NHS Rotherham Hypertension in adults: diagnosis and treatment – background information

Thiazide diuretics

Recommended Choice: Indapamide

Thiazide diuretics can be separated according to their molecular structure into thiazide-type (TT) and thiazide-like (TL) diuretics. NICE guidelines (NG136) state to offer TL diuretic.

Commonly available TT = Bendroflumethiazide and hydrochlorothiazide - only found in combination products

Commonly available TL= Chlorthalidone, Indapamide.

Thiazide-type diuretics achieve their diuretic action via inhibition of the Na+/Cl− co-transporter in the renal distal convoluted tubule.

Thiazide-like diuretics achieve their diuretic action at the proximal segment of the renal convoluted tubule, and some molecules such as indapamide also have vasodilator actions.

Indapamide is the recommended choice due its availability and low acquisition cost. Chlorthalidone is the only other alternative however it is significantly more expensive.

Calcium channel blockers (CCBs):

Recommended Choice: Amlodipine or Lercanidipine

The dihydropyridine (DHP) class of CCBs (amlodipine, felodipine, lacidipine, lercanidipine, nicardipine, nifedipine, and nimodipine) are used in hypertension treatment as they reduce systemic vascular resistance and arterial pressure with less effects on cardiac output and heart rate.

Of the dihydropyridine CCBs there is very little comparative evidence in terms of blood pressure reduction at therapeutic dose.

Side-effects:

Peripheral oedema including ankle oedema, is a recognised adverse effect of the CCBs. Ankle oedema can range from being mild to severely, affecting quality of life. Although the way CCBs give rise to ankle oedema isn't completely understood, it appears to be due to redistribution of fluid from capillaries to interstitial spaces. It is therefore poorly affected by diuretics.
The incidence of ankle oedema appears more frequent in DHP CCBs (reports ranging from 1-15%)[1]. Although the more lipophilic DHPs lercanidipine and lacidipine may have a lower incidence of ankle oedema than less lipophilic ones e.g. nifedipine, amlodipine or felodipine. Ankle oedema appears to be dose related.

Incidence may be >80% in patients taking long-term, high dose DHPs. While longer-acting CCBs appear to have fewer adverse effects (flushing, headache, palpitations) this doesn't seem the case with ankle oedema.

A meta-analysis of 8 RCTs[2] assessed the relative risk of DHP CCB adverse events with lercanidipine versus older DHP CCBs and versus the other lipophilic DHP CCBs (amlodipine, felodipine and nifedipine, lacidipine and manidipine – not available in the U.K). Efficacy outcomes for lowering BP did not differ statistically between lercanidipine and the other medications. Compared with amlodipine, felodipine and nifedipine, lercanidipine was associated with a reduced risk of peripheral oedema but not flushing or headache. There was no statistical difference between adverse effects with lercanidipine and lacidipine or manidipine.

Amlodipine as first choice due to low cost of acquisition followed by Lercanidipine if ankle oedema is an issue.

ACEI's ARB's

Recommended Choice: Ramipril or Lisinopril.

No ACE inhibitor drug appears to be any better or worse than others in terms of blood pressure lowering ability. (https://www.cochrane.org/CD003823/HTN_ace-inhibitors-for-the-treatment-of-high-blood-pressure)

Ramipril or Lisinopril are the preferred options as these are the most cost-effective treatment options.

Alpha blockers

Recommended Choice: Doxazosin followed by Terazosin.

No alpha blocker drug appears to be any better or worse than others in terms of blood pressure lowering ability (https://www.cochrane.org/CD004643/HTN_alpha-blockers-have-a-modest-bp-lowering-effec

Doxazosin and Terazosin are the preferred options as these are the most cost-effective treatment options.

1. NHS Specialist Pharmacy Service (March 2020). What are the reported incidences of ankle oedema with different calcium channel blockers?
2. Makarounas-Kirchmann K, Glover-Koudounas S, Ferrari P. Results of a meta-analysis comparing the tolerability of lercanidipine and other dihydropyridine calcium channel blockers. Clinical Therapeutics 2009;31(8): 1652-1663.