Salt reduction to lower blood pressure in UK Bangladeshi patients with chronic kidney disease: A randomised controlled trial

INTRODUCTION

Chronic kidney disease (CKD) prevalence is three to five times higher in the Bangladeshi population compared to other ethnic groups in the UK.[1] Hypertension is both cause and consequence of CKD[2] and extracellular volume expansion is an important factor in the development and maintenance of hypertension in CKD patients.[3]The British Bangladeshi population has an unusually high salt intake, twice that of the general population, which might contribute to both CKD and hypertension.[4]Patients with resistant hypertension, defined as BP that remains above target despite the use of three or more antihypertensive medications[5], are thought to be salt sensitive.[6]

Meta-analyses of salt restriction studies show a greater blood pressure (BP) lowering effect of salt restriction in hypertensive compared with normotensive subjects; under optimal conditions reductions in systolic/diastolic BP of 7/4 mm Hg[7] can be obtained with salt intake reduced to 100 mmol/day. However, adherence to dietary advice is often poor resulting in smaller changes (<1mm Hg) in blood pressure of dubious clinical value. In previous work we investigated barriers to dietary salt restriction in Bangladeshi CKD patients in East London[8] and developed a strategy intended to reduce salt intake in these patients. This present study set out to test the hypothesis that a low-salt educational intervention tailored to meet the needs, customs and practices of this population in addition to standard hypertension medication management would result in greater blood pressure reduction than standard care alone: a first such intervention with this population group.

METHODS

A parallel-group randomised trial design was selected, and conducted between June 2008 and July 2009. Ethical approval was obtained from the relevant Research Ethics Committee. Participants were patients with established moderate-severe CKD of Bangladeshi origin residing in East London, UK. Inclusion criteria were estimated glomerular filtration rate (eGFR) <60ml/min and mean BP >130/80mmHg on at least two clinic visits or taking antihypertensive medication. Patients on dialysis, those with a body mass index (BMI) <20 or >35 kg/m^2, urinary incontinence, or cognitive impairment or mental problems impairing their ability to participate were excluded.

Participants were recruited at the pre-dialysis clinic of a tertiary renal unit in London by the researcher. Participants were randomly assigned to the salt reduction intervention or usual care by the study statistician. Randomisation was by computer-generated random blocks with block sizes between four and eight to minimise selection bias. This was carried out by the statistician and the final list with group assignment given to the researcher. This was a dietary behaviour intervention, thus, neither participants nor the dietitian administering the intervention could be blinded to treatment allocation. Data analysis was conducted by the research statistician that was blinded to treatment allocation.

Intervention

The intervention group were initially advised by the study dietitian at the hospital. This was followed by practical cooking and educational sessions in the community facilitated by Bengali workers and attended by the researcher (see supplementary file). Community cooking sessions were delivered in conjunction with Community Kitchen UK (CKUK).[9] In the community sessions, intervention participants cooked two versions of their traditional meals: one followed their usual recipe, the other had salt reduced by 50%. Fortnightly telephone calls from a Bengali worker followed, to reinforce advice and set new targets. The control group received usual care from the renal clinic in the form of a low sodium general dietary advice sheet sent by post with the physician's letter. This had not been specifically adapted for Bangladeshi diets.

Data collection

Data collected at enrolment included age, sex, medication use and co-morbidities, including diabetes mellitus. Data collection for the primary outcome was by ambulatory blood pressure measured using TM-2430-13 devices (A&D Medical, Milpitas, CA; graded A/A by the British Hypertension Society) and Doctor Pro software, in accordance with recommendations[10] day time measurements were taken at 30 min intervals, night time measurements every 60 min. Height, weight and body composition (total body water) were measured using the Fresenius Medical Care D GmbH Body Composition Monitor; blood samples were obtained for glycosylated haemoglobin (HbA1c). Physical activity levels were recorded using the YamaxDigi-Walker SW-200 (Yamax Corporation, Tokyo, Japan) pedometer, shown to have an overall mean absolute error of 3% for outdoor normal walking.[11] The accuracy of the pedometer on each participant was checked by a 20 step test at the outset, with an acceptance criterion of +/-2 steps.[11]Data were collected at two time points, at baseline and at end of study – six months later.

