and safety of bladder catheterization for bacteriologic study of the urine. N Engl J Med 255:474–475, 1956
7. Dudley AG, Conrad LL, Markham SM: Continuous intrapartum lumbar epidural block: A comparative study employing propitocaine 2%, lidocaine 1.5% with epinephrine and 1.5% lidocaine. South Med J 64:475–479, 1971
8. Ansell J: Some observations on catheter care. J Chronic Dis 15:675–682, 1962
9. Haskell DL, Sunshine B, Heifetz CJ: A study of bladder catheterization with inguinal hernia operations. Arch Surg 109:378–380, 1974
10. Pryles CV, Luders D, Alkan MK: A comparative study of bacterial cultures and colony counts in paired specimens of urine obtained by catheter versus voiding from normal infants and infants with urinary tract infections. Pediatrics 27:17–28, 1961

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The Pressor Effect of Droperidol on a Patient with Pheochromocytoma

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On theoretical grounds, neuroleptanesthesia seems appropriate for patients who have pheochromocytoma, since droperidol antagonizes the pressor effects of catecholamines[1–3] and prevents catecholamine-induced arrhythmias.[1,4,5] Following this line of thought, we have used neuroleptanesthesia for a patient with pheochromocytoma, in whom administration of droperidol induced an extreme increase in blood pressure.

REPORT OF A CASE

A 13-year-old boy, weighing 31 kg, had had repeated headaches and attacks of nausea for three years. In the three months prior to admission to the Hospital of Osaka University Medical School, the patient had experienced palpitation, exertional dyspnea, and nocturnal sweating. His physician made a tentative diagnosis of pheochromocytoma based on symptoms and a positive phentolamine test. Blood pressure and pulse rate after hospitalization fluctuated between 136/84 and 228/114 torr, and between 90 and 126/min, respectively. Epinephrine in the urine was 46 μg/day; norepinephrine, 391 μg/day, and vanillylmandelic acid in the urine, 16.5 to 40.2 mg/day. Blood volume measured with ^{51}Cr-labelled erythrocytes was 2,760 ml. Basal metabolic rate was +13 per cent. Oral glucose tolerance test showed a diabetic pattern. EKG revealed left ventricular hypertrophy. Examination of the ocular fundi revealed retinal hemorrhages. Results of other routine clinical examinations were within normal ranges.

Six days before operation, the effect of droperidol on the blood pressure was examined. As shown in figure 1, intravenous administration of 1.25 mg lowered the blood pressure from the initial 190/120 to 160/108 torr within 30 seconds, followed by elevation to 216/160 torr one minute later. Within five minutes the patient became dyspneic and restless. He complained of rigidity in the lower extremities. Ten minutes later, when the blood pressure reached 232/160 torr, iv infusion of phenoxybenzamine was begun. The drug was diluted in a 5 per cent glucose solution and administered at the rate of 30 mg/hr. In this manner, the hypertension was easily controlled. When the blood pressure dropped below normal level, 200 ml whole blood was transfused. From the following day, phenoxybenzamine was administered iv at a dosage of 10 mg daily. In addition, 10 mg of propranolol was given orally every 12 hours to control tachycardia of about 130/min. Following these medications, the blood pressure stabilized between 136/76 and 168/128 torr, and the pulse rate between 100 and 110/min.

As surgical premedication, pentobarbital, 100 mg, was given orally one and a half hours before anesthesia; scopolamine, 0.3 mg, was given im an hour later. The patient was calm on arrival at the operating room. An intra-arterial cannula was placed in the right radial artery for direct continuous monitoring of blood pressure. As shown in figure 2, when the patient was given 1.25 mg droperidol, iv, for anesthetic induction, the blood pressure rose from 160/108 to 188/110 torr within 3 minutes. When another 1.25 mg of droperidol was given, the blood pressure reached 206/100 torr within the next minute. The blood pressure decreased without treatment and returned to the initial level in 10 minutes. Then fentanyl, 0.1 mg, and pancuronium, 3 mg, were given successively, and mechanical ventilation with N_2O and O_2 (1:1) was administered for a few minutes, followed by endotracheal intubation. During anesthesia, increases in blood pressure and pulse rate were recorded during manipulations of the tumors. These increases, however, were easily managed by iv administrations of 2 mg phentolamine twice and 1 mg propranolol once. Five minutes after administration of these adrenergic blockers, droperidol, 2.5 mg, was given. This did not induce any further elevation of the blood pressure. An estimated 800 ml blood was lost during the operation. Fourteen hundred milliliters of whole blood were transfused. Throughout the operation, normal sinus rhythm was maintained. Although there was a transient hypotension (70/50 torr) immediately after the resection of all tumors, the blood

