the action is evidenced by a tachycardia which usually requires a beta adrenergic blocking agent such as Inderal® (propranolol). The following case report illustrates an adverse reaction to hydralazine.

The case

A 59-year-old Caucasian male, 80 kilograms, was admitted to the neurosurgical department for evaluation of weakness on the right side, speech difficulty and confusion. A CT scan revealed a left-frontal ring enhancing lesion with moderate midline shift. The patient exhibited expressive aphasia, decreased motor activity on the right side and hyperreflexia. A detailed history was not obtainable.

An increase in blood pressure was found during the physical examination ranging from 150/80 to 160/90. The rest of the physical exam was unremarkable with the exceptions as noted above upon admission. Laboratory values were within normal limits: HCT 43.0; HGB 14.6; PT 11.1; PTT 26.8; Na 139; K 4.5; Cl 105; and CO₂ 23. The preoperative chest x-ray showed a 2-cm mass over the left hemidiaphragm, possibly neoplasm, metastasis, or calcified granuloma. The ECG showed an abnormal Q-wave in lead AVL with the possibility of a previous auricular myocardial infarction. No prior tracings were available for comparison.

A left frontal craniotomy was scheduled and the patient placed on a regimen of dexamethasone, phenytoin (diphenylhydantoin), and antibiotics. Premedication was withheld because of suspected increased intracranial pressure (ICP).

The patient arrived in the operating suite in a confused, semiaphasic state. A large-bore intravenous infusion was started in the right forearm,
an arterial monitor was inserted in the right radial artery and a central venous pressure (CVP) catheter was inserted in the right internal jugular vein. Placement of ECG leads and a Doppler Versatone™ on the patient's chest completed the routine monitoring systems. An intracranial pressure monitor was inserted and transduced with a pressure reading of 17 mmHg.

Anesthesia was induced with the patient in the supine position. The trachea was sprayed with 4% Xylocaine® (lidocaine). During intubation, the mean arterial pressure and ICP remained in the preanesthesia range of 80 and 17, respectively. Pancuronium 6 mg was given for surgical relaxation and anesthesia was maintained with Sublimaze® (fentanyl), nitrous oxide and oxygen. Halothane .2-.5% was required 11/2 hours post-induction to maintain the mean arterial pressure between 75-80 mmHg.

Pulse rate throughout the procedure was 50-60 beats per min and mean arterial pressure varied from 74-82 mmHg. Serial arterial blood gases revealed the PCO₂ in the range of 25-28 mmHg. The case progressed uneventfully and a left-frontal lobe tumor (astrocytoma grade III) was removed without incident. Halothane administration ended 30 min prior to closure of the incision. The patient's mean arterial pressure began a steady increase, and at the time of skin closure, had attained a pressure of 110 mmHg.

Hydralazine was chosen for its antihypertensive effect and 2 mg were administered intravenously (IV). Within a brief period of time (30-45 sec) the patient developed a profound bradycardia from 52-10 beats/min occasioned by premature ventricular contractions (PVCs). Atropine 0.4 mg was given IV and, over a period of 2 min, the pulse returned from bigeminy to a normal sinus rhythm of 58 beats per minute. The mean arterial pressure returned to 110 mmHg.

Five minutes after the pulse returned to normal sinus rhythm, a repeat dosage of 2 mg hydralazine was given IV and the desired antihypertensive effect was obtained without tachycardia. The repeat dosage was given for a two-fold purpose: primarily to obtain the anti-hypertensive effect, and secondarily to see if repeat bradycardia could be elicited in this patient. However, bradycardia did not occur, possibly due to the anticholinergic effect of atropine.

The muscle relaxant was reversed and the patient was suctioned and extubated at the end of the procedure. The patient, responsive and moving all extremities, was moved to the surgical intensive care unit.

**Discussion and summary**

Several variables in this case can be identified as possible etiological factors contributing to the adverse response. First, there is the question of what the patient's cardiac condition was prior to surgery. Other factors to consider include the possibility of a drug interaction with Sublimaze® which was given throughout the three hours, the effect of surgical stimulation and the pain response, the possible presence of an air embolus, and increased intracranial pressure.

Each variable in question can be accounted for with reliable sequential substantiation. Usually, when Sublimaze® is the primary agent used, hydralazine is selected to counteract increasing arterial pressure at the end of neurosurgical procedures. We have never experienced any profound bradycardia with hydralazine in healthy patients or patients with previously diagnosed cardiac abnormalities.

High dose Sublimaze® for induction has been used in open heart and other neurosurgical procedures at our institution without the adverse reaction seen in this patient at the point when hydralazine administration was necessary. The possibility of drug interactions was eliminated because of the sites of action of both drugs. Sublimaze® is primarily a central nervous system stimulant and cholinomimetic in action whereas hydralazine is primarily adrenergic in action.1,4

Surgical stimulation was also discounted in this case because the surgical team was near termination of skin closure. An air embolus was suspect, however, aspiration of the CVP revealed no air extraction and heart sounds; and mean arterial pressure did not vary prior to the episode of bradycardia. The intracranial pressure was continually monitored and remained at 0 prior to, during, and following the incident.

The elimination of possible etiological factors limits the chances that extraneous factors were responsible. It does, however, substantiate the probability that hydralazine was the causative factor of the profound bradycardia. One staff member encountered similar occurrences in the medical intensive care unit when using hydralazine on two occasions. The resultant bradycardia was not of the magnitude experienced by our patient, but still required the use of an adjunctive agent for reversal.*

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*Subsequent to this writing, other instances of bradycardia have occurred with the use of hydralazine IV.
Careful evaluation of this case by anesthesia record review and continuous strip chart recording did not reveal any causative factor other than use of the drug hydralazine. The possibility that this was an idiosyncratic episode by this particular patient remains; however, this case report should alert every CRNA to the fact that possible adverse reactions could occur.

Since hydralazine is used for treatment of moderate hypertension and, in some areas, for prevention of hematomas in plastic surgical procedures, the user should be aware of the possibility of adverse reactions.

REFERENCES


AUTHORS

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