Outcomes

The primary outcome was reduction in systolic blood pressure (SBP) determined by 24hr ambulatory monitoring.
Secondary outcomes were changes in diastolic blood pressure and reduction in estimated glomerular filtration rate (e-GFR).
Measures of 24hr urinary sodium, potassium and creatinine were undertaken using routine methods at baseline and follow-up as indices of adherence to the intervention and determined by assessors blinded to treatment allocation.

Statistical analysis

Sample size calculation showed that a sample of 25 participants per group would convey 80% power to detect a significant reduction in the mean systolic BP of 8 mmHg at $P<0.05$ between the two groups (a clinically relevant difference), assuming a standard deviation of 10 mmHg.[12] Sample size was increased to 26 per group to allow for non-compliance or dropout. Analyses were conducted on an intention to treat basis. We took a P value of 0.05 to be significant.

Changes within groups between baseline and follow-up at 6 months were compared using analysis of covariance and expressed as mean values with 95% confidence intervals. All reported P values were two sided. We used Stata 10 (StataCorp LP, Texas, USA) for data analysis.

RESULTS

Participant recruitment and progress through the trial is shown in Figure 1**.** Of the 56 participants recruited 6 withdrew; 3 cited the inconvenience of 24hr urine collection, 2 were unwilling to undergo ambulatory blood pressure monitoring and one was unwilling to attend the community cooking activity. One intervention group participant died; one control group member relocated to Bangladesh. Data were available for 48 participants. Details are shown in Table 1; groups were well matched including for antihypertensive medication, with most receiving angiotensin converting enzyme inhibitor or angiotensin-receptor blocking medicines and diuretics.

Adherence to the dietary intervention

All participants attended the initial briefing session with the study dietitian. Male participants attended with their wives, daughters or sisters whilst female participants attended with their daughters or daughters-in-law. Participants were split into four groups of six or seven to attend the community cooking sessions; each group were to attend two weekly consecutive sessions. Male participants chose not to attend but sent a female representative; a wife, daughter or sister for single men. The first weekly session was attended by 88% (23/25) of the participants or representatives; the second and final session was attended by 84% (21/25). Overall, all participants attended at least one cooking session.
Adherence to dietary salt recommendations was indicated by urinary sodium excretion. At baseline urinary sodium excretion was approximately 260 mmol/24hr in both groups (Figure 2). Six months later, this had reduced by 122 mmol/24hr (95% CI -140.4,-104.9; P<0.001) in the intervention group, and by 13 mmol/24hrs (95% CI -17.7, -8.2; *P*<0.001) in the control group. At follow-up sodium excretion differed significantly between groups, by 103 mmol (95% CI -131,-76; P<0.001).

Primary and secondary outcomes:

Systolic BP was elevated in both groups at baseline. Comparing changes from baseline to follow up in mean 24hr SBP in both groups, reductions in intervention group values were significantly greater, at 8 (95% CI 5,11; P=0.0003) mm Hg lower. The intervention group showed significant (*P*<0.001) falls in day time and night systolic and diastolic BP compared to the same variables in the control group (Figure 3). Non-dipping, that is loss of the normal nocturnal reduction in night-time systolic blood pressure, with a difference >10 mmHg between night and day time SBP, was observed in 60% (15/25) of the intervention group, 56% (13/23) of the control group at baseline. At follow up this reduced by 40% (6/25; P= 0.02) in the intervention group but remained unchanged in the control group.

There were no differences between groups in changes in eGFR between baseline and follow-up. Kidney function declined by 3.0 (95% C 0.1,6.0) in the intervention compared to 3.4 (95% CI 1.0,5.7) ml/min.1.73m^2 in the control groups.

