Interventions to improve antihypertensive drug adherence: a quantitative review of trials

Morrison A, Wertheimer A I, Berger M L

Authors' objectives
To evaluate the effectiveness of interventions to improve oral antihypertensive drug adherence.

Searching
MEDLINE was searched from 1965 to February 1999 for studies published in the English language, using the following strategies: MeSH terms 'patient compliance' (comparative study OR prospective studies OR clinical trials) AND 'hypertension'; title word 'compliance' OR 'persistence' OR 'adherence'; MeSH terms 'hypertension' AND 'patient compliance' AND 'patient education'.

The bibliographies of review articles were also examined for additional relevant publications.

Study selection
Study designs of evaluations included in the review
Only parallel group randomised (or quasi-randomised) controlled trials published in peer-reviewed literature were considered. The study designs included were randomised controlled trials (RCTs), quasi-randomised trials in which assignment was by an arbitrary method or by minimisation, and crossover designs. Studies in which fewer than 10 participants were randomised were excluded. The length of follow-up ranged from 2 to 29 months.

Specific interventions included in the review
The interventions included the use of electronic vial caps, calendar packaging, patient cards, different dosing regimens, patient reminders, physician education, patient education, worksite care, disease management, counselling, and self-monitoring. The interventions had to be designed to improve adherence with oral drugs in hypertension.

Participants included in the review
The authors did not report the inclusion and exclusion criteria for participants and disease. Participants included ambulatory patients with treated or previously untreated arterial hypertension, patients who were taking one or more antihypertensive medications, non-compliant hypertensive steelworkers, infrequent attenders, and previously non-compliant out-patients. The mean ages of the participants reported in the trials ranged from 47 to 76 years; the median average age was 56 years.

Outcomes assessed in the review
The primary outcome was adherence to medication for lowering blood-pressure.

The methods used to measure adherence were urine sampling, pill counting, self-report, an electronic medication event monitoring system (MEMS), and pharmacy records of prescription refills. The adherence rate was defined as the proportion of prescribed doses taken. The most frequently used definition was that of Sackett et al. (see Other Publications of Related Interest), which defined adherence as greater than 80% pill consumption. Adherence was typically measured at the end of the study (e.g. the last study month), but in several cases adherence was reported for the entire study period. In some trials, adherence was expressed in terms of a Likert scale, based on either self-report or pill counts.

Adherence, as measured by the proportion of prescribed doses taken, was sometimes reported as the medication possession ratio (MPR), i.e. the ratio of the number of days’ supply obtained to the number of days in the study period. A couple of trials used MEMS, but no MEMS data were reported in the review. The secondary outcome was diastolic blood-pressure.

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
Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
Structured data were extracted serially from all twenty-nine articles by one of the study's authors and the process was repeated twice. The authors assumed that the trials were open unless specifically stated otherwise.

Categorical data were extracted in preference to continuous data. This is because the authors wished to compute odds ratios (ORs), which they felt were generally more easily understood than the effect sizes calculated from continuous data. The adherence measure of more than 80% pill consumption was used if reported. For blood-pressure, categorical data were extracted if available; typically, this was the proportion of patients with diastolic blood-pressure less than 90 mmHg, the cut-off regarded as clinically significant according to national guidelines. Otherwise, the mean diastolic blood-pressure was extracted. Studies were tagged 'insufficient data reported' if the effect sizes could not be computed because either the numbers of patients evaluated or a measure of variance were omitted.

ORs with 95 per cent confidence intervals (CIs) were calculated for each individual trial with the categorical data. Effect sizes (Hedges g-statistic) with 95 per cent CIs were calculated for continuous data.

Methods of synthesis
How were the studies combined?
Summary statistics (ORs and effect sizes with 95% CIs) were calculated for trials in the same intervention category, providing all trials in the category reported results and used the same method of measuring adherence. The authors do not describe how studies were selected and weighted. They also do not state any methods for the assessment of publication bias.

How were differences between studies investigated?
The authors do not state a method for assessing any differences between the studies.

