

Anesthesiology
57:540-542, 1982

Refractory Hypertension during Coarctectomy

CAROLYN WILKINSON, M.D.,* AND HOWARD CLARK, M.D.†

Coarctation of the aorta is corrected surgically to prevent sequelae of hypertension. Although rebound hypertension is common during the first 24 hours following surgery and may last for several weeks, repair of the lesion in early childhood or early adolescence does not result in a higher incidence of resting hypertension in late adolescence or early adulthood.¹

Excessive bleeding and hypertension during clamping of the aorta can occur, but anesthesia usually is uncomplicated,² and severe refractory hypertension during operation has not been reported. We describe a patient, who during halothane anesthesia, developed severe hypertension, refractory to sodium nitroprusside and other vasodilators.

REPORT OF A CASE

A 16-year-old 56-kg male adolescent was scheduled for coarctectomy. At one month of age, a difference in arterial pulses in upper and lower extremities was found. He had no symptoms of headache, vertigo, dyspnea, palpitations, or fatigue of legs. He had no prior operations and took no medications.

Physical examination revealed a right arm arterial blood pressure of 160/66 mmHg, left arm 156/68 mmHg, heart rate 65 beats/min, respiratory rate 16/min. His lungs were clear, and examination of the heart revealed a systolic murmur at the base. The electrocardiogram showed sinus arrhythmia. Chest roentgenogram demonstrated dilation of the aorta inferior to the aortic knob, but no notching of ribs. Femoral pulses were not palpable.

Morphine, 10 mg, and 0.4 mg atropine were given one hour prior to surgery. Peripheral venous, arterial, and external jugular catheters were inserted, and electrodes were attached for monitoring EKG and heart rate. After induction of anesthesia with 375 mg thiopental, iv, and tracheal intubation with the aid of 120 mg succinylcholine, iv, arterial blood pressure decreased from 160/80 to 120/80 mmHg, and the heart rate from 120 to 110 beats/min. Anesthesia was maintained with 1.2% halothane and 50% nitrous oxide. Analysis of arterial blood gases after induction of anesthesia showed a pH_a 7.48, Pa_{CO_2} 33 mmHg, Pa_{O_2} 218 mmHg, and base excess 2.0 mEq/l. Arterial blood pressure and heart rate did not vary during the first half hour of anesthesia, but arterial blood pressure rose to 150/80 mmHg during the next 15 min, and stabilized between 140/80 and 150/80 mmHg in the ensuing 90 min, despite administration of 2% halo-

thane. At this time, pH_a was 7.47, Pa_{CO_2} 33 mmHg, Pa_{O_2} 222 mmHg, and base excess 1.0 mEq/l. Before application of the aortic clamp, attempts to lower blood pressure with intravenous nitroglycerin administered at an infusion rate of $9 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ to a total dose of 20 mg caused only a 10 mmHg decrease in systolic blood pressure, a fall in central venous pressure from 12 to 10 cmH₂O, and an increase in heart rate to 120/min. Nitroglycerin was discontinued and sodium nitroprusside (SNP) titrated to $15 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ over 15 min also had little effect on systolic blood pressure. Although the minimal change in arterial blood pressure with clamping of the aorta suggested limited flow through the constricted segment, 15 min after aortic occlusion, the systolic blood pressure rose to 200 mmHg, despite further increased amounts of SNP.

Chlorpromazine, 2.5 mg, and then 5 mg phentolamine were given iv without effect. The pH_a was 7.47, Pa_{CO_2} 30 mmHg, and Pa_{O_2} 145 mmHg. Central venous pressure was 12 cmH₂O. Arterial blood pressure continued to rise to 240/90 mmHg, and the heart rate remained at 120/min. Propranolol was administered in 0.2-mg doses, up to a total of 1 mg, and followed by an additional 5 mg chlorpromazine. Halothane was discontinued and 3% isoflurane was administered. Arterial blood pressure 10 min later remained elevated at 230/95 mmHg, and tachycardia persisted at 120/min.

Sodium nitroprusside, $15 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, was discontinued gradually as trimethaphan $150 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ was begun. Nevertheless, even after more propranolol, 1.0 mg, iv, given in divided doses, arterial blood pressure remained at 250/100 mmHg, although heart rate decreased to 100/min.

Five minutes prior to removal of the aortic cross clamp, all drugs and anesthetic agents were discontinued without change in blood pressure or heart rate. When the aortic cross clamp was removed, arterial blood pressure decreased transiently to 80/40 mmHg, the heart rate to 80/min, and the CVP from 12 to 8 cmH₂O. The arterial blood pressure gradually increased over 10 min to 130/80 mmHg, and heart rate to 105/min. Isoflurane, 0.5 percent, and additional propranolol, 0.4 mg, were administered iv.

