NIFEDIPINE MECHANISM OF ACTION AND USES FOR CARDIOVASCULAR THERAPY

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With the steady rise of global hypertension, medicine to manage blood pressure has never been more in demand [1]. Hypertensive has been known to be a significant contributor to cardiovascular events and kidney disease when left untreated. Nifedipine, an exclusively L-type calcium channel blocker, decreases hypertension by dilating cardiovascular arteries, thus increasing myocardial oxygen supply and decreasing resistance to blood flow within the vascular system [2].

Calcium channel blockers are one of the most important initial monotherapy agents to help control hypertension due to their quick onset [2]. They perform this by directly binding to the α1 subunit of the voltage-gated calcium channel protein embedded in the endothelial membrane. Once bound, calcium is unable to enter the smooth muscle tissue and the formation of myosin-actin bridges for muscle contraction is inhibited [3]. The structure of nifedipine is based on a pyridine ring, a heterocyclic compound of five carbons and one nitrogen. Other calcium channel blockers with a similar structure are categorized under the dihydropyridines family, which includes nimodipine and nisoldipine [3].

There are two types of voltage-gated calcium channels located within the cardiovascular system, T-types and L-types. T-type calcium channels are transient, low-voltage activated channels that are primarily utilized in the sinoatrial node, atrioventricular nodes and the purkinje fibers of the heart [4]. These channels regulate the contraction speed of cardiac myocytes during the cardiac cycle. L-type calcium channels are long lasting, high-voltage activated channels that reside in arterial smooth muscle, particularly coronary arteries, in the vascular system. Nifedipine almost exclusively blocks L-type calcium channels in the arteries [2] due to it having a 10-fold more potent binding ability on L-type channels than T-type channels [3]. This allows nifedipine to greatly affect the vascular system while providing little interference to cardiac function. L-type calcium channels have four classes based on their specific subunits; Cav1.1, Cav1.2, Cav1.3, Cav1.4. Only dihydropyridines-sensitive Cav1.2 subunit are expressed in high concentration in the cardiovascular system [5]. Cav1.2 class can be further spliced into two different isoforms. CaV1.2a corresponds to the calcium channels contained in the cardiac muscles and Cav1.2b corresponds to the smooth muscle calcium channels contained in the arterial vessels [3]. Due to the low concentration of CaV1.2a in the heart and high concentration of Cav1.2b in the arterial vessels, nifedipine has a much more potent effect on the arterial smooth muscle.

The therapeutic benefits of nifedipine stems from its ability to selectively dilate coronary and afferent arterial vessels. By decreasing systolic blood pressure via vasodilation, a decrease in afterload (resistance) pressure lowers the force needed to be exerted by the left ventricle [1].

With the decrease in ventricle exertion, nifedipine has also been utilized as a angina pectoris therapy due to the decreased myocardium oxygen consumption of the left ventricle [4]. Patients with hypertension have shown a significant decrease in blood pressure than patients that were non-hypertensive patients when given 10mg of nifedipine orally[1].

Although nifedipine has been shown to be efficient at managing blood pressure, there are some drawbacks. Nifedipine effectiveness is only for a short period of time. Although recent nifedipine formulas have enabled nifedipine to be utilized for long-term blood pressure management [1], other antihypertensive drugs, such as ACE inhibitors and diuretics, are typically also prescribed along with the calcium channel blocker for more effective long-term management [2]. Also, due to the quick vasodilation and increased sympathetic tone, indirect cardio-stimulation occurs which could result in tachycardia-induced heart failure [2]. In addition, nifedipine trait of binding primarily to L-type channels in afferent arteries results in an elevated glomerular pressure and damage to the kidneys [2]. With continuous nifedipine usage, other side effects include predominant hypotension, cardiodepression and lower extremity edema [4].

Nifedipine is a strong, short-term arterial vasodilator for the cardiovascular system. Its specificity in targeting only L-type Cav1.2 channels in arterial smooth muscles is beneficial by not affect other processes that utilize calcium channels in the cardiovascular system. However, it is not an infallible antihypertensive drug. Its powerful, short-term effects can strain kidney function after prolong usage. Nifedipine is commonly used for first line of defense when lowering blood pressure quickly, but other antihypertensive drugs have been shown to be much more effective for long-term blood pressure management [4].

References

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