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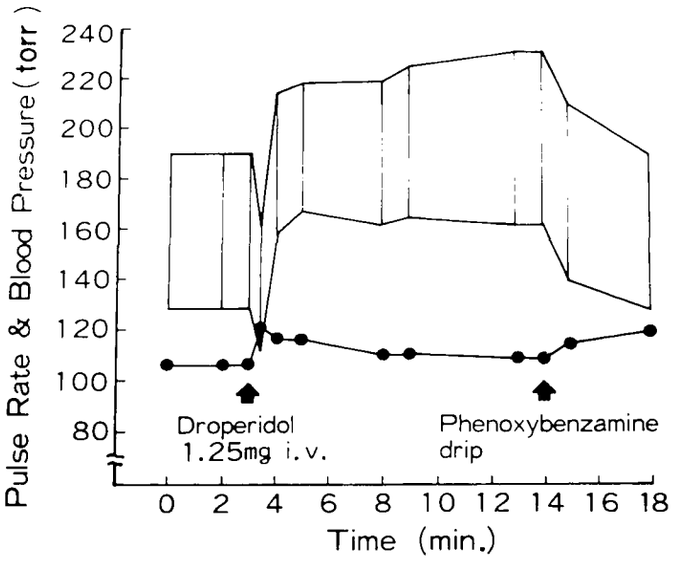

FIG. 1. The increase in blood pressure caused by droperidol. The patient was given 1.25 mg droperidol, iv, prior to administration of phenoxybenzamine, in his room.

pressure promptly returned to normal without vasopressors. A total of five tumors was found in the paraganglia bilaterally. Histologically, they were benign pheochromocytomas. The patient made an uneventful recovery and was discharged on the nineteenth postoperative day in good condition.

DISCUSSION

Jansen *et al.*[1] showed, in animal experiments, that droperidol antagonized the effects of epinephrine and norepinephrine. Subsequently, the ability of the compound to reduce the pressor effects of catecholamines was confirmed in dogs[2] and man.[3] This action of droperidol was ascribed to a specific α-adrenergic receptor blocking effect[3] or a nonspecific local anesthetic effect.[6] Furthermore, an antiarrhythmic action of droperidol was confirmed in animals[2,4] and man.[5] It was reported to be particularly effective in cases of epinephrine-induced ventricular arrhythmia.[2,4]