Table 1. Baseline characteristics for the Intervention and Control groups

	Control (n=23)		Intervention (n=25)	
	Mean	SD	Mean	SD
Age (years)	60.7	12.0	55.7	15.1
Male:female (numbers)	14:9		14:11	
Mean 24 hr systolic BP mmHg	156.0	10.7	149.3	15.2
Mean 24 hr diastolic BP mmHg	85	5.8	85	6.3
Diabetes (%)	14	(60)	17	68
Glycosylated Hb (%)	8.6	1.8	8.9	1.9
GFR ml/min/1.73m^2	42	15.3	41	17.2
Urinary sodium mmol/24hr	259	47.1	263	54.0
Urinary Potassium mmol/24hr	39	6.9	43	4.0
Urinary creatinine mmol/24hr	11.15	1.9	10.75	1.3
Number BP medication/patient[1]	3	(2,4)	3	(2,4)
Total body water (kg)	33.1	5.9	33.4	5.2
BMI (kg/cm^2)	27.1	5.2	26.6	5.4
Physical activity (steps/day)1	2,534	1,101	2,471	1,419

[1]Median with interquartile range

GFR - Glomerular filtration rate, BMI-body mass index. No statistical significant differences between the two groups

Covariate findings

Potassium excretion was low (40 mmol/d) in both groups and unchanged at follow-up. Physical activity levels were low in both groups and remained unchanged during the study. Glycosylated haemoglobin concentrations remained elevated at >8.0%, indicating poor but unchanging diabetic control in both groups. Body weight did not change in either group, but there was a modest but statistically significant reduction in mean total body water in the intervention group (0.50L, P<0.01) compared to no change in the control group (0.26L, n.s.).

DISCUSSION

Dietary advice to lower salt intake is routinely given to patients with CKD in the form of an information sheet; this study suggests this is ineffective at changing behaviour. By contrast, the dietitian-led intervention which identified the sources of salt in the Bangladeshi diet and developed strategies to lower intake, achieved a reduction in dietary salt intake of over 100 mmol/d. Whilst mean urinary sodium excretion still remained well above the UK target of 100 mmol/day,[13] post-intervention group results were more similar to those seen in the UK white population. This reduction in salt intake led to a highly significant fall in blood pressure of 8/3 mmHg; very close to the figure predicted by meta-analyses.[7]

The dietary approach used has also been shown to be effective in blood pressure reduction with other ethnic groups with high dietary salt intakes.[14] Behavioural intervention studies have previously demonstrated that knowledge is a key contributing factor to adherence to low-salt diet[12] and that lack of knowledge is a key barrier in dietary modification and adherence.[15, 16] However, knowledge of the need to reduce dietary salt intake is not always enough to ensure dietary modification and adherence. This study shows that knowledge tailored to recipients' needs and contexts, delivered in a practical and acceptable manner, can effect behavioural change and achieve health benefits.

Our previous studies showed that Bangladeshi CKD patients have much higher intakes of salt than the general population, with much of the salt being added during home preparation of food rather than during processing, as is the case in the general population. Consequently, routine advice for salt reduction designed for predominantly white European populations was not appropriate for this group of patients, for whom the engagement of family members was crucial. This was particularly relevant for these study participants, who almost exclusively ate home-prepared meals in family groups.

We noted that over half of the Bangladeshi CKD patients had raised BP throughout the day and night: the 'non-dipping' effect. Previously 'non-dipping' prevalence has been found to increase with worsening CKD, with 15% of normal subjects affected increasing to 75% in those with stage 5 CKD.[17] Non-dipping has been associated with increased target-organ damage (heart, brain, kidney[18-20]), raised frequency of stroke and myocardial infarction,[21] and higher cardiovascular mortality.[20] Decreased salt intake and urinary sodium excretion led to greater reduction in night time SBP compared to daytime, and the restoration of the normal physiological night-time dip in blood pressure in many patients. In black salt-sensitive hypertensive patients salt restriction improved the circadian rhythm of blood pressure with a return to dipping pattern.[22] Our study confirmed that salt reduction can change the pattern from 'non-dipper' to 'dipper', and a recent review has concluded that the South Asian population are

salt sensitive.[23] A return to a 'dipping' BP pattern may lead to a significant reduction in the risk of vascular events for this patient group but long-term follow up is required to demonstrate this.

