Continuous-Infusion Labetalol vs Nicardipine for Hypertension Management in Stroke Patients

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Background: Labetalol and nicardipine are antihypertensives commonly used in the management of elevated blood pressure (BP) following an acute stroke, but there is limited evidence to suggest which agent as a continuous infusion should be used preferentially in this setting. *Objective:* This study aimed to compare the safety, efficacy, and ease of administration of continuous-infusion labetalol with continuous-infusion nicardipine following an acute stroke. *Methods:* This retrospective cohort study of patients with acute ischemic stroke or intracerebral hemorrhage included patients if they received either study agent within 24 hours of admission. The primary outcome was percent time spent at goal BP. Secondary outcomes included time to goal BP, the number of dose adjustments, and use of rescue antihypertensives. *Results:* The analysis included 99 patients who received labetalol- (n = 34) or nicardipine- (n = 65) continuous infusions. Intracerebral hemorrhage was the most common stroke subset (n = 81) followed by acute ischemic stroke (n = 18). There was no statistical difference in time at goal BP (labetalol 68.0%, nicardipine 67.0%; $P = .885$), rescue antihypertensive use (labetalol 14.7%, nicardipine 24.6%; $P = .2570$), time spent 10% above or below mean systolic BP (labetalol 35.5%, nicardipine 33.5%; $P = .885$), time to goal BP (labetalol 81.4 minutes, nicardipine 56.3 minutes; $P = .162$), and mean number of dose adjustments (labetalol 5.9, nicardipine 6.9; $P = .262$). *Conclusions:* Labetalol- and nicardipine-continuous infusions were comparable in the studied safety and efficacy outcomes including time at goal and BP variability. Further prospective studies are needed to validate these safety and efficacy findings and to assess clinical outcomes. **Key Words:** Beta-adrenergic blockers—calcium-channel blockers—stroke—hypertension—antihypertensives—cerebrovascular disorders—critical care.

Introduction

Stroke is one of the leading causes of death in the United States with more than 795,000 people affected each year.[1] Elevated blood pressure (BP) occurs in nearly 80% of patients acutely poststroke and results in increased rates of recurrent stroke, rebleeding, hematoma expansion, and treatment failure.[2-5] Although the importance of BP management is well established, there remains less evidence to guide the choice of antihypertensive agent. Labetalol and nicardipine are recognized as the preferred intravenous (IV) agents in national guidelines, but this is largely based on expert opinion.[6-8]

Selection of an antihypertensive agent is an important consideration when treating acute stroke patients.

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Factors such as rapidity of BP reduction, BP variability, drug tolerability, and ease of administration can all potentially influence outcomes. For example, a positive correlation in morbidity and mortality has been found with BP control that showcases the importance of rapid BP control while avoiding hypotension.[2-12] A consideration when selecting an agent is the method of IV administration. Nicardipine is administered strictly as a continuous infusion, whereas labetalol can be administered either as a continuous infusion or repeat IV boluses. In terms of labetalol administration, both continuous and intermittent dosing have been compared with nicardipine.[13-15]

Despite these studies, questions still loom among practitioners because of the differing administration techniques of labetalol used in head-to-head studies, the small sample sizes studied, and the trend toward superiority of nicardipine. This retrospective cohort study aimed to address some of these concerns and to determine if a continuous infusion of labetalol offers a safe and effective alternative to nicardipine in acute stroke patients.

Methods

This study was a retrospective cohort study of patients admitted between April 1, 2011 and July 31, 2014 to St. Joseph Mercy Hospital, Ann Arbor, MI, a 537-bed, nonuniversity affiliated, community-teaching hospital. This study was approved by the Institutional Review Board and a waiver of informed consent was granted. Adult patients with an acute intracerebral hemorrhage (ICH) or acute ischemic stroke (AIS) were eligible for inclusion if they received a labetalol- or nicardipine-continuous IV infusion for any amount of time within the first 24 hours of admission to the hospital. Exclusion criteria were history of intracranial neoplasm, concomitant administration of both study agents, or stroke secondary to a traumatic event. Patients were studied from the time of drug initiation until the infusion was discontinued or 24 hours, whichever came first. BP goals for the analysis were determined primarily by the consulting neurologist or neurosurgeon recommendations. National guideline recommendations were used to determine goal BP if neurology or neurosurgery recommendations were not made. Based on these guidelines the goal BP used for AIS was below 180/105 mmHg when fibrinolytic therapy was administered, a 15% reduction in systolic blood pressure (SBP) if fibrinolytic therapy was not administered, and a goal BP of below 160/90 mmHg for ICH.[7,8]

Baseline information collected included age, sex, history of stroke, contraindication to beta-blocker therapy, history of hypertension, home antihypertensive agents, receipt of an antihypertensive agent before study drug, starting infusion rate, heart rate (HR) in beats per minute (bpm), BP at initial presentation, and the last BP reading before study drug initiation. All available BP readings within the defined study period were included in the analysis. Arterial line BP monitoring was the preferred modality for recording BP, but noninvasive readings were included when invasive measurements were not available. Mean infusion rates of the study agents were calculated by collecting the total dose of the agents received over the study period and dividing by the time spent on the study agent.

The primary efficacy outcome was the percentage of time spent at goal BP during the study period. Secondary efficacy outcomes included time to goal BP in minutes, BP variability defined as the percentage of time spent 10% above or below the mean SBP, rescue IV antihypertensive use, and the number of dose adjustments which was defined as any change in infusion rate. The mean amount of time spent on each study agent was recorded as well. Secondary safety outcomes were the incidence of bradycardia (defined as HR <60 bpm), tachycardia (defined as HR >120 bpm), and hypotension (defined as SBP <90 mmHg).

Statistical Analysis

The outcome of time at goal BP and time to goal BP were modeled using linear regression. Adjusted characteristics were partitioned into 2 categories: patient (age and sex) and clinical (baseline BP, stroke subset, and infusion drug). The number of dosage adjustments required and BP variability were assessed using the Wilcoxon rank sum test. The analysis of BP variability was then adjusted for differences in total time spent on study agent. All other safety and efficacy outcomes were assessed using a chi-square test of independence with significance set at P value of .05.

Results

Patient Characteristics

A total of 99 patients were available for the final analysis with 34 in the labetalol arm (34.3%) and 65 patients in the nicardipine arm (65.7%) (Fig 1). ICH was the most common stroke type at 81.8% of patients (n = 81) and 18.2%

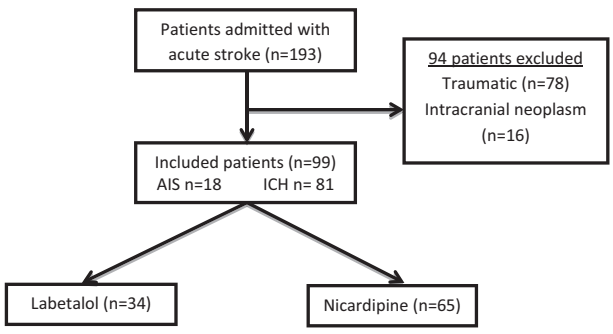

Figure 1. *Flow diagram of study population. Abbreviations: AIS, acute ischemic stroke; ICH, intracerebral hemorrhage.*