Elevated vascular resistance after labetalol during resection of a pheochromocytoma (Brief report)

[Élévation de la résistance vasculaire générale après l'administration de labétalol pendant la résection d'un phéochromocytome]

Peter C.H. Chung MD, Allen H. Li MD, Chih Chung Lin MD, Ming Wen Yang MD

Purpose: To report a case of pheochromocytoma exhibiting an increase in systemic vascular resistance index (SVRI) and decreased cardiac index (CI) after use of labetalol.

Clinical features: A 36-yr-old male underwent adrenectomy for pheochromocytoma. Midazolam 5 mg, fentanyl 100 μg and labetalol 20 mg were administrated intravenously for premedication upon arrival in the operating theatre. After induction of anesthesia with fentanyl, thiopental and atracurium, 30 mg *iv* labetalol was administered. The blood pressure gradually rose to 178/101 mmHg with mildly increased SVRI (1958 dn-sec^{-1}·m^2·cm^5) and stable CI (3.8 L·min^{-1}·m^2). The blood pressure reached 247/150 mmHg after intubation with an increase in SVRI (3458 dn-sec^{-1}·m^2·cm^5) and a decrease in CI (3.6 L·min^{-1}·m^2). The SVRI increased further to 4986 dn-sec^{-1}·m^2·cm^5 and CI declined to 2.4 L·min^{-1}·m^2 after the administration of additional labetalol 20 mg. Sodium nitroprusside was administered and the blood pressure declined immediately to 108/72 mmHg, with a decreased SVRI (2526 dn-sec^{-1}·m^2·cm^5) and stable CI (2.3 L·min^{-1}·m^2).

Conclusions: The elevated SVRI with low CI was considered to result from increased -adrenergic activity secondary to ß- adrenergic blockade with labetalol. Clinicians should be aware of the possibility of a hypertensive crisis after *iv* labetalol. We suggest that labetalol should be replaced promptly with -adrenergic blockers or other vasodilators when such a condition arises.

Objectif : *Rapporter un cas de phéochromocytome présentant une augmentation de l'index de résistance vasculaire générale (IRVG) et une baisse de l'index cardiaque (IC) à la suite de l'usage de labétalol.*

Éléments cliniques : *Un homme de 36 ans a subi une surrénalectomie pour un phéochromocytome. On lui a administré par voie intraveineuse 5 mg de midazolam, 100 ìg de fentanyl et 20 mg de labétalol comme prémédication à l'arrivée au bloc opératoire. Après l'induction anesthésique avec du fentanyl, du thiopental et de l'atracurium, 30 mg de labétalol iv ont été donnés. La tension artérielle est montée graduellement à 178/101 mmHg et l'IRVG a augmenté légèrement à 1958 dn-sec^{-1}·m^2·cm^5 tandis que l'IC est resté stable à 3,8 L·min^{-1}·m^2 . La tension a atteint 247/150 mmHg après l'intubation, l'IRVG s'est élevé à 3458 dn-sec^{-1}·m^2·cm^5 et l'IC a baissé à 3,6 L·min^{-1}·m2. L'IRVG a augmenté encore à 4986 dn-sec^{-1}·m^2·cm^5 et l'IC a baissé à 2,4 L·min^{-1}·m^2 après l'administration de 20 mg supplémentaires de labétalol. Du nitroprussiate de sodium a été administré et la tension artérielle a immédiatement baissé à 108/72 mmHg, l'IRVG a baissé à 2526 dn-sec^{-1}·m^2·cm^5 et l'IC est demeuré stable à 2,3 L·min^{-1}·m^2.*

Conclusion : *L'IRVG élevé, accompagné d'un IC faible, a été jugé comme le résultat d'une augmentation de l'activité -adrénergique secondaire au blocage ß-adrénergique provoqué par le labétalol. Il faut penser à la possibilité d'une crise hypertensive avec l'usage iv de labétalol. Dans ce cas, le labétalol devrait être remplacé rapidement par des inhibiteurs -adrénergiques ou d'autres vasodilatateurs.*