Comparison with other studies

Data supporting our findings were reported by MacGregor et al,[24] who demonstrated that when urinary sodium excretion dropped by 100mmol/24hr, subjects supine BP declined by 8/5 mm Hg ($P<0.01$); a sodium reduction of 150mmol/24hr led to a larger decline of 16/9mm Hg. Similarly, a modest salt reduction of 50 mmol/24hr (from a much lower baseline than in our participants: an average of 177 mmol/24hr) resulted in 7/3 mm Hg drop in blood pressure in a randomised trial in older people.[25] A recent meta-analysis of 17 trials in hypertensive individuals over ≥4 weeks supports the approximate magnitude of this effect.[7] A recent study of modest dietary sodium restriction in patients receiving angiotensin converting enzyme medicines showed an 11mm Hg reduction in SBP in non-diabetic nephropathy.[26] Our study confirms this magnitude of association between reduction in sodium excretion and blood pressure values.

Strengths and limitations

The strength of this study is that it delivered an effective salt reduction dietary intervention for this group of patients, and demonstrated participants' adherence to dietary advice through 24hr urinary sodium excretion. However, only single 24hr urine collections and 24hr ambulatory blood pressure recordings were made. Further, treatment allocation could not be blinded. It remains uncertain whether reducing blood pressure may translate into slowing of disease progression or reduction in cardiovascular events.

Applicability and generalizability

The Bangladeshi population and indeed the South Asian group are known for a high dietary salt intake, are at a high risk of CKD and thus, hypertension development. Dietary salt reduction can safely and usefully be extended to other family members who may in time also be at risk of developing hypertension. Other ethnic groups with a high prevalence of CKD and hypertension, such as Black African and Afro-Caribbean populations, may also benefit from tailored dietary interventions to reduce salt intake.

CONCLUSION

This study demonstrates the importance of tailoring dietary advice to patients' contexts, cultures and needs, particularly for minority and high-risk groups. Healthcare professionals need education and training in methods to enable them to translate generic principles of healthy living and health promotion in such a way as to successfully deliver education and promote its application in the daily lives of their patients. Policy-makers need to recognise the importance of resourcing complementary approaches to medication for effective blood pressure control. An

integrated approach, drawing on multiple successful approaches to hypertension reduction, offers the best option for blood pressure management in CKD patients.

Legends

Figure 1: CONSORT flowchart of participant recruitment, allocation and assessment

Figure 2. 24hr urine sodium excretion for intervention and control groups at baseline and end study

Figure 3. Changes in mean blood pressure between baseline and end study for intervention and control groups

List of abbreviations

CKD: Chronic kidney disease; BP: Blood pressure; eGFR: Estimated glomerular filtration rate; BMI: Body mass index; SBP: Systolic blood pressure; DBP: diastolic blood pressure; CI: Confidence Interval

Contributorship

IdeBA, researcher, designed the study and data collection tools, conducted educational intervention, collected data for whole trial, drafted and revised the paper. MV, statistician, wrote the statistical analysis plan, analysed the data, drafted and revised paper. MMY, LP, HD, TABS & JET – were supervisors. The supervisors contributed to the design of study and data collection tools, monitored data collection for whole trial, drafted and revised paper.

Data sharing

The original article was prepared from a database established by the corresponding author and it is accessible to all listed authors. This data remain the intellectual property of Barts and The London NHS Trust, but confidential data sharing agreements may be entered to address any questions in relation to the trial. All data relevant to this author is presented here.

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Competing interests

All authors declare that for this submitted work: IdeBA received salary support from a grant made to Barts and The London NHS Trust by the trustees of Barts and The London Charitable Foundation; no other financial support was received from any organisation for the submitted work; no financial relationships with any organisations might have an interest in the submitted work in the previous three years, no other relationships or activities influenced the submitted work.

