

Effects of low sodium intake on the anti-proteinuric efficacy of olmesartan in hypertensive patients with albuminuria (ESPECIAL)

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ABSTRACT

Background: Blockade of the renin angiotensin aldosterone system (RAAS) reduces albumin excretion rate. The antiproteinuric effect of RAAS blockade can be magnified by dietary salt restriction. We tried to determine the effect of low salt diet in non-diabetic hypertensive patients with albuminuria on blood pressure and urine protein excretion.

Methods: This study is an open-label randomized controlled trial. After a run-in period of eight weeks, patients received angiotensin-II receptor blocker (ARB) olmesartan, 40 mg daily. And then, patients were divided into two groups. One group was treated for another eight weeks with Olmesartan plus conventional low-salt diet (LSD) education and the other group was treated for eight weeks with Olmesartan plus weekly intensive education on LSD. A total of 269 adult recipients were enrolled, and we performed the final analyses with 235 completed patients.

Results: The amount of daily albuminuria was significantly decreased with 8 weeks of ARB treatment (930.0 ± 969.2 mg/day vs. 515.7 ± 685.5 mg/day; p<0.001). Twenty-four-hour urinary sodium excretion was decreased by 34.8 mmol/day in the intensive education group and 9 mmol/day in the conventional education group. Patients who completed intensive LSD education exhibited greater decreases in urinary albumin excretion than the control group (Δalbuminuria, 154.4 mg/day vs. 2.6 mg/day; p=0.02). The proportion of patients with a greater than 25% reduction in albuminuria was higher in the intensive LSD education group (60.9% vs. 39.2%; p=0.001). Urinary albumin excretion tended to decrease as the 24 h urinary sodium excretion amount decreased.

Conclusion: The reduction in salt intake induced by intensive LSD education effectively reduced urine albumin excretion in RAAS blockade-treated patients with hypertension. Weekly intensive education for LSD would be a suitable method for clinical practice.

BACKGROUND

- CKD is a potent risk factor of end-stage renal disease (ESRD), cardiovascular disease (CVD), all cause & cardiovascular mortality and hospitalization Go AS et al. N Engl J Med 2004;351:1296-1305
- Blockade of the renin-angiotensin- aldosterone system (RAAS) is well known to reduce albumin excretion rate and considered a mainstay of therapy in the prevention of ESRD. The antiproteinuric effect of RAAS blockade can be magnified by dietary salt restriction. Slagman MC et al. BMJ 2011;343:d4366
- Koreans are heavy consumers of sodium; with a dietary sodium level of 4790.7 mg/day, the country leads all other nations in terms of daily sodium intake Korea Health Statistics 2011 - Korea National Health and Nutrition Examination Survey (KNHANES V-2)
- Several studies have shown an added effect of dietary salt restriction with RAAS blockade on blood pressure and proteinuria but most of the studies were proceeded with a small number of patients and the methods of low-salt diet (LSD) were not suitable to apply to clinical practice.

