The effect of self-measurement of blood pressure on medication adherence and lifestyle factors: a systematic review and meta-analysis. [2,900 words not including tables, figures or appendices]

Abstract [247 words]

Background

Self-measurement of blood pressure (SMBP) can contribute to improved blood pressure (BP) control in hypertensives. Potential mediators include improvement in medication and non-pharmacologic treatment adherence/lifestyle factor change (dietary change, increased physical activity and/or change in smoking status).

Methods

We searched electronic databases through February 2014 to identify all randomised controlled trials that compared SMBP to control/usual care in ambulatory hypertensive patients. Trials were required to report medication or non-pharmacologic treatment adherence measures.

Results

Twenty-eight trials with 7,021 participants fulfilled our inclusion criteria. Medication adherence was assessed in twenty-five trials, dietary outcomes in eight, physical activity in six and medication persistence in one. BP was assessed in twenty-six studies.

SMBP interventions were associated with significantly better adherence to antihypertensive medication adherence in 32% of trials. Pooled results demonstrate a small but significant overall effect in favour of SMBP interventions (SMD 0.21, 95%CI 0.08 to 0.34), with moderate heterogeneity (I2=43%).

Where SMBP interventions had a significant effect on lifestyle factor change, the effect was unlikely to be clinically significant.

Office systolic BP at six months was significantly reduced in those who used SMBP (WMD -4.07mm, 95%CI -6.71 to -1.43).

Conclusions

The evidence from this review demonstrates that SMBP may aid in improving adherence to medication adherence in hypertensives. Evidence for the effect of SMBP on lifestyle factor change and medication persistence is scarce and of poor quality.

A number of methodological issues mean that judging the true impact of SMBP difficult. Future trials should address these issues.

Keywords: blood pressure; self-measurement; adherence; meta-analysis; non-pharmacoligic

Background

It is widely accepted that self-measurement of blood pressure (SMBP) can contribute to improved blood pressure control in hypertensives [1-3]. However, how SMBP brings about this change is less well understood. Potential mediators include improvement in adherence to antihypertensive medication, and/or adherence to non-pharmacologic treatment (i.e. dietary change, increased physical activity and/or change in smoking status).

A systematic review published in 2006 found that of eleven included trials investigating the impact of SMBP on antihypertensive medication adherence, six showed a statistically significant improvement [4]. There have to date been no reviews of the effect of SMBP on other intermediate outcomes such as lifestyle change. There is limited evidence from qualitative research that the use of SMBP can influence compliance with diet and exercise regimes [5,6], and a review of trial data is needed to further investigate this. It has been estimated that a diet and weight loss approach can be at least as effective as single drug therapy at reducing BP in hypertensives[7].

The primary objectives of this review were to determine the effect of SMBP on medication adherence, medication persistence, and lifestyle factors in hypertensives, in order to better understand the mechanisms through which SMBP may achieve better BP control.

Methods

Information sources and study selection

A protocol was developed and made available on the PROSPERO database prior to commencing the review [8]. Electronic databases were searched in February 2014 (DARE, Cochrane Database of Systematic Reviews, MEDLINE, EMBASE, CINAHL, PsycINFO, Dissertation and Theses). Ongoing and completed studies without related publication were identified through searches of clinical trial databases (i.e. ClinicalTrials.gov, WHO trials portal, UKHTA, Current controlled trials).

There were no language or time restrictions to the search. The Medline search strategy was translated for use in the other databases (Supplementary material: Appendix 1). Studies were also identified through citation searches of related reviews, and relevant trials, and authors were contacted for further information where necessary.

Randomised or quasi-randomised trials were eligible for inclusion if the intervention included self-measurement of BP; if usual care did not include self-measurement; if the participants were hypertensive and receiving care in ambulatory/outpatient settings; and if medication adherence and/or lifestyle factor outcomes were available. Two reviewers independently screened the reports for inclusion (BF, JHB).

Data extraction and risk of bias assessment

Data were extracted on: recruitment and setting; baseline characteristics; intervention and control characteristics; and outcome measures. Raw unadjusted data were extracted where available for outcome measures, and where only adjusted results were given this is reported as such in the results.

Primary outcomes of interest were antihypertensive medication adherence and persistence, dietary outcomes (including alcohol consumption), physical activity and smoking. Medication adherence measures were divided into four groups to aid analysis: electronic monitoring, pill counts, pharmacy fill data, and self-reported measures. Secondary outcomes included BP, BP control and adherence to the SMBP component of interventions.

When extracting information on intervention characteristics, studies were classified according to whom the intervention was aimed at (patients and/or healthcare professionals [HCPs]), and any co-interventions beyond self-measurement of BP.

