



ORIGINAL ARTICLE

Assessment of postoperative changes in antihypertensive drug consumption in patients with primary aldosteronism using the defined daily dose



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Summary *Background:* The number of antihypertensive drug classes cannot accurately reflect the total consumption of antihypertensive drugs used to control blood pressure. The defined daily dose has been adopted to permit consumption analysis of many prescribed drugs. The aim of the present study was to assess postoperative changes in antihypertensive drug consumption in patients with primary aldosteronism using the defined daily dose as the unit of measurement.

Methods: This retrospective study included 110 Japanese patients who underwent unilateral laparoscopic adrenalectomy between 1995 and 2012. Antihypertensive drug doses were calculated according to the standard of the defined daily dose recommended by the World Health Organization to compare drug use. After assessing postoperative changes in antihypertensive drug consumption, univariate and multivariate analyses were performed to identify clinical predictors for a 75% or greater decrease in the defined daily dose.

Results: Consumption of antihypertensive drugs decreased postoperatively in 95.4% of patients. The median decrease in the defined daily dose was 76.8%. A postoperative decrease

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of 75% or greater in the defined daily dose was confirmed in 52.7% of patients. Multivariate analysis identified no medical history of cardiovascular disease, low body mass index, and short duration of hypertension as independent predictors of a postoperative decrease of 75% or greater in the defined daily dose.

Conclusion: The defined daily dose is a useful tool for assessing total changes in the consumption of antihypertensive drugs in patients with primary aldosteronism. Using the defined daily dose, clinicians could explain in detail to patients with primary aldosteronism the predicted postoperative change in antihypertensive drug consumption.

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1. Introduction

Primary aldosteronism (PA) is caused by the autonomous secretion of aldosterone from adrenocortical lesions, and it is associated with hypertension due to sodium retention and hypokalemia due to increased potassium excretion.^{1–3} Aldosterone excess leads to cardiovascular damage, independent of its effects on blood pressure (BP).^{1–3} Primary aldosteronism is primarily caused by an aldosterone-producing adenoma (APA) or by bilateral adrenal hyperplasia (also known as idiopathic hyperaldosteronism).^{1–3}

Laparoscopic adrenalectomy is the preferred approach to treat patients with unilateral PA such as APA.^{4–6} Despite normalization of the endocrine abnormalities, not all patients with PA have their hypertension cured completely by laparoscopic adrenalectomy.^{1–3} Many predictors of hypertension cure in PA patients have been reported.⁷ The number of antihypertensive drug classes can be a robust predictor for postoperative hypertension cure in PA patients.^{7–11} However, it cannot reflect the total consumption of antihypertensive drugs to control BP accurately.

Using the number of antihypertensive drug classes as a unit of measurement, the following two types of patients can be regarded as taking an equivalent amount of antihypertensive drugs: (1) patients who take 50 mg of eplerenone and 5 mg of amlodipine and (2) patients who take 100 mg of eplerenone and 10 mg of amlodipine. However, the second type of patient apparently has more severe hypertension, despite taking the equivalent two classes of antihypertensive drugs.

The defined daily dose (DDD) has been adopted to assess the consumption of many prescribed drugs.^{12,13} The doses of diverse drugs were calculated in accordance with the standard of the DDD recommended by the World Health Organization (WHO) to compare drug use.¹⁴ At present, clinicians can search each drug's DDD at the web address http://www.whocc.no/atc_ddd_index. The DDD system is often applied at the population level; however, in many studies, it can be used to compare individual drug utilization as a unit of measurement.^{12–18}

The aim of this study was to assess postoperative changes in antihypertensive drug consumption in PA patients, using the DDD as the measurement unit, and to identify clinical predictors for decreased antihypertensive drug consumption.

2. Methods

2.1. Patient selection

The clinical variables associated with a postoperative decrease in antihypertensive drug consumption were surveyed retrospectively among PA patients seen at the Chiba University Hospital Chiba, Japan. One hundred and ten patients with PA who underwent unilateral laparoscopic adrenalectomy between 1995 and 2012 were analyzed. The criteria used to establish the diagnosis of PA were a history of hypertension resistant to antihypertensive drugs with or without hypokalemia, and increased plasma aldosterone concentration (PAC) and suppressed plasma renin activity (PRA). In this study, patients had a confirmed PAC:PRA ratio of at least 20.0 ng/dL per ng/mL/hour as a biochemical screen for PA.^{1–3} Additional confirmation of the diagnosis was obtained using the saline-loading test, the captopril-challenge test, and/or the upright furosemide-loading test.^{1–3} Differentiation between APA and idiopathic hyperaldosteronism was obtained by computed tomography or by magnetic resonance imaging. Furthermore, lateralization of aldosterone overproduction was demonstrated through adrenal vein sampling (AVS) and/or adrenal dexamethasone-suppression scintigraphy with ¹³¹iodine (¹³¹I) cholesterol in all patients.^{1–3,5} The result of AVS was used to identify unilateral hypersecretion. When the finding of scintigraphy was equivocal or contrary to that of AVS, the AVS results were given precedence over the results of scintigraphy.

Postoperative normalization of plasma aldosterone levels was defined as decreased concentration of plasma aldosterone (<15.0 ng/dL). In this study, all patients were confirmed to have normalized plasma aldosterone levels after laparoscopic adrenalectomy. Hypokalemia cure was achieved after surgery in all patients with preoperative hypokalemia. The underlying adrenocortical lesion was pathologically identified in all patients after surgery. Pathological findings revealed cortical adenoma in 95 patients and nodular hyperplasia in 15 patients.

2.2. Definitions

The BP of each patient was classified in accordance with WHO 1999 guidelines as normal BP (<140/90 mmHg) or

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