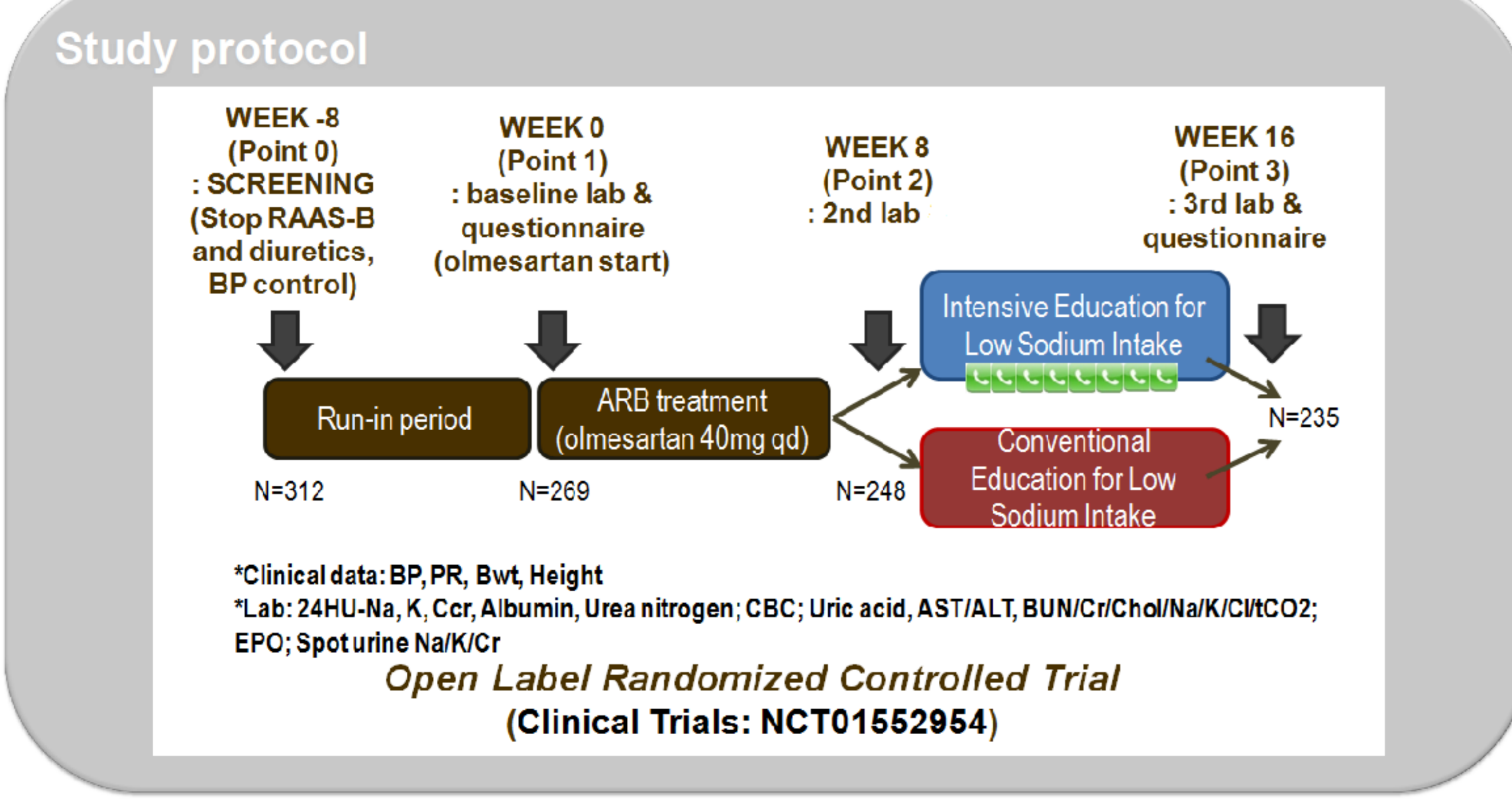
PURPOSE

- To determine the effect of low salt diet in patients who is taking RAAS blockade (olmesartan) on
 - Urine Protein Excretion
 - Blood Pressure
- To determine the effect of interventions with regular reinforcement for low salt diet (weekly 30 minutes phone call education)

METHODS

- ### Inclusion criteria
- Age of 19–75 years
 - The use of antihypertensive medication or a diagnosis of hypertension
 - Modification of Diet in Renal Disease Study (MDRD) estimated GFR (eGFR) ≥ 30 mL/min/1.73 m²
 - Random urine albumin/creatinine (Cr) ratio ≥ 30 mg/gCr more than twice with ≥ 1-week interval in the last 6 months
 - An ability and willingness to provide written informed consent.

- ### Exclusion criteria
- Patients with uncontrolled hypertension (BP > 160/110 mm Hg) at the time of screening
 - Pregnant women
 - Patients with serum potassium > 5.5 mmol/L, a malignancy, a diagnosis of cardiovascular disease (cerebral infarction, hemorrhagic infarction, acute myocardial infarction or unstable angina, coronary angioplasty, or coronary artery bypass surgery) within the last 6 months
 - Contraindication for angiotensin II receptor blockers (ARBs)
 - Diabetes mellitus
 - Continuous users of steroids, nonsteroidal anti-inflammatory drugs, or other immunosuppressive agents at the time of registration.

