

## Low-dose landiolol for hypertension with tachycardia following neurosurgery

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*To the editor:* Hypertension with tachycardia is a common complication after neurosurgery. This is due to a significant increase in sympathetic tone, resulting in various electrocardiographic changes and an increased risk of myocardial ischemia [1]. Therefore, a beta adrenergic antagonist is rational therapy for these patients [1]. Unfortunately in Japan, no titratable short-acting intravenous beta-antagonists were available before landiolol was introduced in July 2002.

Since then, landiolol has been successfully used for controlling hemodynamic responses during anesthesia [2]. However, until October 2006, when the postoperative use of landiolol was approved [3], it was limited to intraoperative use. The safety and efficacy of landiolol in the postoperative setting have not been fully evaluated, especially for the neurosurgical population. We present details of three neurosurgical patients, in whom low-dose landiolol successfully controlled postoperative tachycardiac hypertension without adverse effects.

The first patient was a 69-year-old man who underwent a craniotomy after developing an acute subdural hematoma. Thirteen hours after the craniotomy, the blood pressure (BP) was 168/90 mmHg and the heart rate (HR) was 121 beats·min<sup>-1</sup> using 5 mg·h<sup>-1</sup> of nicardipine. An infusion of landiolol was initiated at 10 µg·kg<sup>-1</sup>·min<sup>-1</sup>, the lowest dose recommended, without administration of an initial bolus [3]. Fifteen minutes after initiation of the infusion, the BP and HR improved, to 120/58 mmHg and 76 beats·min<sup>-1</sup>, respectively. Landiolol was continued at a rate of 5 µg·kg<sup>-1</sup>·min<sup>-1</sup> with HR of 60–80 beats·min<sup>-1</sup> until postoperative day (POD) 2, when the HR and BP were stable using only low-dose nicardipine.

Similar hemodynamic effects were observed in the second patient, a 51-year-old woman who underwent an emergency craniotomy for a hypertensive intracerebral hemorrhage. On POD 4, the administration of 10–15 µg·kg<sup>-1</sup>·min<sup>-1</sup> of landiolol with low-dose nicardipine had hemodynamic effects similar to those observed in patient 1. On POD 5, landiolol was discontinued, when hemodynamic stability was achieved with oral carvedilol and azelnidipine.

The third patient was a 57-year-old man who underwent a craniotomy after developing a subarachnoid hemorrhage (SAH). On POD 5, the BP was 140/60 mmHg and the HR was 118 beats·min<sup>-1</sup>. Following the administration of 10–30 µg·kg<sup>-1</sup>·min<sup>-1</sup> of landiolol, the HR was stable at 100

beats·min<sup>-1</sup>, with no apparent changes in the BP. The cardiac index (CI) measured by an arterial-pressure-based cardiac output monitor system (FloTrac/Vigileo; Edwards Lifesciences, Irvine, CA, USA) did not decrease significantly (5.2 to 4.8 l·min<sup>-1</sup>·m<sup>2</sup>). On POD 8, landiolol was withdrawn, and oral metoprolol was initiated.

In all three patients, landiolol initiated at the minimum dose without initial bolus administration, was efficacious for controlling the HR in the presence of hypertension. Both patients 1 and 2 seemed somewhat sensitive to landiolol, probably due to decreased intravascular volume with the concomitant use of a vasodilator. For these sensitive patients, the titratable character of landiolol is a potential benefit.

In contrast, the BP and CI in patient 3 did not change significantly with landiolol, suggesting that the intravascular volume was maintained for the treatment of vasospasm. In patients with SAH who must maintain sufficient BP and cerebral blood flow, landiolol has therapeutic potential as a safe and effective antitachyarrhythmic medication.

In patients 2 and 3, the conversion from landiolol to oral beta-blocker therapy was successful. Rebound hypertension and tachycardia after the cessation of landiolol should be avoided.

The rationale behind beta-blocker therapy for neurosurgical patients has been described in the literature. Numerous lines of evidence suggest that beta-blocker therapy reduces perioperative myocardial ischemia and may reduce the risk of myocardial infarction and death in high-risk patients [4]. In the neurosurgical population, beta-blocker therapy improved both neurological outcome after SAH [5] and survival after traumatic brain injury [1], despite some limitations in these available studies.

In conclusion, as a rational therapy, low-dose landiolol successfully controlled sympathetic-mediated hypertension and tachycardia in patients undergoing neurosurgery. Caution must be exercised during landiolol infusion to avoid hypovolemia-induced hypotension and a rebound hyperdynamic state. Further clinical trials are needed to establish the role of landiolol in the neurosurgical population.

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