Data extraction and risk of bias assessment was carried out independently by two reviewers (BF, JHB). Following guidance from the Cochrane Collaboration, studies were deemed to be at high, low or unclear risk of bias based on random sequence generation, allocation concealment, blinding of outcome assessment, selective reporting, attrition and other risks of bias[9].

Statistical analysis

Meta-analyses were performed using RevMan 5 using random-effects models for a comparison of SMBP versus usual care/control for medication adherence and BP outcomes. As medication adherence was measured using different measures, standardised mean differences (SMD) were calculated in order to compare the effect of SMBP on adherence across studies. Cohen (1988)

proposed guidelines for interpreting standardised mean difference effect sizes, stating that: 0.2 is a small effect, 0.5 is a medium effect, and 0.8 is a large effect [10]. Subgroup analysis was used to group studies that measured medication adherence using different measures. Where studies report a number of adherence measures, the most objective measure was used in meta-analysis to avoid double counting.

For office systolic and diastolic BP at six months, weighted mean differences were calculated for overall change between intervention and control. Weighting depended on the standard deviation of the change in BP from baseline to final reading. Where data were only available on baseline and outcome standard deviation, the standard deviation for mean change could be imputed according to the methods suggested in the Cochrane Handbook [9]. The correlation between baseline and final result was estimated from studies where all standard deviations were reported and then used to estimate the standard deviation for the mean change.

The I^2 statistic was used to present statistical heterogeneity, and was interpreted using the guidelines presented by the Cochrane Handbook [9].

Results

Included studies

Twenty-eight trials with a total of 7,021 participants fulfilled our inclusion criteria (Figure 1)[11-38]. Of the included studies: medication adherence was assessed in twenty-five; dietary outcomes in eight; physical activity in six; smoking in three; and medication persistence in one study. The secondary outcome of BP was assessed in twenty-six studies.

Characteristics of the included studies are summarised in Table 1. SMBP was the sole component of interventions in eleven studies (39%), with SMBP combined with co-interventions in seventeen (61%). Co-interventions were coded and grouped and are summarised in Table 1, and in more detail in the supplementary material (Appendix 2). The most common co-intervention was education delivered either verbally (in eleven studies) or using either printed or on-line materials (in six studies).

Patients alone were the target of the intervention in eight studies[13,18,19,21,23,24,30,36], whilst interventions targeted both patients and healthcare professionals in the remaining twenty. In the majority of cases where healthcare professionals were also targeted, intervention participants' GPs received self-measured BP results from patients, or were informed when patients exceeded target BP, and were able to act accordingly[11,16,20,25-29,32,35,38,39]. Three studies involved pharmacists implementing the intervention, two involved nurses, and one involved dieticians. The theoretical basis for the development of the intervention was reported in only four studies [17,28,31,33]

Participants were initiated on new anti-hypertensive medications in four studies [14,23,35,36], and medication titration protocols based on self-measured BP measurements were reported in five studies [14,22,33,35,38].

Protocols for self-measurement varied across studies, ranging from participants being asked to measure their BP twice daily every day[21], to four occasions per year (twice in morning on four consecutive days)[29]. The SMBP protocol was not reported in five studies[14,24,30,39].

Follow-up ranged from two weeks to twelve months with a median of 6 months, and was deemed to be adequate (i.e. >80% of participants available for outcome assessment at follow-up) in 75% of studies.

[insert Figure 1 and Table 1 here]

Risk of bias

Two studies were judged to be at low risk of bias across all domains [22,33]; twelve studies were judged to be at high risk of bias in at least one domain [15,19,20,25,27-29,31,32,34,36,39]. The remaining fourteen studies were at unclear risk of bias in at least one domain, most commonly due to allocation concealment. Risk of bias is across studies is presented in Figure 2.

[insert Figure 2 here]

Adherence to antihypertensive medication

Adherence to antihypertensive medication was assessed by electronic monitoring in five studies [14,23,33,35,36], by pill count in eight [11,15,16,18-20,24,35], using pharmacy fill data in six [21,22,26,30,32,34], and by self-report in nine [17,21,28,31,34,37-39]. Three trials used two categories of measure [21,34,35]. Full results of medication adherence are presented in Table 2.

[insert Table 2 here]

Overall, SMBP interventions were associated with significantly better adherence to antihypertensive medications in eight of twenty-five studies (32%) [13,15,18,19,23,24,33,35]. The independent effect of SMBP on medication adherence (i.e. SMBP was the sole component of the intervention) was tested in nine studies [11,13,19-21,23,24,26,30], and was associated with significantly better adherence in four of those studies (44%) [13,19,23,24]. In contrast, when SMBP was part of a complex intervention, a significant effect on medication adherence was demonstrated in four of sixteen studies (25%)[15,18,32,35].