At the end of surgery, arterial blood pressure was 155/95 mmHg and heart rate 100/min; trimethaphan was restarted at $100 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, and continued during transport to the recovery room. The final intraoperative vital signs were an arterial blood pressure of 130/85 mmHg, a heart rate of 90/min, and a spontaneous respiratory rate of 20/min.

Intraoperative blood loss was 400 ml and 3.0 l lactate Ringer's solution and 0.25 l albumin were given during the 4-hour procedure. Urinary output was 215 ml. Total intraoperative drug dosages were, 20 mg nitroglycerin, 50 mg nitroprusside, 7.5 mg chlorpromazine, 5 mg phentolamine, 2.4 mg propranolol, and 250 mg trimethaphan, iv.

Postoperatively, blood pressure remained difficult to control despite administration of 15 mg propranolol and 35 mg hydralazine, iv, in divided doses during the first six hours in the intensive care unit. Trimethaphan was discontinued over an 18-hour period. Systolic blood pressure ranged between 144 and 174 mmHg, and heart rate between 110 and 124/min. Propranolol, 10 mg, and 25 mg hydralazine were given every six hours orally after leaving intensive care. The patient went home on the eight postoperative day, with a systolic blood pressure ranging between 154 and 188 mmHg and a heart rate between 90 and 100/min. His medications at discharge were 50 mg hydrochlorothiazide, 0.25 mg reserpine, and 25 mg hydralazine, to be

* Assistant Professor, Department of Anesthesia.

† Resident in Anesthesia.

Received from the Department of Anesthesiology, Northwestern University Medical School, 303 East Superior, Chicago, Illinois 60611. Accepted for publication June 30, 1982.

Address reprint requests to Dr. Wilkinson.

Key words: Blood pressure: hypertension. Complications: hypertension. Surgery: vascular, coarctectomy. Sympathetic nervous system: sympatholytic agents.

taken three times a day. Six weeks after surgery, his systolic pressure was normal and all medications were discontinued. A normal blood pressure has persisted.

DISCUSSION

The mechanisms of hypertension in coarctation of the aorta and of postoperative rebound hypertension following repair are not understood completely. Three theories have been postulated. The mechanical theory suggests that preoperative hypertension is caused by the high resistance of the narrowed segment proximal to the coarctation,³ but this does not explain elevated mean arterial pressure distally⁴ or development of rebound hypertension after surgery. The neural theory proposes that increased pressure proximal to coarctation alters carotid and aortic baroreceptors structurally or functionally, preventing normal reflex decrease in sympathetic stimulation when buffer nerves are stimulated.⁵ Although a marked increase in plasma noradrenaline concentration occurs after coarctectomy,⁶ evidence does not indicate that this increased sympathetic nervous system activity is mediated by baroreceptors set at a higher level. The renal theory postulates that underperfusion of the kidney secondary to aortic coarctation produces a Goldblatt phenomenon. In dogs, autotransplantation of one kidney to a site proximal to aortic stricture causes significant lowering of arterial pressure.⁷ Although renal blood flow is not decreased in coarctation of the aorta,⁸ implication of the renin-angiotensin system (RAS) may have some credence.⁹

Past studies of the RAS and plasma renin activity (PRA) have not shown consistently elevated PRA in patients with coarctation of the aorta,¹⁰⁻¹² but the role of sodium balance was not appreciated and assessment of RAS with specific blocking agents was not available. After a low salt diet and administration of furosemide to patients with coarctation of the aorta, significantly higher levels of PRA (compared to those in a control group of healthy patients) have been reported, and preoperative and postoperative administration of saralasin (1-sarcosin-8-alanine-angiotensin II), a specific blocker of angiotensin II, to these patients significantly reduced arterial pressure and confirmed the presence of excess angiotensin II.^{13,14} The hypotensive response to saralasin suggests the RAS has a role in the hypertension of patients with coarctation of the aorta. We speculate that RAS may also have played a role in the severe hypertensive episode in our patient.

Both halothane² and sodium nitroprusside¹⁵ (SNP) have been proposed for use during coarctectomy. Since halothane depresses the sympathetic nervous system, decreases cardiac output, and slightly decreases peripheral vascular resistance,¹⁶ it has been favored for control of hypertension during coarctectomy in the young. During resection, maintenance of arterial pressure between

a mean of 80 mmHg enables the patient's normal blood pressure to be obtained with halothane. If not, administration of SNP prior to aortic occlusion usually reduces hypertension and the elevated left ventricular filling pressure.