Results of the review
Twenty-nine trials with a total of 12,835 participants were included. The included studies evaluated: electronic vial caps (1 study, n=70), calendar packaging (5 studies, n=796), patient cards (2 studies, n=303), dosing regimen (4 studies, n=8,288), physician education (2 studies, n=301), patient education (5 studies, n=1,512), disease management (1 study, n=39), worksite care (2 studies, n=651), counselling (5 studies, n=524), and self-monitoring (2 studies, n=351).

Electronic vial cap (1 study): the odds of a patient being compliant in the electronic vial cap group were about six times higher that those in the control group; both groups had a similar effect on diastolic blood-pressure (no exact data reported).

Calendar packaging (5 studies): the summary OR for pill counts was 1.7 (95% CI: 1.4, 2.0, p-value not reported) for 3 trials. The remaining 2 trials either did not show a statistically-significant result or did not report adherence.

Patient cards (2 studies): both trials resulted in statistically-significant positive effects with a combined OR of 2.9 (95% CI: 2.7, 3.1, p-value not reported). One study reported data for blood-pressure, but the result was non significant.

Dosing regimen (4 studies): adherence results could only be calculated for one of the studies (OR 1.0, 95% CI: 0.7, 1.44, p-value not reported). The effect on blood-pressure was not statistically significant. The authors felt that the data do not provide support for the effectiveness of a simplified dosage regimen.

Reminders (3 studies): the results were statistically significant in the 2 studies that used mixed interventions (no exact data reported). The authors stated that there was insufficient evidence to demonstrate the effectiveness of reminders.
alone.

Physician education (2 studies): one study showed that the odds of a patient of a physician being compliant in the experimental group was 3.2 times higher than for those in the control group (no exact data reported), whereas the results of the other study were not statistically significant. Both studies showed statistically-significant results for blood-pressure (no exact data reported).

Patient education (5 studies): there were conflicting results of trials of patient education in hypertension (no exact data reported).

Worksite care (3 studies): in each of these trials, the summary statistics suggested a small statistically-significant positive effect on adherence and an improvement in blood-pressure was reported (no exact data reported).

Counselling (7 studies): adherence could be calculated for 6 of the 7 studies. Two studies showed statistically-significant positive results (exact data not reported). However, the results were conflicting and, overall, did not demonstrate that counselling per se was effective.

Self-monitoring (5 studies): adherence could only be calculated for 3 of the 5 studies. Only one of these showed a statistically-significant effect for both adherence and blood-pressure (no exact data reported).

Authors’ conclusions
The authors state that statistically-significant improvements in adherence were observed in single-blind trials of worksite care, physician education, and an electronic vial cap, and in unblinded trials of patient cards and calendar packaging. There was insufficient evidence to support the effectiveness of mailed reminders alone, according to unblinded trials. Adherence results were conflicting for patient education and inconclusive for patient counselling. Self-monitoring was deemed ineffective according to single-blind trials. The results for meeting the goal diastolic blood-pressure, when evaluated (if data were available), were generally in accordance with those for adherence.

CRD commentary
This review aimed to summarise the evidence for the effectiveness of interventions to improve antihypertensive drug adherence. The authors provided little information on the process of study selection, the validity assessment, and the methods used for statistical pooling. They did not mention any methods to assess differences between the studies or publication bias. However, the authors were aware of some of these limitations and mentioned these in the discussion. The review included only English language publications in MEDLINE, and an attempt should have been made to search other databases for articles published in all languages.

This was an important review and dealt with a very relevant question. Although the authors’ conclusions appear to be supported by the data, only a very limited amount of data was provided in the paper. Perhaps there should have been more emphasis placed on the fact that some of the included studies were small in number, were very heterogeneous with regard to participants, interventions and outcomes, and that their comparison was very difficult. The results of this review should, therefore, be interpreted with caution.

Implications of the review for practice and research
The authors did not state any implications for further research and practice.

Bibliographic details

Other publications of related interest
Indexing Status
Subject indexing assigned by CRD

MeSH
Antihypertensive Agents /therapeutic use; Hypertension /drug therapy; Patient Compliance

AccessionNumber
12000000668

Date bibliographic record published
31/03/2002

Date abstract record published
31/03/2002

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.