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THERAPEUTICS INITIATIVE Evidence Based Drug Therapy

therapeutics letter
January - February 2007

Mild Hypertension

An approach to using evidence in the decision making process

We think health care professionals should try to practice evidence based medicine and shared-informed decision making whenever possible. But how often is that truly possible? The case below illustrates a common presentation in family practice and an attempt to approach it using the principles of evidence developed by the Cochrane Collaboration.

Case

Mr. EBP is a 55-year-old man, who you have been following for the last 15 years. He has been healthy, except for an occasional upper respiratory tract infection. He has no history of heart disease or stroke. Family history reveals that his mother died of a stroke age 79, and father died of colon cancer age 75. He is a non-smoker, drinks 2 ounces of scotch daily and does no regular exercise. He is 5'8" (173 cm) tall and weighs 200 lb (91 kg). His general physical examination is normal, except for resting BP, which averaged 150/98 mmHg on repeated measurements in the sitting position. On review of his chart you discover that BP was 138/88 mmHg 1 year ago. You recommend an exercise program and a reduced calorie, no added salt diet.

Laboratory investigations: CBC, creatinine, electrolytes, FBS, urinalysis, and EKG are normal. Over the next 6 months you repeat the BP measurements during three office visits. He is reducing calories and exercising, his weight has decreased by 5 lbs and his average seated BP is 146/94. You diagnose primary mild (Stage 1) hypertension.

Dialogue

Physician (beginning to fill out a prescription): *Despite the non-drug measures your BP remains elevated and you should start drug therapy to lower your BP.*

Patient: *I am a cautious person. Before I start something I want to know the chances of my benefiting or being harmed with drug therapy.*

Physician (gently escorting him out of the office): *I will get the information and provide it at your next appointment.*

What do you need to provide the answer to his question? You are hoping that you can find the answers in The Cochrane Library. You remember that most questions for systematic reviews come from clinical practice and you realize that you need a systematic review that answers the following question: How much does antihypertensive drug therapy as compared to placebo or no treatment change mortality and morbidity in randomized controlled trials of men with BP in the range of 140-160/90-100 mmHg?

The Cochrane Library

You fortunately have access to The Cochrane Library Issue 1, 2007. When you do a search for "pharmacotherapy" and "hypertension" you find 2 completed reviews: Pharmacotherapy for hypertension in women of different races[1] and Pharmacotherapy for hypertension in the elderly[2]. Neither is particularly relevant to your patient as the first is the wrong gender and the latter review is limited to patients 60 years of age and above. However, you discover in The Library that the Hypertension Review Group is based at the University of BC. You send an e-mail to the Review Group Coordinator describing your case and question.

The Cochrane Hypertension Group

The following is their reply. The Cochrane Hypertension Group keeps a record of all the relevant RCTs related to hypertension. There are 5 RCTs that were designed to test the effect of antihypertensive treatment versus placebo in "mild hypertension".[3-7] According to the inclusion and exclusion criteria of these 5 trials, your patient would have been eligible for each of them. In these trials 23,000 people were studied, 54% male, average age 51

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years, the average baseline BP was 160/98 mmHg and most subjects had no evidence of cardiovascular disease. The first-line drugs studied were thiazides in all 5 RCTs, the only exception being one RCT which also had a beta blocker arm. The average duration of follow-up was 5 years.

Quantitative evidence

The key pooled outcomes from these 5 trials reveal the following:

1. Total mortality, RR 0.95 [0.71 - 1.11].
2. Total serious adverse events were not reported in any of the trials.
3. Total cardiovascular events (fatal and non-fatal strokes plus fatal and non-fatal coronary heart disease) were reduced from 4.0% to 3.2%, RR 0.81 [0.71 - 0.92], ARR 0.8%, NNT 125 for 5 years.
4. Withdrawals due to adverse events, RR 4.8 [4.2 - 5.6], ARI 9%, NNH 11 for 5 years.
5. Removing the first-line beta blocker arm did not materially change the estimates.

You now feel you are in a position to explain the benefits and harms to your patient.

Back to the case

When your patient comes to his next appointment you explain what you have done and what evidence is available as follows. In the 5 trials there was no benefit in terms of total mortality, but there was a reduction in total strokes and heart attacks from 4% to 3.2%. The magnitude of the absolute reduction was 0.8%, meaning that 125 people like him would have to be treated for 5 years to prevent one heart attack or stroke. On the harm side there was a 9% absolute increase in withdrawals due to adverse effects with drug treatment as compared to placebo. That means that for every 11 people treated one would stop the drug because of a side effect. That side effect would resolve after the drug was stopped. After discussing the magnitude of the potential benefits, harms and costs associated with therapy, you and the patient come up with a shared-informed decision. Whatever decision is made, you support the decision of the patient.

Discussion

Randomized trials provide an assessment of the average response one can expect from an intervention. This is simply an estimate and may be limited by the amount of data that is reported in a published trial. However, if we use the RCT evidence and outcomes that are specific and meaningful to our patient, it is likely the best that we have. In this case the 5 trials included 46% women and 54% men with an average age a little less than our patient. Since risk is higher in men and increases with age, the patient might expect a somewhat higher absolute benefit than the average. However, the patient's blood pressure is 14/4 mmHg lower than the average patient in the trial suggesting that his absolute benefit might be less than in the trials. A more precise estimate of the benefits and harms could be achieved by looking at the outcomes in a subgroup limited to males, aged 50 to 60 and with blood pressure in the range of 140-160/90-100 mmHg at baseline. This is possible, and it is one of the projects being worked on by the Cochrane Hypertension Group.

The approach presented might appear challenging and time consuming for the health professional. **However, we think patients need to know this information when it comes down to making decisions about long-term drug therapy.** We also think that this evidence based and shared-informed decision making approach needs to be compared to usual care in a randomized controlled trial.

Conclusions

- Using the best available evidence, the magnitude of benefit for drug treatment of mild hypertension can be estimated and presented to a patient.
- Shared-informed decision making can only truly be done if one can provide reasonable estimates of the potential benefits and harms of a proposed therapy.
- RCTs are needed to test whether using this evidence and shared-informed decision making approach changes mortality and morbidity as compared to usual care.

RR = Relative risk
ARR = Absolute risk reduction
NNH = Number needed to harm
NNT = Number needed to treat
ARI = Absolute risk increase

In a future Letter we will review a different approach: the use of risk calculators to estimate the benefits of risk factor modification.

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The draft of this Therapeutics Letter was submitted for review to 40 experts and primary care physicians in order to correct any inaccuracies and to ensure that the information is concise and relevant to clinicians.