Halothane and SNP, however, may not always be effective during coarctectomy. A preliminary report of patients receiving halothane for coarctectomy suggested a greater incidence of postoperative rebound hypertension than in those receiving nitrous oxide, muscle relaxants, and thiopental,¹⁷ although no controlled randomized studies of these two agents have been performed. During halothane anesthesia, the RAS plays a significant role in maintaining blood pressure. The use of SNP alone or during anesthesia stimulates renin release and subsequent production of angiotensin II, which causes partial recovery of blood pressure and may be partially responsible for rebound hypertension after withdrawal of SNP.¹⁸⁻¹⁹ Indeed, in rats, administration of saralasin during halothane anesthesia will block both the partial recovery of blood pressure during administration of SNP and the rebound hypertension after discontinuation of SNP, verifying that the RAS antagonizes the combined hypotensive effects of halothane and SNP.²⁰ In addition, SNP has been reported to increase blood catecholamine levels²¹ and elevate heart rate and stroke volume.²²

Although anesthesia *per se* does not activate the RAS in humans, surgical trauma, renal perfusion pressure, fluid and blood loss, plasma sodium concentration, renal sympathetic stimulation, and centrally released catecholamines influence renin release. Our patient was normovolemic preoperatively. Although he received liberal quantities of fluid iv ($9 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$), postoperatively his central venous pressure ranged from 4-6 cmH₂O and chest roentgenogram and arterial blood gases did not reflect interstitial pulmonary edema.

The clue to control of hypertension after occluding the thoracic aorta is manipulation of systemic vascular resistance and cardiac output. Generally, peripheral vasodilators are effective in controlling hypertension even though part of the peripheral vascular bed is excluded by the aortic clamp.²³ In our patient alpha-adrenergic blockers were not effective, and are not advised because they can increase stroke volume and heart rate. Also, isoflurane was not effective, possibly due to the fixed resistance presented by the occluded aorta.

We believe that drugs affecting the RAS may more likely allow control of refractory hypertension in thoracic vascular operations. Although the use of propranolol has not been advised in coarctectomy because the chronotropic and inotropic effects may prevent restoration of cardiac output in the event of sudden blood loss,²⁴ propranolol can control heart rate and block sympathetic activity at the juxtaglomerular apparatus,

thereby inhibiting renin release. In our patient, larger doses may have been more effective but were limited by anticipation of severe hypotension when the aortic clamp was removed.

Ganglionic blocking drugs may allow more effective control of hypertension than SNP, because they decrease sympathetic activity and thus also inhibit renin release. Knight *et al.* were able to prevent increases in PRA, circulating levels of angiotensin II, and catecholamines using ganglionic blockade, propranolol in young children using morphine anesthesia, and deliberate hypotension during correction of scoliosis.²⁵ Indeed, when compared with chlorpromazine, nitroprusside, and nitroglycerin, trimethaphan is especially effective in decreasing systemic vascular resistance and cardiac index.²²

Captopril, a competitive inhibitor of angiotensin I converting enzyme, and effective in patients requiring multi-drug regimens for control hypertension, may prove to be useful in patients with coarctation of the aorta since preliminary evidence suggests that angiotensin II may play a role in development of postoperative rebound hypertension and mesenteric vasculitis.²⁶

Hydralazine, a direct-acting vasodilator, also reflexly causes tachycardia and increased cardiac output, and is not a drug of choice for treating rebound hypertension after coarctectomy, unless combined with propranolol. Reserpine causes a slowly developing fall in blood pressure, a decreased peripheral vascular resistance, and is associated with a reduced cardiac output. This drug, along with propranolol, may be more appropriate for the postoperative period.

The etiologic factors of hypertension secondary to coarctation of the aorta and its surgical repair is exceedingly complex and multifactorial. Increased activity of sympathetic nervous system and RAS have been documented. The activity of both systems may best be decreased by the use of ganglionic and beta receptor blockade. Although these drugs seem preferable for intraoperative and postoperative hypertension, the use of competitive inhibitors of angiotensin I converting enzyme and blockers of angiotensin II may ultimately prove to be more effective.

