The crucial role of calcium channel blockers in the management of essential hypertension. Hypertension is a major cause of death worldwide; it exists when the pressure on blood vessels is too high if left untreated it can lead to other serious health conditions.

Essential hypertension: A prevalent multi factorial condition in which persistently raised blood pressure exists with no secondary cause identified.

Calcium channel blockers (CCBs): Widely prescribed first-line agents in the management of essential hypertension. Treatment of essential hypertension involves lifestyle changes and medications, including diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, and calcium channel blockers.

A prevalent condition in which persistently raised blood pressure exists with no secondary cause identified is known as essential hypertension. Hypertension is divided into two categories: Essential hypertension, which represents between 85% and 95% of human cases and has an unidentified cause (Harrison et al., 2021). Secondary hypertension is caused by identifiable underlying conditions, including renal artery stenosis, pheochromocytoma, adrenal adenoma or single gene mutations(Harrison et al., 2021). Irvine Page, a prominent pioneer of hypertension research, proposed the Mosaic Theory of Hypertension and advocated that hypertension is the result of many factors of organ damage when interacting with raised blood pressure (Harrison et al., 2021). This Essay will focus on essential hypertension and the role of calcium channel blockers in its management. Hypertension involves the impairment of renal pressure natriuresis, the feedback system in which high blood pressure induces an increase in sodium and water excretion by the kidney that leads to a reduction of the blood pressure. (Hall et al., 2019). Blood pressure homeostasis involves receptors monitoring blood pressure and control centres initiating changes in the effectors to keep regulation and maintenance of blood pressure within a range of values appropriate for the system. (Lumen Learning, 2019) The 2017 Hypertension Clinical Practice Guidelines describe a healthy blood pressure range as being a systolic less than 120 and a diastolic less than 80 (Muntner et al., et al., 2019). The pathophysiology of hypertension involves complex interactions between genetic, environmental, and lifestyle factors that lead to sustained high blood pressure (Harrison et al., 2021). Central to its development is increased peripheral vascular resistance, which is often due to narrowing or stiffening of the blood vessels. This can result from endothelial dysfunction, where the inner lining of blood vessels fails to regulate vascular tone properly. Additionally, overactivity of the renin-angiotensin-aldosterone system (RAAS) contributes by increasing blood volume and causing vasoconstriction. Sympathetic nervous system overactivity also plays a significant role by promoting vasoconstriction and increasing heart rate. Other contributing factors include obesity, insulin resistance, high salt intake, and certain genetic predispositions. There is still much uncertainty about the pathophysiology of hypertension. (Beevers et al., 2021).A small number of patients (between 2% and 5%) have an underlying renal or adrenal disease as the cause for their raised blood pressure (Beevers et al., 2021). A number of physiological mechanisms are involved in the maintenance of normal blood pressure, and their derangement may play a part in the development of essential hypertension. (Beevers et al., 2021) The sympathetic nervous system regulates arterial blood pressure (ABP) by functionally influencing the vasculature, kidney, and heart. Indeed, altered sympathetic function is firmly established in the development, maintenance, and pathophysiology of numerous cardiovascular diseases, including hypertension (DeLalio et al., 2020). Sympathetic and parasympathetic nervous system activity and/or vasopressin release are the major mechanisms by which the CNS influences blood pressure, although other minor mechanisms may also be involved (Takahashi et al., 2011). The management of hypertension is subdivided into pharmacological and Non-pharmacological management. Non-pharmacological and lifestyle management is recommended for all individuals with raised BPs regardless of age, gender, comorbidities, or cardiovascular risk status(Iqbal & Jamal, 2023). Patient education has been shown to be paramount in effective management (Iqbal & Jamal, 2023). Lifestyle changes alone can account for up to a 15% reduction in all cardiovascular-related events (Iqbal & Jamal, 2023). Pharmacological therapy consists of angiotensin-converting enzyme inhibitors (Ace), angiotensin receptor blockers (ARBs), diuretics (usually thiazides), calcium channel blockers (CCBs), and beta-blockers (BBs), which are instituted considering age, race and comorbidities such as the presence of renal dysfunction, LV dysfunction, heart failure, and cerebrovascular disease. (Iqbal & Jamal, 2023). Calcium channel blockers (CCBs) are commonly prescribed in the management of essential hypertension. (McKeever & Hamilton, 2022)Calcium channel blockers include both dihydropyridines, such as Nifedipine and amlodipine (Basile, 2004). Non‐dihydropyridines (verapamil and diltiazem)(Basile, 2004). The main goal of treatment is to decrease the risk of mortality and cardiovascular\ renal morbidity. (Basile, 2004). Calcium channel blockers act by blocking the influx of calcium ions into vascular smooth muscle and cardiac muscle cells during membrane depolarization (Zimmerman HJ, 2012). Because muscle contraction is largely dependent upon the influx of calcium, its inhibition causes relaxation, particularly in arterial beds. Thus, the major effects of calcium channel blockers are the relaxation of vascular and arterial smooth muscle cells, resulting in arterial vasodilation (Zimmerman HJ, 2012). The major use of calcium channel blockers is for hypertension and angina. (pubmed, 2012). Calcium channel blockers are medicines used to lower blood pressure. They stop calcium from entering the cells of the heart and arteries. Calcium causes the heart and arteries to squeeze more strongly. By blocking calcium, calcium channel blockers allow blood vessels to relax and open. (Mann JFE, et al. 2023)