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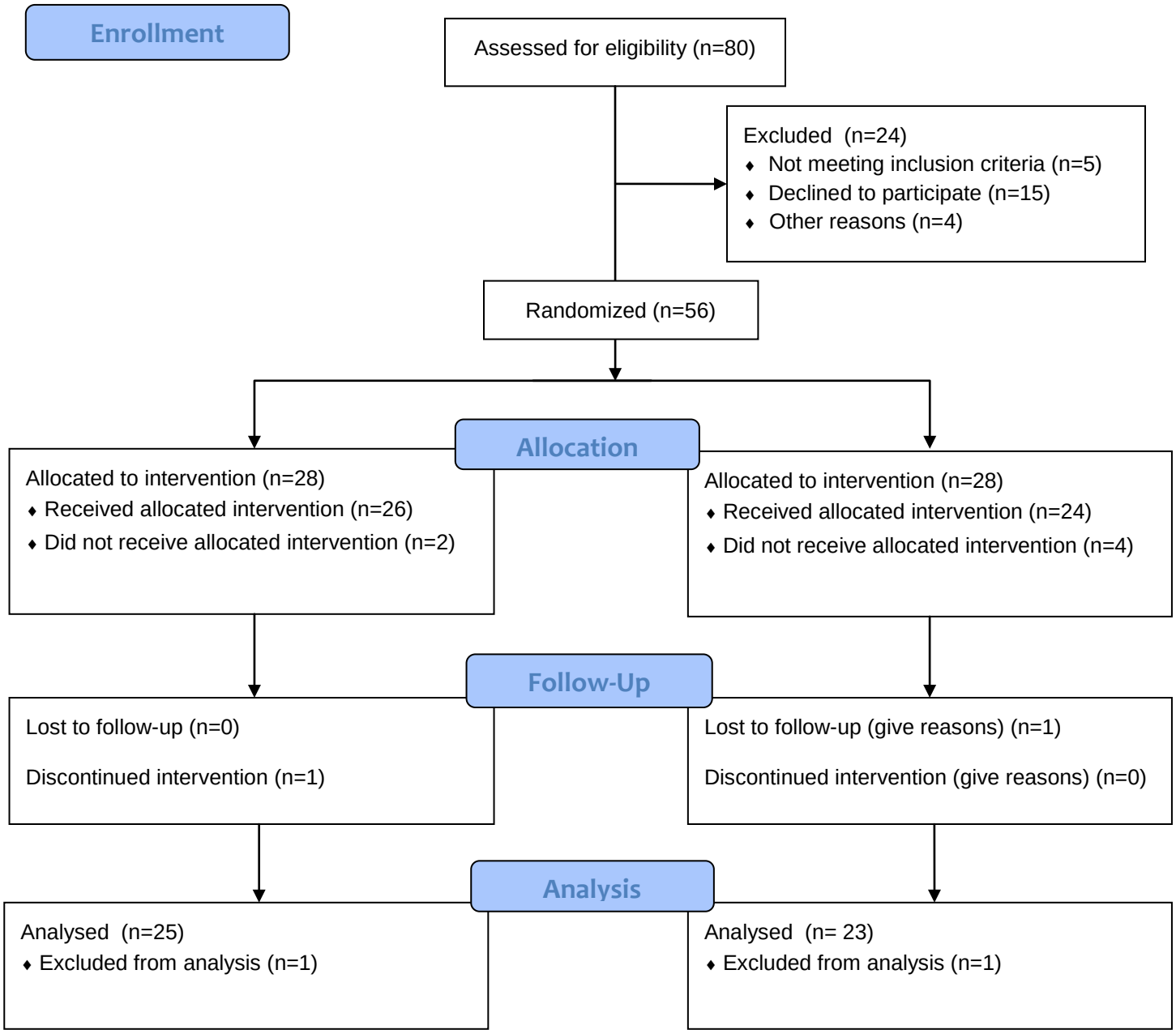
Patient allocation and evaluation



