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Non-Invasive Hemodynamic Analyses to Guide Pharmacotherapy of High Blood Pressure: Mini-Review

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Abstract

Hypertension is the biggest risk factor to cardiovascular events, stroke and kidney disease, despite a numerous antihypertensive drugs, control rates still suboptimal. In the present mini-review, we will analyze an emergent method to control high blood pressure using hemodynamic parameters. We found seven trials since 1996 to 2106, a total of 1087 patients were studied comparing the standard method with the hemodynamic method with a success rate mean of 72, 6% in control blood pressure values using hemodynamic method. Hemodynamic guided pharmacotherapy has demonstrated be superior to standard recommendations con control high blood pressure, the assessment of more hemodynamic variables aloud to the physician to analyses more detailed the accurate parameter to guide antihypertensive therapy, however, more controlled trials are needed to increase evidence of this emergent method.

Keywords: Hypertension; Resistant hypertension; Hemodynamics; High blood pressure; Goal therapy; Hemodynamic individualized therapy

Introduction

Hypertension is the most common chronic health disease and is well related to high risk factor for cardiovascular events, strokes and kidney disease. European hypertension guidelines, defines hypertension when values are equal or superior to 140mmHg to systolic blood pressure and or 90mmHg to diastolic blood pressure based on epidemiological studies that suggest that treatment-induced blood pressure reduction in this patients are beneficial [1]. A more extended definition of hypertension may be a complex syndrome than alters vascular resistance affecting all circulatory systems, related to many pathophysiological factors like oxidative stress, increased sympathetic nervous system activity, altered sodium-retaining hormones, dysregulation in renin-angiotensin-aldosterone system [2].

Blood pressure is the product of cardiac output and total peripheral vascular resistance, so any change in this elements will have a direct effect on blood pressure, in the other hand, cardiac output depends on three important factors, stroke volume, heart rate, and preload [3]. Because all the possibilities that can create is disease in this system to rise blood pressure and product organ damage, we need to identify which parameter is failing to guide therapy more accurate and control blood pressure.

In the present article we will review all literature about use of hemodynamic measurements to adjust antihypertensive therapy to control blood pressure and its outcome in control blood pressure compared with standard protocols. We use Medline and PubMed database to search all articles, and keywords used to search were “hypertension”, “resistant hypertension”, “hemodynamics”, “therapy individualization” and “goal-directed therapy”.

Discussion

Seven trials were founded between 1996 and 2016, randomized trials only 3, the oldest trial form Sramek B et al. [4], a non-randomized trial in 1996, enrolled 322 patients previously treated by conventional therapy, non-controlled using at least 2 antihypertensive drugs, they observed a 75% became “normodynamic” or controlled after 3 weeks follow up. Next study was the Teler’s et al. [5] study, in 2002, in this study, the first randomized trial in 104 patients with resistant hypertension divided in 2 groups, one treated with conventional therapy with certified hypertension specialist and the other one, treated with hemodynamic goal-directed therapy in 3 months follow up, in this study they reached a 56% control of blood pressure in hemodynamic arm and 33% of control in conventional therapy arm with a statistical significant result P<0,05.

In 2004, Mehra M et al. [6] published a series of 56 clinical cases previously non-controlled patients enrolled in a non-randomized trial and applied the hemodynamic goal-therapy protocol to archive blood pressure control, they fund a 57,1% (P<0,001) of success. The fifth study in the list was the Smith's et al. [7] trial in 2006, a randomized study with 164 enrolled patients, non-controlled with standard therapy and before start study, patients had a 2 weeks washout of antihypertensive medication and there were no differences between groups in blood pressure parameters before start protocols, they found a 77% of blood pressure control in the hemodynamic arm, compared with a 57% of control in standard therapy (P<0,01).

Table 1: Hemodynamic algorithm to control blood pressure.

Treatment Options	Cardiac Index	Systemic Vascular Resistance Index	Thoracic Fluid Content	Pattern
Angiotensin converting enzyme I, Angiotensin II receptor blocker, calcium channel blocker or direct vasodilator	Normal or low	High	-	Vasoconstricted
B-blocker or non-dihydropyridine calcium channel blocker	High	Normal or low	-	Hyperdinamic
Diuretic	Normal or high	Normal or high	High	Fluid retention

The second trial, published in 2008 by Sremek et al. [8] studied 56 patients with uncontrolled hypertension and applied the hemodynamic method classifying patients in 4 groups based on intravascular volume, inotropy and vasoactiviy (Table 1) and adjusted medications according the result with a success in control blood pressure of 84% and 87,5 & of no side effects reported. Another non-randomized trial was performed by Aoka et al. [9] in 2009, enrolling 113 uncontrolled patients with hypertension and a follow up of 4, 7 months with a 72% of success using hemodynamic goal-directed therapy. The last trial in medical database consulted was the Krazesinsky's trial from 2016, a randomized trial with 272 enrolled patients, they had a 87, 7% of control of blood pressure compared with the 69, 1% of the standard therapy (P=0,012).

Table 2: Trials using hemodynamic assessment of high blood pressure.

Trial	Year	n	Intervention	Outcome
Sramek et al. [4]	1996	322	Prospective nonrandomized trial	75% of patients with blood pressure controlled
Taler et al. [5]	2002	104	1:1 randomized, 3 months prospective, specialist vs hemodynamic protocol in refractory hypertension subjects	56% of patients with resistant hypertension with blood pressure controlled
Mehra et al. [6]	2004	56	Prospective trial with non-controlled patients using 2 antihypertensive agents and apply hemodynamic protocol to control blood pressure.	57, 1% of patients with blood pressure controlled
Smith et al. [7]	2006	164	3:2 randomized prospective, 3 months follow standard vs hemodynamic protocol	77% of patients with blood pressure controlled
Sramek et al. [4]	2008	56	Prospective non-randomized trials with 3 months follow up	84% of patients with blood pressure controlled
Aoka [9]	2009	113	prospective non-randomized trial, 4, 7months duration	72% patients with blood pressure controlled
Krzesinski	2016	272	1:1 Randomization, 12 weeks prospective, conventional Vs Hemodynamic protocol with previous captopril washout in hypertensive patients.	87, 7% of patients with blood pressure controlled

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After all search, seven trials in 20 years, 1087 patients with a success rate mean of 72, 6% in control blood pressure values (Table 2). Hemodynamic approaches of blood pressure have its rationale in all different hemodynamic mechanism of hypertension, this mechanisms were described by Tarazi [10] in 1983, according to him, hypertension can be explained by alterations in vascular resistance, cardiac output or intravascular volume; in agreement of this, antihypertensive agents are classified in order of its mechanism of actions, for example, diuretics reduces intravascular volume, angiotensin converting enzyme inhibitors have his primary effect on vascular tone, and B-blockers on cardiac output. According to this hypothesis, the hemodynamic assessment of high blood pressure can be a more pathophysiological accurate method to guide antihypertensive therapy.

Conclusion

Hemodynamic guided pharmacotherapy has demonstrated be superior to standard recommendations con control high blood pressure, the assessment of more hemodynamic variables aloud to the physician to analyses more detailed the accurate parameter to guide antihypertensive therapy, however, more controlled trials are needed to increase evidence of this emergent method and outcomes like mortality, side effects and reduction in organ damage.

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