Specific drug – Nifedipine

Brand Name: APO-Nifedipine XR

Generic name: Nifedipine

Chemical name: Dimethyl 2,6-dimethyl-4-(4-nitrophenyl)pyridine-3,5-dicarboxylate

Nifedipine is a calcium channel blocker in the dihydropyridine subclass. It is primarily used as an antihypertensive and as an anti-anginal medication (Khan et al., 2021). Indications include chronic stable angina and hypertension (Khan et al., 2021). Nifedipine is used as monotherapy or in combination with several different medications, such as ACE inhibitors, ARB and thiazide diuretics to manage hypertension. (Khan et al., 2021). Nifedipine is taken orally and can come in 30 mg extended-release tablets, 60 mg extended-release tablets, 90 mg extended-release tablets,10 mg oral capsules and 20 mg capsules (Khan et al., 2019). Tolerance has been shown to be better with extended-release preparations than with immediate-release preparations of Nifedipine (Khan et al., 2019). During the depolarization phase of smooth muscle cells, there is an influx of calcium ions through voltage-gated channels (Khan et al., 2021). Nifedipine inhibits the entry of calcium ions by blocking these voltage-dependent L-type calcium channels in vascular smooth muscle and myocardial cells (Khan et al., 2021). Reduced intracellular calcium reduces peripheral arterial vascular resistance and coronary arteriey dilation, Reduces systemic blood pressure and increases myocardial oxygen delivery (Khan et al., 2021). Nifedipine thus has hypotensive and anti-anginal properties. (Khan et al., 2021) Nifedipine is almost completely absorbed from the gastrointestinal tract after sublingual, oral, and rectal administration (Raemsch & Sommer, 1983c). Nifedipine displays zero-order kinetics across the dosing range from 30 mg to 180 mg with an estimated elimination half-life of 1.7 hours. (Swanson et al 1987; Pfizer 2003). This is significant considering the effect on heart rate and BP corresponds to plasma drug concentration (Swanson et al. 1987; Pfizer 2003). Sixty to eighty per cent of the dose is excreted as an inactive metabolite in the urine (Pfizer 2003). Nifedipine is hepatically metabolized and is 92% to 98% protein-bound. Due to significant first-pass metabolism, Nifedipines' bioavailability is between 45%–68% (Chung et al, 1987; Pfizer, 2003). Nifedipine is mainly metabolized in the liver (Khan et al., 2021). If liver function is deficient, the metabolism of Nifedipine can suffer (Khan et al., 2021). This can lead to increased blood levels of the medication for longer periods of time, resulting in toxicity and severe side effects. Nifedipine should be used with caution in individuals with hepatic dysfunction (Khan et al., 2021). Chronic liver disease may also prolong the disposition half-life and increase the bioavailability. Individuals with renal disease cannot excrete nifedipine normally. So, this medication can stay in circulation for longer time and can be toxic. Nifedipine should be used with caution in individuals with compromised renal function. Nifedipine may also be contraindicated in people who have a blockage in the digestive tract, a history of stomach surgery, coronary artery disease, or congestive heart failure.Nifedipine can be fatal when taken in conjunction with other medications such as St. John's Wort as it alters bioavailability and efficiency. Common side effects include flushing, peripheral edema, dizziness, headache. Hypersensitivity reactions, such as pruritus, urticaria, and bronchospasms, are relatively rare. (Khan et al., 2021) Abrupt discontinuation of the drug after prolonged use may lead to rebound hypertension or angina. (Khan et al., 2021) Nifedipine should not be used with medications that can lower heart rate, such as, Beta-blockers or vasodilation, such as, Isosorbide and Hydralazine Mann JFE, et al. (2023) . Using them together can result in episodes of low heart rate and BP and can present a medical emergency. Mann JFE, et al. (2023).

Overall, it is evident that Essential hypertension is multifaceted and a highly complex disease. The analysis presented in this essay demonstrates the importance of pharmacological and non-pharmacological intervention in the treatment and management of essential hypertension.

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