A review of the literature showed that neuroleptanesthesia has been used in some patients with pheochromocytoma.[7–13] In most of the cases, anesthetic management was successful, but in two, extreme hypertension, possibly due to neuroleptanesthesia, was found.[11,12] In the present case, we carefully observed the action of droperidol on the arterial blood pressure in a patient with pheochromocytoma. The increase in blood pressure induced by droperidol was prompt and extreme, but controllable with an α-adrenergic receptor blocker. Though the mechanism of this action of droperidol is not clear, the following explanations may be advanced: 1) Droperidol may stimulate the sympathoadrenal system by a central mechanism. Pheochromocytoma tissue probably is not innervated,[14] but the releasable stores of catecholamines in the sympathetic nerve endings are expanded because the nerve endings constantly are exposed to abnormally high concentrations of catecholamines in plasma.[14] The psychic excitement of the patient observed subsequent to the first administration of droperidol resulted in neurologic changes, and this might accelerate an increase in blood pressure. But this would appear to be an incomplete assessment of the mechanism, because the increase in blood pressure preceded the excitement, and in the operating room the blood pressure increased in spite of sufficient sedation with premedicant drugs. 2) Droperidol may directly stimulate the tumor cells or sympathetic nerve endings to evoke catecholamine release. If this is the mechanism, then the drug may be compared to chlorpromazine, which evokes catecholamine release from the adrenal medulla by mobilizing calcium pools within the chromaffin cell.[15] Chlorpromazine, however, was used successfully in patients with pheochromocytoma.[16] 3) A positive feedback mechanism due to droperidol may play a role. As shown in figure 1, the administration of droperidol initially lowered the blood pressure, and this reduction might trigger a feedback mechanism. But as shown in figure 2, observation of the patient in the operating room did not disclose decreases in blood pressure when the direct arterial pressure was monitored continuously. 4) Droperidol may inhibit the uptake of catecholamines into the nerve terminals. If this is the case, then the drug may be compared to cocaine and imipramine, which have been shown to pro-

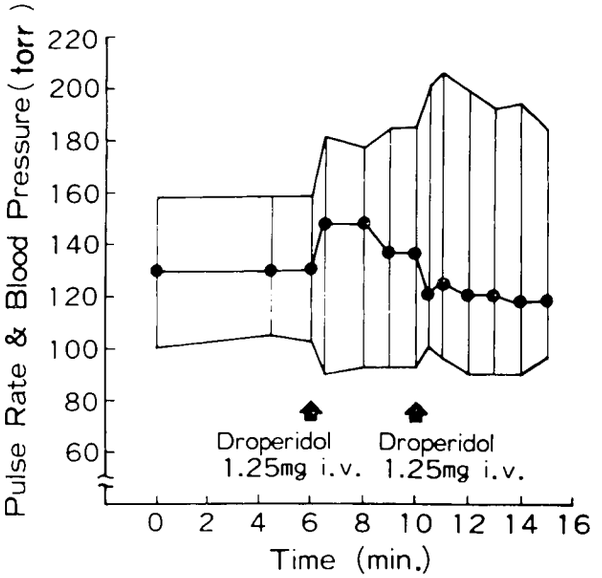

FIG. 2. The increase in blood pressure caused by droperidol. The patient was given 1.25 mg droperidol, iv, twice for induction of anesthesia in the operating room.

duce hypersensitivity to norepinephrine by preventing uptake.[17]

In normal subjects, the effects of droperidol on catecholamines in plasma and urine have been studied only in combination with fentanyl,[18] and there is evidence to suggest that neuroleptanesthesia increases plasma levels[19] and urinary excretion[20] of epinephrine. No appropriate explanation of this has been reported.

Although it was recommended to give phenoxybenzamine orally at the rate of 1 mg/kg per day,[21] we administered it iv because prompt and reliable action was necessary when a hypertensive episode was encountered following the trial administration of droperidol. Initially, a dose of 30 mg was given. This was subsequently adjusted to the minimum amount necessary to maintain the desired blood pressure. The small dose used, 0.3 mg/kg/day, caused no side effect and was sufficient to prevent extreme hypertension during the surgical procedure. Although mild hypertension was inevitable, it was easily controlled with phentolamine.

The present case has made it evident that droperidol causes extreme hypertension in patients who have pheochromocytoma. The site of the action of droperidol is unknown. In spite of the known pressor effect of the drug in this patient, we applied neuroleptanesthesia using droperidol for the following reasons: 1) The increase in blood pressure induced by droperidol was controllable with an α-adrenergic receptor blocker. 2) Neuroleptanesthesia does not sensitize the heart to catecholamines as do the other halogenated volatile anesthetics. 3) It has little depressant effect on cardiac[22] and renal functions.[23]

