Health-related quality of life in patients treated for hypertension: a review of the literature from 1990 to 2000

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Authors' objectives
To synthesise the available data on the impact of antihypertensive therapy on health-related quality of life (HRQL), and to provide recommendations for future research.

Searching
MEDLINE was searched using terms such as 'quality of life', 'health-related quality of life', 'hypertension', 'essential hypertension' and 'clinical trial'. In addition, the reference lists of relevant reviews and other trials were examined. Only studies published in English between 1990 and January 2000 were sought.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials were included. No study length was defined, but in the included studies the median follow-up period was 16 weeks (mean 26.1 weeks, range: 4 weeks to 5 years).

Specific interventions included in the review
Any antihypertensive pharmacological intervention was eligible for inclusion. In the included studies, the medications (singularly or in combination) were: betaxolol, verapamil, nifedipine, nifedipine GITS, enalapril, atenolol, diltiazem, chlorthalidone, reserpine, hydrochlorothiazide (HCTZ), bisoprolol, altizide-spiroolactone, lisinopril, HCTZ-triamterene, chlorthalidone, celiprolol, captoril, isradipine, metoprolol, pinacidil, bendrofluazide, citazapril, methyldopa, hydralazine, doxazosin, acebutolol, amlodipine, clopamide, telmisartan, propranolol, carvedilol, quinapril, and losartan. The comparisons were made between drugs or against placebo.

Participants included in the review
Patients with essential hypertension. In the included trials, the participants were male and female, and black and white. However, there was no indication of their ages or severity of illness or hypertension.

Outcomes assessed in the review
For inclusion in the review, HRQL had to be an explicitly stated outcome and a description of the HRQL assessment had to be provided. The authors do not define HRQL (and this is not clearly stated in most of the included studies). However, to be included, a 'specific' HRQL instrument or a subscale of a 'specified instrument' must have been identified and used. Full details of those used in the included studies (108 separate instruments or scales) were tabulated. The reported outcomes included:

- general well-being, i.e. anxiety, depression, general health perception, mental health and mood;
- cognitive function, i.e. memory, attention, complex cognitive/language ability, visual-spatial and motor skills;
- sleep;
- sexual function; and
- 'symptoms', i.e. tiredness, dry mouth, palpitations, dizziness, headache, cough and so on.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.
Assessment of study quality
The authors do not report the method used to assess validity, or how the validity assessment was performed.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

The data extracted included: reference and country of study; sample size, the number evaluable for HRQL and demographic characteristics (percentage male and female, black and white); the duration of the trial; treatments; and results. The scales and instruments used in the studies were tabulated separately.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative. The results were presented both in tabular format and in the narrative, where they were grouped according to the outcomes.

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.

Results of the review
Forty-eight studies were included; of the 23,985 participants, only 17,181 were 'evaluable for HRQL', i.e. 'either completed the study or for whom complete HRQL data were available'. Fifty-seven per cent of the studies had less than 100 participants per treatment arm.

General well-being.
Forty-two studies were included. These used 29 questionnaires to measure a variety of general well-being dimensions. The use of diuretics had either a positive effect or no effect on general well-being. Beta-blockers, calcium-channel blockers and angiotensin-converting enzyme (ACE) inhibitors appeared generally to have positive results on general well-being (details of the individual studies and drugs are given in the paper).

Cognitive function.
Twenty-three studies using 41 different tests were included. No treatment group differences were noted in the majority of the studies (17). The results of beta-blockers on cognitive function were mixed, showing both increases and decreases in performance (3 studies). Calcium-channel blockers had a positive effect on cognitive function (3 studies), while ACE inhibitors had a positive effect on memory/attention tests (3 studies). In general, although some studies reported changes within, or differences between treatment groups, most suggested that antihypertensive regimens have no effect on cognitive function. Specifically, there is little evidence that antihypertensive treatments are associated with significant cognitive impairment.

Sleep.
Twenty-two studies using 14 different questionnaires were included, but no statistically-significant treatment group differences were noted in 15 of these. Data on the effects of beta-blockers, ACE inhibitors and calcium-channel blockers were inconsistent, but there was some evidence to suggest that beta-blockers interfered with sleep (7 studies). Diuretics did not appear to have any adverse effect on sleep.

Sexual function. Twenty-one studies using 13 different questionnaires were included, but many of these did not appear to differentiate sexual function by gender. In 10 (48%) of the studies there were no differences between the treatment groups. In the remaining studies; diuretics were associated with a significant negative effect in comparison with placebo and atenolol (2 studies); propranolol and atenolol were associated with a decrease in sexual function (2 studies); and atenolol was found to both increase and decrease sexual interest (2 studies). One study found that amlodipine did not
affect sexual function, whereas another found that it caused a significant decrease. In 2 separate studies, enalapril was found to decrease sexual interest among women, but not sexual function. In men, enalapril was associated with both decreased sexual function (2 studies) and a significant increase in morning erections (one study). One study showed that captopril significantly increased sexual performance in men, but did not affect sexual functioning in women.

Symptoms.

Twenty-five studies reported self-reported symptoms or side-effects using 9 different questionnaires. In general, the results reported on individual studies of differing drugs (and comparisons) and a wide variety of symptoms; details are given in the paper. Studies comparing beta-blockers with calcium-channel blockers (3 studies) and ACE inhibitors (4 studies) demonstrated no treatment group differences in the incidence of symptoms. The most frequent and well documented complaint of ACE inhibitors was a dry cough. Two studies found that captopril was associated with a decrease in symptoms (compared to baseline), while one study showed that it had a significantly better side-effect profile than enalapril.

Authors’ conclusions

The results among the studies were frequently inconsistent, most likely because of the wide variety of dimensions studied and instruments used, as well as the methodological weaknesses in the studies. These weaknesses included small sample sizes, short-term assessments, and a failure to account for missing data. A standardised approach to the assessment of HRQL in hypertensive patients is needed, so that research in this area can be of value to clinical practice and to patients and their families.

CRD commentary

This review covered a complex but important subject area of particular interest to patients and those trying to improve adherence to antihypertensive therapies. The scope of the review was very broad (all antihypertensive agents and all aspects of HRQL). The authors stated their aims although they acknowledged that a clear definition of HRQL is lacking. The database search was limited to MEDLINE and to English language papers published between 1990 and 2000. In addition, the search terms appeared to be limited. It is therefore possible that studies were missed.

The authors did not state how the review process was conducted, how the papers were selected, how the data were extracted, or how papers were assessed for validity. This could affect the validity of the results. The authors discussed an intention-to-treat analysis, but they accept that the vast majority of the studies did not account for this. Failure to take account of drop-outs or withdrawals in the studies can lead to bias in the results; in 9 studies a loss in sample size of 25% or more occurred. A narrative synthesis was appropriate given the wide range of treatments and methods of assessing or describing the outcomes. There was little information on the participants in the studies, such that it is difficult to generalise from the results. In addition the differences between the studies (drugs, comparison treatments, scales used) were not given any weighting in the results. The authors acknowledged these problems in the discussion and also the considerable problems related to drop-outs and intention-to-treat analysis, which could lead to significant bias in the results.

Taking these comments into consideration, the authors’ conclusions would appear to be valid.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors state that professional organisations and leaders in the field (of hypertension) should set guidelines for HRQL evaluation in hypertension. These should include a consensus on the dimensions of HRQL in relation to hypertension, as well as an agreement on a core set of HRQL instruments to be used in this research.

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