Clinical features

A 36-yr-old male with a history of hypertension for six years and occasional syncope for four months was admitted. His 24-hr urine VMA was 12.9 ng·mL^{-1} (normal range: 2–7 ng·mL^{-1}). A right adrenal tumour of 3.5 cm in diameter was visualized with computer tomographic scanning, and I^{131}-metaiodobenzyl guanidine scintigraphy showed a positive shadow. Under the impression of pheochromocytoma, adrenectomy was scheduled. Preoperative physical examination revealed no apparent abnormality. Blood sugar was normal, but electrocardiography (ECG) showed sinus tachycardia with ventricular premature contractions. Labetalol (200 mg) 1# bid and nifedipine (10 mg) 1# qid were prescribed and the cardiac rhythm became regular. His 48-hr in-hospital blood

From the Department of Anesthesiology, Chang Gung Memorial Hospital, Tao-Yuan, Taiwan.

Address correspondence to: Dr. Peter C.H. Chung, Department of Anesthesiology, Chang Gung Memorial Hospital, 5 Fu-Hsing Street, Kwei-Shan, Tao-Yuan, 333, Taiwan. Phone: +886-3-3281200, ext. 2389; Fax: +886-2-28737816; E-mail: steve226@ms23.hinet.net

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pressure remained between 120/80 and 130/90 mmHg. On the morning of surgery, oral medications were administered as usual. Upon arrival in the operation theatre, blood pressure was 156/92 mmHg and heart rate 70 beats·min^{-1}. Midazolam 5 mg, fentanyl 100 µg and labetalol 20 mg were administered intravenously for premedication. Blood pressure was 150/95 mmHg. Monitors included ECG, pulse oximetry, continuous arterial blood pressure via a radial artery catheter, and a pulmonary artery catheter inserted via the right internal jugular vein. After insertion of the pulmonary artery catheter under local anesthesia with 1% lidocaine, systolic blood pressure was between 160 and 170 mmHg. The cardiac output (CO) was monitored with a continuous CO monitor (Vigilance monitor, model VGS, Edwards Critical Care Division, Baxter Healthcare Corperation). Anesthesia was then induced with fentanyl 200 µg, 2.5% sodium thiopental 250 mg, and atracurium 40 mg intravenously. After loss of eyelash reflex, isoflurane 3.5% in oxygen 3 L·min^{-1} was administered via a face mask, with an expired concentration of isoflurane between 1.2 and 1.5%. Ventilation was easy with an oxygen saturation of 100%. Blood pressure was 147/85 mmHg. Labetalol was administered in 10 mg *iv* boluses, up to a total dosage of 30 mg. Blood pressure gradually increased to 178/101 mmHg. Mildly increased SVRI (1958 dn-sec^{-1}·m^2·cm^5) and stable CI (3.8 L·min^{-1}·m^2) were recorded. After intubation, blood pressure increased to 247/150 mmHg with a further increase in SVRI (3458 dn- sec^{-1}·m^2·cm^5) and a mild decrease in CI (3.6 L·min^{-1}·m^2), as shown in the Figure. After an additional dose of labetalol 20 mg *iv*, the blood pressure declined to 219/133 mmHg with a CI of 2.4 L·min^{-1}·m^2. However, the SVRI remained elevated (4986 dn-sec^{-1}·m^2·cm^5). Sodium nitroprusside was administered and the blood pressure declined immediately to 108/72 mmHg, with a decreased SVRI (2526 dn-sec^{-1}·m^2·cm^5) and stable CI (2.3 L·min^{-1}·m^2).

During tumour manipulation and resection, sodium nitroprusside was administered to control the elevated blood pressure (216/137 mmHg) and SVRI (5029 dn-sec^{-1}·m^2·cm^5). The blood pressure drop after tumour resection (blood pressure 77/52 mmHg and SVRI 1635 dn-sec^{-1}·m^2·cm^5) was treated with dopamine. In the postoperating room, blood pressure was elevated mildly due to wound pain, and subsided after 25 mg of *iv* meperidine.