When the results of all adherence measures are pooled, a small but significant overall effect in favour of the intervention is demonstrated (SMD 0.21, 95% CI 0.08, 0.34), with moderate heterogeneity (I^2=43%) (Figure 3). A test for subgroup differences did demonstrate a significant effect of adherence measure on the overall effect size (Chi^2=5.47, df=3, p=0.14). The pooled effect size (ES) estimates increase in size with more objective measures of adherence, with the largest ES seen when adherence is measured using electronic monitoring, this is reflected in the proportion of studies showing a significant effect in medication adherence across measures (i.e. 60% for electronic monitoring, 50% for pill counts, 0% for pharmacy fill, 11% for self-report).

When assessed by electronic monitoring (i.e. medication event monitoring systems), SMBP was associated with significantly better adherence to antihypertensive medications in three of five studies (60%)[23,33,35]. Medication adherence was generally high in these studies, for example proportion of days with correct dosing: >83% (Marquez-Contreras), >62% (Rudd), >77% (Dusing); >90% (van Onzenoort). The pooled result of two studies detected a significant effect in favour of the intervention (SMD 0.45, 95% CI 0.10 to 0.79), with moderate statistical heterogeneity (I^2=59%). This effect size (ES) represents a medium effect according to Cohen (1988)[10].

When pill counts were used to measure adherence, SMBP interventions were associated with significantly better adherence in four of eight studies (50%)[15,18,19,24]. Again adherence was generally high: proportion of available medication taken >97% (Hosseininasab), >88% (Bailey), >93% (McKenney); >85% (Fikri-Benbrahim), >87% (van Onzenoort). The pooled result of five studies detected a small significant ES in favour of the intervention (SMD 0.30, 95% CI 0.01 to 0.59), with moderate statistical heterogeneity (I^2=42%).

Of the six studies that used pharmacy fill data (i.e. medication possession ratio), none demonstrated a significant effect of SMBP interventions on medication adherence. A pooled estimate of two studies reflects this with no significant effect in favour of the intervention (SMD 0.12, 95% CI -0.05 to 0.29), with low statistical heterogeneity (I^2=0%).

SMBP interventions were associated with significantly better medication adherence in one of nine studies (11%) where self-reported measures were used [13]. A pooled estimate of four studies showed no significant effect in favour of the intervention (SMD 0.05, 95% CI -0.13 to 0.22), with low statistical heterogeneity (I^2=0%).

[insert Figure 3 here]

Medication persistence, diet, physical activity and smoking

Diet, physical activity and smoking outcomes are presented in Table 4. Medication persistence was assessed in one study [14]. No significant effect in favour of SMBP was found in the proportions not discontinuing their medication by the end of the trial (9 months). Similarly to the studies where medication adherence was measured, medication persistence was high (i.e. >83% of participants were still taking their medication at the end of the nine month study period).

Dietary outcomes were reported by eight studies [13,17,21,25,27-29,38]. Two studies investigated the effect of SMBP on the proportion of participants who reported food intake according to dietary guidelines, and reported no significant effect in favour of the intervention [13,21]. One study investigated the impact of SMBP on mean change from baseline in overall diet quality score and found a significant effect in favour of the intervention (+3.5 points on a 100 point composite scale, p<0.03)[28].

One study demonstrated the effect of a complex SMBP intervention on mean change from baseline in the average number of daily fruit and vegetables consumed, and found a significant effect in favour of the intervention, +2.3 daily servings, p<0.01[17]. SMBP was found to have no significant impact on coffee consumption [27].

Four studies reported alcohol consumption outcomes: three studies found no effect of interventions on mean change in daily alcohol consumption [27,29,38]; and one study reported no effect on mean change in alcohol consumption according to guidelines (i.e. <21 units/week for men, and <14 units per week for women) [25].

Physical activity was an outcome in six studies [13,17,25,27-29]. In two studies SMBP had no effect on the proportion of participants exercising more than three times a week [13,25]. Two studies used the proportion engaging in regular exercise as an outcome, which again was not significantly affected by the intervention [17,27]. Finally, two studies investigated the impact of SMBP on the mean change in energy expenditure in MJ/day: in one study there was no significant effect[29], and in the other there was a significant increase in favour of the intervention, mean difference +80MJ/day, p<0.05 [28].