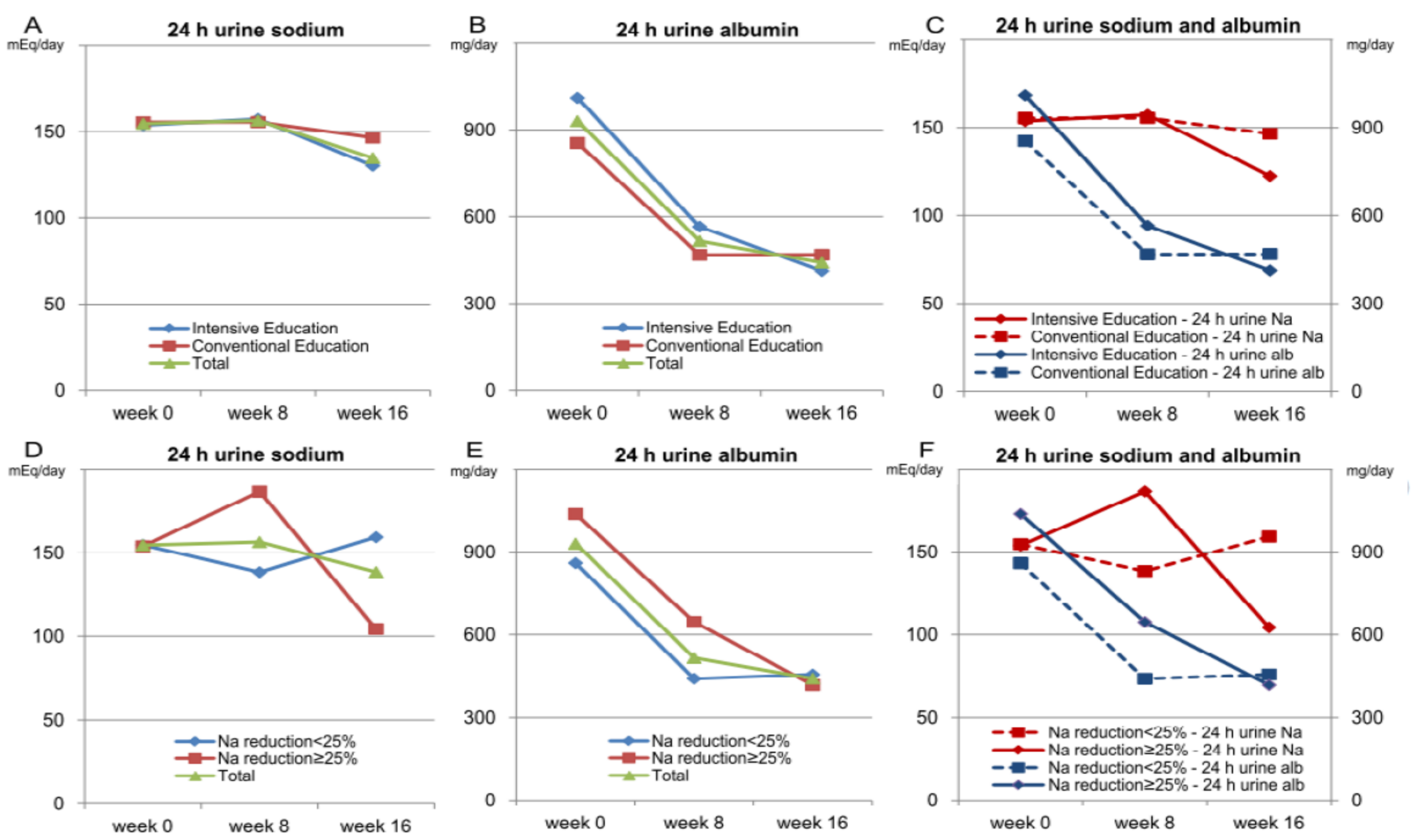


RESULT

Baseline characteristics and parameters

	Intensive Education (n=115)	Conventional Education (n=120)	Total (n=235)	p value
Characteristics				
Age	48.5 (12.1)	51.5 (13.9)	50.0 (13.1)	0.075
Male	55 (47.8%)	62 (51.7%)	117 (49.8%)	0.603
Weight (kg)	68.4 (13.6)	67.6 (13.3)	68.0 (13.4)	0.618
Height (cm)	163.8 (8.8)	162.9 (9.0)	163.4 (8.8)	0.442
Systolic BP (mm Hg)	130.9 (11.1)	131.0 (12.6)	130.9 (11.9)	0.951
Diastolic BP (mm Hg)	79.7 (8.2)	79.0 (10.0)	79.3 (9.1)	0.603
Pulse Rate (bpm)	77.3 (11.4)	76.9 (12.5)	77.1 (11.9)	0.799
Menopause in Women	33 (45.2%)	35 (53.8%)	68 (49.3%)	0.394
Blood measurements				
WBC (x/mm ³)	6506.7 (1676.3)	6306.8 (1814.5)	6404.6 (1747.4)	0.374
Hemoglobin (g/L)	140 (18)	138 (17)	139 (17)	0.304
Hematocrit	41.2 (4.7)	40.5 (4.4)	40.9 (4.6)	0.289
Platelet (x1000/mm ³)	243.4 (58.8)	235.2 (60.4)	239.2 (59.7)	0.282
BUN (mmol/L)	5.85 (2.25)	6.46 (2.25)	6.18 (2.25)	0.04
Creatinine (μmol/L)	99.01 (34.48)	104.31 (37.13)	101.66 (36.24)	0.276
eGFR (mL/min/1.73 m ²)	68.5 (23.3)	65.4 (24.8)	66.9 (24.1)	0.356
Cholesterol (mmol/L)	4.77 (0.91)	4.73 (0.93)	4.75 (0.92)	0.737
Uric acid (μmol/L)	374.8 (107.1)	380.7 (107.1)	374.8 (107.1)	0.493
AST (μkat/L)	0.41 (0.25)	0.39 (0.13)	0.4 (0.2)	0.445
ALT (μkat/L)	0.43 (0.32)	0.4 (0.24)	0.41 (0.28)	0.464
Na+ (mmol/L)	140.7 (2.2)	140.6 (2.1)	140.7 (2.2)	0.718
K+ (mmol/L)	4.3 (0.4)	4.3 (0.4)	4.3 (0.4)	0.457
Cl- (mmol/L)	104.4 (2.6)	103.8 (4.7)	104.1 (3.8)	0.257
tCO ₂ (mmol/L)	26.5 (2.8)	26.4 (2.7)	26.4 (2.8)	0.795
Urine Measurements				
Random Urine Na+ (mmol/L)	90.9 (42.9)	85.6 (41.4)	88.2 (42.1)	0.352
24 h Urine Na+ (mmol/day)	153.7 (69.1)	155.4 (71.7)	154.6 (70.3)	0.823
Random Urine K+ (mmol/L)	56.6 (27.4)	57.7 (31.8)	57.2 (29.7)	0.825
24 h Urine K+ (mmol/day)	53.5 (21.4)	56.0 (22.5)	54.8 (22.0)	0.36