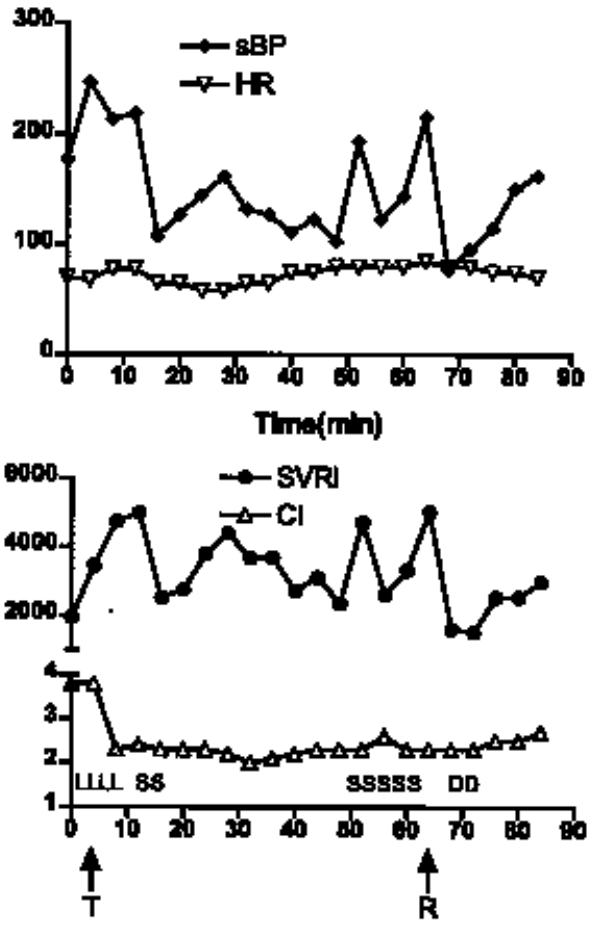

FIGURE Changes in systolic blood pressure (sBP, mmHg), heart rate (HR, beats·min^{-1}), systemic vascular resistance index (SVRI, dn-sec^{-1}·m^2·cm^5) and cardiac index (CI, L·min^{-1}·m^2) during intubation and resection of pheochromocytoma, and the timing of administration of labetalol, sodium nitroprusside and dopamine.

Discussion

During the induction of anesthesia, the elevated SVRI with a low CI was considered to result from increased -adrenergic activity secondary to ß-adrenergic blockade with labetalol.

Generally, during the treatment of hypertension, if ß-adrenergic receptors are blocked first, norepinephrine and epinephrine will produce unopposed -adrenergic stimulation. ß$_2$-mediated vasodilation will not be able to offset $_1$ vasoconstriction, and peripheral vascular resistance will increase.[1] Theoretically, without adequate -adrenergic blockade, ß-adrenergic blockade may result in high peripheral vascular resistance and hypertension. Therefore, weak -adrenergic blockade and strong ß-adrenergic blockade are not an ideal combination for an anti-hypertensive agent. However, labetalol is such an agent and has been used effectively for years as an anti-hypertensive agent without

reports of high vascular resistance,[2–5] even in patients with norepinephrine-secreting pheochromocytoma.[6] But, as the use of continuous CO monitoring becomes more widespread, hemodynamic changes following the use of labetalol can be demonstrated more clearly. It can provide more accurate and reliable information on CO than the traditional devices,[7] especially in a hemodynamic emergency such as during pheochromocytoma resection. With a coiled heater at the tip of the pulmonary artery catheter, CO can be estimated every ten seconds, and the average value of the last few CO measurements can be displayed, as can 30 min to 24 hr trends of CO.

In this case, the blood pressure increased while CO remained stable after administration of labetalol before intubation, and the blood pressure continued to increase despite a decrease in CO after increasing doses of labetalol after intubation. In our experience, the combination of fentanyl (5 $\mu g \cdot kg^{-1}$), thiopental (5 $mg \cdot kg^{-1}$), labetalol (0.5–1 $mg \cdot kg^{-1}$), and isoflurane with an expired concentration between 1.2 and 1.5% provides adequate anesthesia for intubation. So, we concluded that the increase in blood pressure was related mainly to the administration of labetalol.

The aim of this report is to remind clinicians of the possibility of SVRI elevation and hypertensive crisis after *iv* labetalol. We suggest that labetalol should be replaced promptly with -adrenergic blockers or other vasodilators when such a condition arises, in order to prevent the possible cardiac and pulmonary complications induced by further ß-blockade.

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