REVIEW ARTICLE

NSAIDs and hypertension

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SUMMARY

Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used to alleviate pain of the patients suffering from inflammatory conditions such as osteoarthritis, rheumatoid arthritis, and other painful conditions. An ample amount of studies put forth evidence that NSAIDs reduce the efficiency of antihypertensive drugs plus aggravate pre-existing hypertension or make the individuals prone to develop high blood pressure through renal dysfunction. This review therefore works as an for evidence the practitioners to keep in mind the interaction between NSAIDs and hypertensive drugs. Also, this review suggests regular monitoring of blood pressure when NSAIDs and antihypertensive drugs are used simultaneously.

Key words: Non-steroidal anti-inflammatory drugs; NSAIDs; Pain; Hypertension; Osteoarthritis

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INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are the most common and the most effective drugs used to relieve pain of the patients suffering from arthritis, low back pain and soft tissue pain. These drugs work by blocking the class of the enzymes called cyclo-oxygenases (COX) and subsequently the production of prostaglandins. However, along with their beneficial effects, these drugs carry a lot of adverse effects such as gastrointestinal bleeding,[1,2] peptic ulcers,[3] renal dysfunction,[4,5] edema[6] and high blood pressure.[7,8] NSAIDs produce analgesic, antipyretic and anti-inflammatory effects. Therefore, these drugs are used as a first line drug therapy for the patients with rheumatoid arthritis (RA).

Hypertension is one of the major health problems affecting about one billion people all over the world.[9] It is a common medical condition in older people, especially in obese and diabetic patients.[10] Similarly, RA is also the disease of elderly people, for which NSAIDs are prescribed frequently.[11] In other words, the use of NSAIDs and development of hypertension are both associated with old age. However, studies have suggested that NSAIDs contribute to the risk factors of hypertension and even aggravate high blood pressure.[6,8,12] Therefore, identification of NSAIDs as a risk factor for hypertension would lead practitioners to limit these drugs in hypertensive patients.

NSAIDs may affect blood pressure in two ways; by antagonizing the anti-hypertensive effect of the drugs or by damaging the renal function. Fournier et al have reported that NSAIDs antagonize the effects of hypertensive drugs like angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs).[13] Similarly, NSAIDs have been reported to cause acute renal failure or to aggravate pre-existing renal dysfunction stimulating the renin-angiotensin system and the subsequent worsening of hypertension.[14] Here, in this review we will present as much as evidence as we could for NSAIDs contributing to or aggravating hypertension.

OVERVIEW

In order to collect data on the relationship of NSAIDs and hypertension, we conducted an online search on the most used database PubMed, using the combination of different keywords such as 'non-steroidal anti-inflammatory drugs' or NSAIDs and 'hypertension' or 'renal dysfunction' or 'antihypertensive drugs'. We also collected data from free full text articles.

NSAIDs Antagonize Antihypertensive Drugs

Use of NSAIDs and antihypertensive drugs increases with age and 12-15% of the elderly patients take an NSAID and an antihypertensive concurrently.[15] Studies reveal that the patients taking NSAIDs are at increased risk of initiating antihypertensive drugs as compared to those who do not use NSAIDs. In other words, use of NSAIDs significantly increases the risk of blood pressure. These drugs are attributed to antagonize the effects of antihypertensive drug, thus leading to sustained high blood pressure or an

increased demand of the antihypertensive drugs. Recently, Fournier et al conducted a population based cohort study and reported that NSAIDs lead to an intensification of hypertension treatment, especially in those who are on ACE inhibitors or ARBs.[13] In a Russian study, Savonkov et al studied 30 patients with arterial hypertension of degree I-II and reported competitive interaction of NSAIDs and antihypertensive activity of ACE inhibitors (i.e. analapril and lisinopril).[16] Aljadhey et al carried out a large retrospective cohort study, comprising of 2640 adult hypertensive patients and reported a small rise in systolic blood pressure in those who used ibuprofen as compared to acetaminophen.[17] Salort-Llorca et al also demonstrated that ibuprofen interacts with antihypertensive drugs, leading to the elevation of both systolic and diastolic blood pressures.[18] Ibuprofen inhibits the synthesis of inflammatory and vasodilatory prostaglandins and decreases renal blood flow and thus reduces the excretion of water and sodium leading to high blood pressure. Polonia demonstrated that NSAIDs affect the efficacy of antihypertensive drugs; however, she reported that calcium channel blockers are probably not affected by these drugs.[19] Therefore, calcium channel blockers may be preferred over other antihypertensive drugs while using NSAIDs concurrently. Morgan and Anderson reported too, that dihydropyridine calcium channel blocking drugs were more effective when used with NSAIDs.[20] In a nutshell, NSAIDs reduce the efficacy of antihypertensive drugs through competitive interactions, keeping blood pressure at high levels.

NSAIDs, Renal Dysfunction and Salt Retention

prostaglandins play a key role in the renal hemodynamics and renal tubular function. Therefore, impaired prostaglandin synthesis would badly affect the kidney functions. In this regard, NSAIDs block cyclo-oxygenase enzyme and subsequent synthesis of prostaglandins. Therefore, NSAIDs have long been known to cause renal toxicity along with many other side effects. Renal toxicity increases with increase in risk factors like diabetes, heart failure, and the old age.[21] These effects are referred to the presumption that NSAIDs cause renal vasoconstriction due to the blockade of vasodilatory prostaglandins plus strong vasoconstrictor forces such as angiotensin II, catecholamines and increased sympathetic activity. Moreover, about one fourth of the patients receiving NSAIDs therapy retain sodium in the body, leading to hypertension.[22] Ejaz et al has demonstrated that patients with or without acute or chronic renal failure develop reduced ability of clearing creatinine and concentrating urine.[23]

Griffin et al conducted a nested case-control study in order to evaluate risk of renal function deterioration with the use of NSAIDs.[24] They reported that out of 1799 patients with renal failure, 18.1% were using NSAIDs, as compared to 11.3% of 9,899 controls who were selected randomly. In the same way, Bouvy et al studied the effects of NSAIDs on the renal function of the patients on ACE inhibitors.[25] Their study strongly suggested that NSAIDs are associated with renal dysfunction in hospitalized patients taking ACE inhibitors. Ulinski et al reported that NSAIDs play havoc in condition with a stimulated renin-angiotensin system, leading to renal dysfunction through prostaglandin inhibition.[26] Similarly, other authors have demonstrated that COX-2 inhibitors reduce sodium excretion, leading to acute renal failure in the patients whose kidney functions are "prostaglandin-dependent".[27] Wei et al conducted a population-based longitudinal analysis and reported that estimation of glomerular filtration rate (GFR) lead to decreased use of NSAIDs and subsequently improved renal function.[28]

CONCLUSION

Long term use of NSAIDs contributes to high blood pressure either by antagonizing antihypertensive drugs or by affecting the renal functions and subsequent stimulation of renin-angiotensin system leading to hypertension. As NSAIDs are commonly used and are the first-line treatment in arthritis, there is an unmet need of an recommendation referring to renal insufficiency. Moreover, further research may lead to discovery of safer anti-inflammatory drugs for these conditions.

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