

DRUG & THERAPEUTICS LETTER



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First-line Antihypertensive Agents

Hypertension should not be diagnosed on the basis of single blood pressure measurement. Hypertension requiring treatment exists when a patient's blood pressure, measured on at least three separate occasions, exceeds the threshold pressures which predict an increased cardiovascular risk, in the absence of complicating features such as diabetes mellitus and overt cardiovascular disease.

While there is no absolute cut-off between normal and elevated blood pressure, current guidelines advise treatment for patients whose systolic pressure is 160 mmHg or greater, or

whose diastolic pressure is 95-100 mmHg or greater. If other risk factors for cardiovascular disease are present, such as hyper-lipidaemia, smoking, obesity or a family history, treatment should be started at 140/90-95 mmHg.

Once a decision has been taken to intervene, and provided that urgent reduction of the blood pressure is not needed, a period of non-drug treatment is recommended such as reduction of excess weight, salt and alcohol intake coupled with increased exercise.

In hypertension, all the five major drug classes (low-dose thiazides, beta blockers, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor antagonists) are efficacious in reducing blood pressure and cardiovascular events.

Recent results from various studies and meta-analyses show that it is the reduction in blood pressure itself that

leads to lower cardiovascular morbidity and mortality. It is the reduction in blood pressure that counts and not the drug class used to reduce it.

Patients with hypertension are often overweight and have an increased likelihood of developing diabetes, independent of treatment. The highest quality trials suggest that diabetes incidence is unchanged or increased by thiazides and beta blockers, and unchanged or decreased by ACE inhibitors, calcium channel blockers and angiotensin receptor blockers. However, there are no data on long-term outcomes using the very low doses of diuretic now recommended (daily doses of hydrochlorothiazide, chlorthalidone and indapamide not exceeding 12.5 mg, 12.5 mg and 1.5 mg respectively) although it would be expected that the metabolic effects would be less.

If we combine the evidence from each of the selection criteria, it is difficult to escape the conclusion that treatment of patients with uncomplicated hypertension should be started with low-dose thiazide type diuretics. Failure to respond adequately will probably require the addition of another drug, while the emergence of unacceptable adverse effects is a reason

for changing to an alternative class of drug.

A prudent approach is to measure serum potassium, uric acid and fasting glucose before prescribing and not use diuretics (or beta blockers) if the fasting blood glucose is at, or above, 6.1 mmol/L. Fasting glucose should be monitored periodically in patients on continuing diuretic treatment.

Conclusion: For most patients with uncomplicated hypertension low-dose thiazide-type diuretics should be first-line therapy. World Health Organization / International Society of Hypertension (WHO/ISH) in 2003 also advises: 'for the majority of patients without a compelling indication for another class of drug, a low dose of a diuretic should be considered as the first choice of therapy on the basis of the comparative trial data, availability and cost.'

Sources:

- Suzanne R Hill and Anthony J Smith. First-line medicines in the treatment of hypertension. *Aust Prescr* 2005;28(2):34-7
- Whitworth JA. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. *J Hypertens* 2003;21:1983-92

Brief Information:

Antibiotic Prophylaxis in Surgery

Wound infections are the commonest hospital-acquired infections in surgical patients. They result in increased antibiotic usage, increased costs and prolonged hospitalisation. Appropriate antibiotic prophylaxis can reduce the risk of postoperative wound infections, but additional antibiotic use may favour the emergence of antimicrobial resistance. Judicious use of antibiotics in the hospital environment is therefore essential.

It was reported from a study of eight German hospitals, approximately 30-50% of antibiotic use in hospital practice was for surgical prophylaxis. However, between 30% and 90% of this prophylaxis was inappropriate. Most commonly, the antibiotic was either given at the wrong time or continued for too long.

Widely accepted indications for antibiotic prophylaxis are contaminated and clean-contaminated surgery and operations involving the insertion of an artificial device or prosthetic material. Less well-accepted indications for prophylaxis include clean operations in patients with impaired host defences or patients in whom the consequences

of infection may be catastrophic, for example neurosurgery, open heart surgery and ophthalmic surgery.

Most importantly, the antibiotic should be active against the bacteria most likely to cause an infection. Most post-operative infections are due to the patient's own bacterial flora. Prophylaxis does not need to cover all bacterial species found in the patient's flora, as some species are either not particularly pathogenic or are low in numbers or both.

It is important to select an antibiotic with the narrowest antibacterial spectrum required, to reduce the emergence of multi-resistant pathogens and also because broad spectrum antibiotics may be required later if the patient develops serious sepsis. The use of third generation cephalosporins such as ceftriaxone and cefotaxime should therefore be avoided in surgical prophylaxis. Often several antibiotics are equal in terms of antibacterial spectrum, efficacy, toxicity, and ease of administration. If so, the least expensive drug should be chosen.

The use of an appropriate single antibiotic dose is usually sufficient if the operation lasts for four hours or less. In prolonged surgery of greater than four hours, further antibiotic doses may be required to maintain the

concentration, particularly if the antibiotic has a short half-life. Continuing antibiotic prophylaxis until surgical drains have been removed is illogical and also of unproven benefit. Inappropriate use of antibiotics for surgical prophylaxis increases both cost and the selective pressure favouring the emergence of resistant bacteria.

Drug Committee, TUTH

The present Drug Committee, TUTH which was constituted about 2 years back has accomplished following activities:

- selection of drug manufacturers based on the list of the manufacturers provided by various departments of the hospital for the procurement of drugs for the hospital pharmacy
- developing policies and strategies for minimizing expiry of

drugs in the hospital pharmacy

- taking steps in getting approval for disposal of drugs expired in the hospital pharmacy since the establishment of the hospital up to 2061/62
- developing proposal for the extension of hospital pharmacy services including in-patient supply of drugs (the proposal is already accepted by the Management Committee, TUTH)
- updating hospital formulary
- conducting study on prescribing practices, patients' knowledge on drug use, and pharmacy services at TUTH and dissemination of findings to the heads of departments as well as in the bulletin, "Drugs and Therapeutics Letter" (Vol. 11 No. 1, October – December, 2004).

"Drug and Therapeutics Letter" is also available now in the following websites :
<http://www.teachinghospital.org.np/diu.html>, <http://www.iom.edu.np/diu.html>

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