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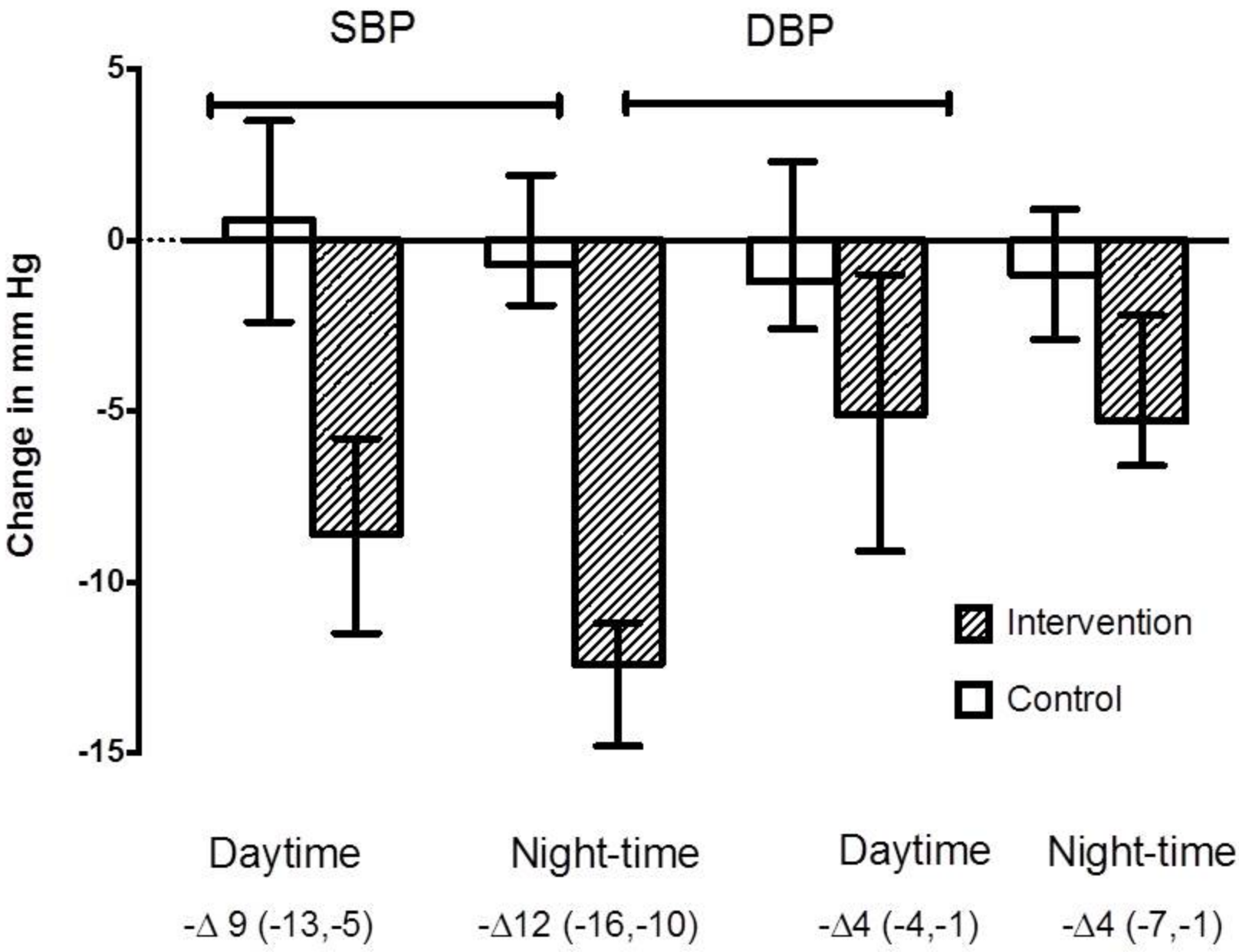
SBP
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Change in mm Hg
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-Δ4 (-4,-1)
-Δ4 (-7,-1)