REFERENCES

- Hubbell MM, O'Brien RG, Krovetz LJ, Mauck HP, Tompkins DG: Status of patients 5 or more years after correction of coarctation of the aorta over age 1 year. *Circulation* 60:74-80, 1979
- Smith RM: *Anesthesia for infants and children*. St. Louis, CV Mosby, 1980, pp 358
- Bing RJ, Handelsman JC, Campbell JA, Griswold HE, Blalock A: The surgical treatment and the pathophysiology of coarctation of the aorta. *Ann Surg* 128:803-824, 1948
- Harris JS, Sealy WC, DeMaria W: Hypertension and renal dynamics in aortic coarctation. *Am J Med* 9:734-746, 1950
- Sealy WC: Coarctation of the aorta and hypertension. *Ann Thorac Surg* 3:15-28, 1967
- Benedict CR, Phil D, Grahame-Smith DG, Fisher A: Changes in plasma catecholamines and dopamine beta-hydroxylase after corrective surgery for coarctation of the aorta. *Circulation* 57:598-602, 1978
- Scott HW, Bahnson HT: Evidence for a renal factor in the hypertension of experimental coarctation of the aorta. *Surgery* 30:206-217, 1951
- Culbertson JW, Eckstein JW, Kirkindall WM, Bedell GN: General hemodynamics and splanchnic circulation in patients with coarctation of the aorta. *J Clin Invest* 36:1537, 1957
- Sealy WC, Panijayanomid P, Alexander J, Seaber AV: Activity of plasma angiotensin II in experimental coarctation. *J Thorac Cardiovasc Surg* 65:283-291, 1973
- Amsterdam EA, Albers WH, Chritlieb AR, Morgan CL, Nadas AS, Hickler RB: Plasma renin activity in children with coarctation of the aorta. *Am J Cardiol* 23:296-309, 1969
- Werning, C, Schonbeck M, Weidman P, et al: Plasma renin activity in patients with coarctation of the aorta. *Circulation* 40:731-737, 1969
- Markiewicz A, Wojczuk D, Kokof F, Cicka A: Plasma renin activity in coarctation of the aorta before and after surgery. *Br Heart J* 37:721-725, 1975
- Parker FB, Streeten DHP, Sondheimer HM, Anderson GH: Hypertensive mechanisms in coarctation of the aorta. *J Thorac Cardiovasc Surg* 80:568-573, 1980
- Ribeiro AB, Krakoff LR: Angiotensin Blockade in coarctation of the aorta. *N Engl J Med* 295:148-150, 1976
- Will RJ, Walker OM, Traugott RC, Treasure RL: Sodium nitroprusside and propranolol therapy for management of postcoarctectomy hypertension. *J Thorac Cardiovasc Surg* 75:722-724, 1978
- Eger EI II, Smith NT, Cullen DJ, Cullen B, Gregory GA: A comparison of the cardiovascular effects of halothane, fluroxene, ether and cyclopropane in man. *ANESTHESIOLOGY* 34:25-41, 1971
- Davis TB, Morrow DH, Hebert CL, Cooper T: An increased incidence of paradoxical hypertension following resection of aortic coarctation under halothane. *ANESTHESIOLOGY* 22:132-133, 1961
- Miller ED, Ackerly JA, Vaughn ED, Peach MJ, Epstein RM: The renin-angiotensin system during controlled hypotension with sodium nitroprusside. *ANESTHESIOLOGY* 47:257-262, 1977
- Kaneko Y, Ikeda T, Takeda T, Inoue G, Tagwa H, Ueda H: Renin release in patients with benign essential hypertension. *Circulation* 38:353-362, 1968
- Delany TJ, Miller ED Jr.: Rebound hypertension after sodium nitroprusside prevented by saralasin in rats. *ANESTHESIOLOGY* 52:154-156, 1980
- Rawlinson WAL, Loach AB, Benedict CR: Change in plasma concentration of adrenaline and noradrenaline in anaesthetized patients during sodium nitroprusside-induced hypotension. *Br J Anaesth* 50:937-943, 1978
- Stinson EB, Holloway EL, Derby G, et al: Comparative hemodynamic responses to chlorpromazine, nitroprusside, nitroglycerin, and trimethaphan immediately after open-heart operations. *Circulation (Suppl I)* 51, 52:I-26-I-33, 1974
- Kouchoukos NT, Lell WA, Karp RB, Samuelson PN: Hemodynamic effects of aortic clamping and decompression with a temporary shunt for resection of the descending thoracic aorta. *Surgery* 85:25-30, 1979
- Jones SEF: Coarctation in children, controlled hypotension using labetalol and halothane. *Anaesthesia* 34:1052-1055, 1979
- Knight PR, Lane GA, Nicholls MG, et al: Hormonal and hemodynamic changes induced by pentolinium and propranolol during surgical correction of scoliosis. *ANESTHESIOLOGY* 53:127-134, 1980
- Rocchini AP, Rosenthal A, Barger AC, Castaneda AR, Nadas A: Pathogenesis of paradoxical hypertension after coarctation resection. *Circulation* 54:382-384, 1976