References

1. Jansen PA, Niemegeers CJ, Schellenkens KH, et al: The pharmacology of Dehydrobenzperidor (R 4749), a new potent and short acting neuroleptic agent chemically related to haloperidol. Arzneim Forsch 13:205–211, 1963
2. Yelnosky J, Katz R, Diertrich EV: A study of some of the pharmacologic actions of droperidol. Toxicol Appl Pharmacol 6:37–47, 1964
3. Whitwam JG, Russell WJ: The acute cardiovascular changes and adrenergic blockade by droperidol in man. Br J Anesth 43:581–591, 1971
4. Bertoló L, Novaković L, Penna M: Antiarrhythmic effects of droperidol. ANESTHESIOLOGY 37:529–535, 1972
5. Long G, Dripps RD, Price HL: Measurement of antiarrhythmic potency of drugs in man: Effects of dehydrobenzperidol. ANESTHESIOLOGY 28:318–323, 1967
6. Puddy BR: Effects of droperidol on the vasoconstriction produced by noradrenaline, histamine, sympathetic nerve stimulation and potassium ions in the isolated rabbit auricular artery. Br J Anaesth 43:441–444, 1971
7. Simone M, Barusco G, Coan B: Impiego della NLA tipo II nel traffamento chirurgico del feocromocitoma. Acta Anesthesiologica 19:233–243, 1968
8. Kaniak J, Kuczynska-Sekita K, Shora K, et al: A case of emergency surgical removal of a pheochromocytoma under type II neuroleptanalgesia. Pol Tyg Lek 24: 602–603, 1969
9. Clarke AD, Tobias MA, Challen PD: The use of neuroleptanalgesia during surgery for pheochromocytoma, Report of two cases. Br J Anaesth 44:1093–1096, 1972
10. Ogawa R, Fujita T: Neurolept-anesthesia for the surgery of pheochromocytoma. Jap J Anesth 21:174–178, 1972
11. Morikawa S, Hikita K, Marukawa S, et al: α-blocking and anti-arrhythmic effect of droperidol. Jap J Anesth 21:1268–1274, 1972
12. Yusa T, Hashimoto Y, Shima T, et al: Droperidol and pheochromocytoma. Jap J Anesth 22:474–479, 1973
13. Gotoh F, Miyashita K, Ogawa R, et al: Anesthesia for pheochromocytoma: Roles of catecholamines and histamine. Jap J Anesth 22:1293–1297, 1973
14. Melmon KL: Catecholamines and the adrenal medulla, Textbook of Endocrinology. Fifth edition. Edited by RH Williams. Philadelphia, London, Toronto, W. B. Saunders, 1974, pp 283–322
15. Rahwan RG, Borowitz JL, Miya TS: The role of intracellular calcium in catecholamine secretion from the bovine adrenal medulla. J Pharmacol Exp Ther 184: 106–118, 1973
16. Bingham W, Elliott J, Lyons SM: Management of anesthesia for phaeochromocytoma. Anaesthesia 27:49–60, 1972
17. Trendelenburg U: Mechanism of supersensitivity and subsensitivity to sympathomimetic amines. Pharmacol Rev 18:629–640, 1966
18. Tammisto T: Effects of neuroleptanesthesia of catecholamines, International Anesthesiology Clinics. Neuroleptanesthesia. Edited by T Oyama. Boston, Little, Brown, 1973, pp 185–195
19. Tammisto T, Takki S, Nikki P, et al: Effect of operative stress on plasma catecholamine levels during neuroleptanalgesia. Anaesthesist 22:158–161, 1973
20. Giesecke AH Jr, Jenkins MT, Crout JR, et al: Urinary epinephrine and norepinephrine during Innovar–nitrous oxide anesthesia in man. ANESTHESIOLOGY 28: 701–704, 1967
21. Ross EJ, Prichard BNC, Kaufman L, et al: Preoperative and operative management of patients with pheochromocytoma. Br Med J 1:191–198, 1967
22. Zauder HL, Del Guercio LRM, Feins N, et al: Hemodynamics during neurolept analgesia. ANESTHESIOLOGY 26:266, 1965
23. Hirasawa H: Effects of anesthetics on blood flow of the renal cortex and medulla. Jap J Anesth 20:539–548, 1971