Random Urine Cr (mg/dL)	139.6 (91.5)	126.3 (72.5)	132.8 (82.5)	0.237
24 h Urine Cr (mg/day)	1225.4 (415.0)	1272.3 (668.7)	1249.5 (559.0)	0.438
Albumin/Cr ratio (mg/g Cr)	682.1 (995.5)	647.6 (899.8)	664.5 (855.6)	0.745
24 h Urine Albumin (mg/day)	1010.1 (1056.3)	854.5 (877.1)	930.0 (969.2)	0.242
Creatinine Clearance (mL/min)	82.1 (31.3)	78.7 (34.8)	80.4 (33.1)	0.605
Comorbidities				
HTN	115 (100.0%)	120 (100.0%)	235 (100.0%)	1.000
Dyslipidemia	64 (56.6%)	68 (60.7%)	132 (58.7%)	0.589
Angina	0 (0.0%)	1 (0.8%)	1 (0.4%)	0.368
Stroke	2 (1.7%)	4 (3.3%)	6 (2.6%)	0.684

Changes in 24 h urine sodium and albumin excretions by group



A–C: Change in the mean 24 h urine sodium and albumin excretion amounts by group
 D–F: Change in the mean 24 h urine sodium and albumin excretion amounts according to the extent of 24 h urine sodium amount reduction between the 8th and 16th weeks

Changes in Variables According to the Randomised Groups

	Week 0	Week 8	Week 16	p value (0–8)	p value (8–16)	p value (0–16)
24 h Urine Na+ (mmol/day)						
Intensive Education	153.7 (69.1)	157.3 (74.9)	122.5 (60.4)	0.577	<0.001	<0.001
Conventional Education	155.4 (71.7)	155.5 (72.4)	146.5 (66.9)	0.987	0.062	0.149
Total	154.6 (70.3)	156.4 (73.5)	134.7 (64.8)	0.667	<0.001	<0.001
p value	0.853	0.857	0.005	-	-	-
24 h Urine Albumin (mg/day)						
Intensive Education	1010.1 (1056.3)	565.5 (727.5)	412.7 (602.7)	<0.001	0.001	<0.001
Conventional Education	854.5 (877.1)	467.9 (642.1)	468.7 (686.7)	<0.001	0.942	<0.001
Total	930.0 (969.2)	515.7 (685.5)	441.2 (646.0)	<0.001	0.009	<0.001
p value	0.221	0.276	0.51	-	-	-

Conclusion

- LSD effectively reduced proteinuria in nondiabetic hypertensive patients who received ARB therapy.
- Feedback and education by telephone for 30 minutes weekly would be a suitable method for educating LSD in actual clinical practice.