Three studies investigated the impact of SMBP interventions on smoking status, however no significant effect was found in favour of SMBP interventions [13,25,27].

[insert Table 3 here]

Blood pressure

Twenty six trials reported BP outcomes. SMBP interventions had a significant effect on office systolic BP in six of twenty-three studies (26%)[11,15,22,26,33,34]. Pooled data for mean change in office systolic BP at six months are presented in Figure 4. Office systolic BP was significantly reduced in those who used SMBP; mean difference -4.07 mmHg (95% CI -6.71 to -1.43), with substantial statistical heterogeneity (I^2=67%). Full BP results are available in the supplementary material (Appendix 3,4 and 5).

[insert Figure 4 here]

Medication adherence and BP outcomes were both measured in twenty three studies (all but [21,25,27,29,36]. In the eight trials where SMBP had a significant effect on medication adherence [13,15,18,19,23,24,33,35], office systolic BP was measured in seven and office diastolic BP in all eight. Office systolic BP significantly improved in favour of the intervention in three of the seven studies where adherence was also significantly improved (28%) [15,33]; and office diastolic BP improved in three of the eight studies (38%) [15,23,33].

Office systolic BP significantly improved in three of fifteen studies (20%) where SMBP interventions had no effect on medication adherence [22,32,34]. Similarly, office diastolic BP was significantly improved in two of fourteen studies (14%) where SMBP had no effect on medication adherence [26,32].

DISCUSSION

This is the first review to include carry out pooled analysis of the effect of SMBP interventions on medication adherence. SMBP was shown to have a small but significant effect on medication adherence, SMD=0.21 (95%CI 0.08 to 0.34). Whilst the overall effect size is small, this could represent a significant effect on clinical outcomes and healthcare costs. A recent study estimated the reduction in healthcare costs that would be associated with increasing medication adherence in hypertensives in five European countries[40]. In England it was estimated that by increasing the proportion of patients adherent to treatment to 70% (i.e. 70% taking >80% of their medication),that €36 billion could be saved over ten years, representing 6,553 fewer cardiovascular events[40].

Studies using more objective measures of medication adherence showed a greater effect size in favour of intervention. The pooled estimate when electronic monitoring was used (SMD=0.45 (95%CI 0.10 to 0.79) is almost double the overall estimate, and approaching ten times larger than the estimate from studies where the least objective self-reported measures were used. It may be the case that self-reported medication adherence is under/over-reported equally across intervention and control groups due to randomisation, while more objective measures allow the true effect of the intervention to be estimated.

Only one study included evidence on medication persistence. Helping patients take their medication correctly on a day-to-day basis is important (adherence), but in conditions that require long term treatment such as hypertension making sure patients keep taking the medication over time (persistence) is of equal if not greater importance.

Evidence for the effect of SMBP on diet, physical activity and smoking was available in only nine studies, and where significant effects in favour of the intervention were found, they were not likely to be clinically significant. Overall, the quality of evidence of the impact of SMBP on lifestyle factors was poor. UK guidance for the management of hypertension recommends that lifestyle advice should be offered to all people undergoing treatment for hypertension. SMBP could potentially help hypertensives see the benefits of a healthier lifestyle, potentially delaying the need medication, and reducing the medication in those already on treatment.

The interventions tested were heterogeneous, with varying target, SMBP protocol, medication titration protocol and other co-interventions. Studies were often aimed at hypertensives, but also required the input of healthcare professionals to interpret the SMBP measurements and act accordingly (sometimes using trial specific protocols and sometimes according to usual care). Using complex interventions and targeting both patients and HCPs together complicate the investigation of the independent effect of SMBP on patient behaviour.

The theoretical basis for intervention development only reported in 4 studies (14%). As SMBP interventions target behaviour change in patients and/or HCPs, conceptual models are needed to provide a framework for the development of interventions. As it stands it is difficult to understand how many SMBP interventions have been developed, for example the justification for the frequency of self-measurement of BP and what patients/HCPs are expected to do with these readings.

CONCLUSIONS

Self-measurement of BP leads to an increase in medication adherence, and this effect is seen best in those studies where objective measures are used. Evidence for the effect of SMBP on lifestyle factor change and medication persistence is scarce.

Future trials should isolate patients or HCPs as the target of the SMBP intervention and use methods that allow for the potential incremental effects of co-interventions to be determined (i.e. factorial design). There needs to be more transparency in reporting the basis of the intervention development.

A better understanding of the mediators of the effect of self-measurement of blood pressure is needed, in order to optimise SMBP interventions to be tested in trials and translated into "real-world" use.

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Tables and figures

Supplementary material