

The effect of cilnidipine on intradialytic blood pressure in intradialytic hypertensive patients: A multicenter, prospective randomized open-label study

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Background

- Intradialytic hypertension (HTN) is one of the poor prognostic markers in hemodialysis (HD) patients and may be associated with sympathetic overactivity.
Kidney Int 2007;71:454-461
Kidney Int 2009;76:1098-1107
Am J Kidney Dis 2009;54:881-890
- L/N-type calcium channel blocker cilnidipine was reported to suppress sympathetic nerves activity *in vivo*.
Clin Exp Hypertens 2009;31:241-249

Purpose

To clarify cilnidipine attenuate intradialytic systolic blood pressure (SBP) elevation through the suppression of sympathetic nerves activity in intradialytic HTN patients.

Participants

- Fifty-one chronic hemodialysis patients with intradialytic HTN (SBP elevation > 10mmHg during HD) and proper fluid volume
- Exclusion criteria
 - Pre HD SBP < 120mmHg, Post HD SBP < 130 mmHg
 - Severe heart failure, recent myocardial infarction, severe valvular heart disease, active malignancy disease, atrial flutter/fibrillation, ventricular arrhythmia, signs of infection

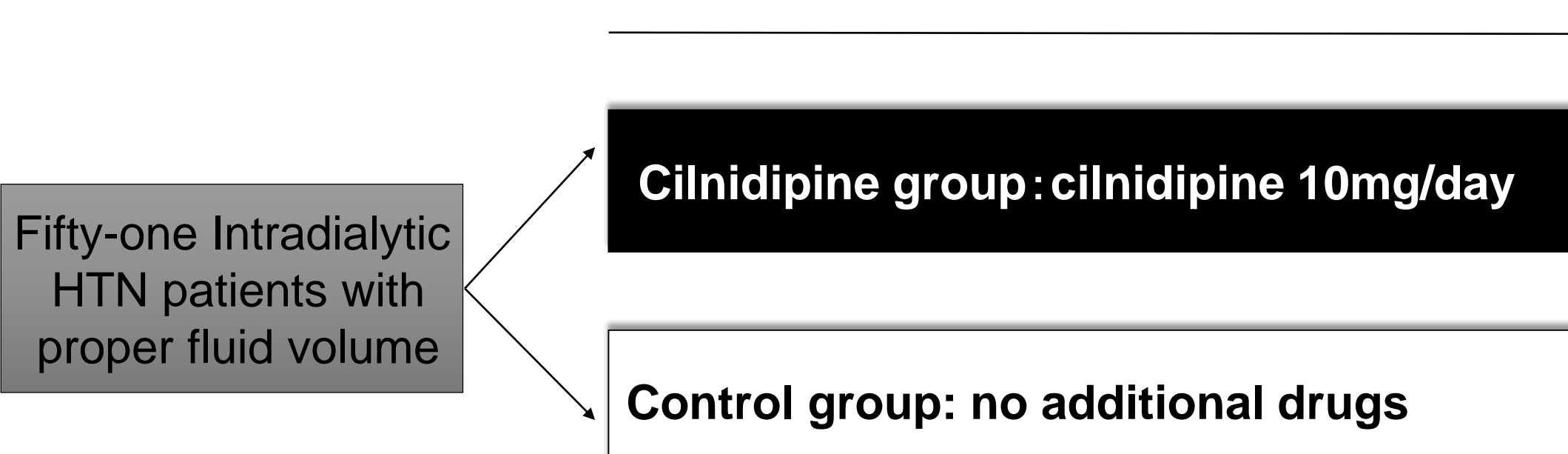
Intradialytic HTN with proper fluid volume

- SBP >10mmHg elevation from pre- to post-HD
- CTR < 55% or hANP < 200pg/ml at post-HD
- No use of vasopressor

Methods

- A total of 749 patients were screened in 3 HD center, and 51 of those patients were randomly assigned in a 2:1 fashion to a cilnidipine or a control group and tracked for 12 weeks.
- Cilnidipine group: taking cilnidipine 10mg /day for 12 weeks.
- Control group: continue taking the same drugs
- Primary endpoint: the change in intradialytic SBP elevation from the baseline to the 12th week.
- Secondary endpoint: changes in humoral factors; norepinephrine, epinephrine, PRA, and PAC.

baseline → 12weeks

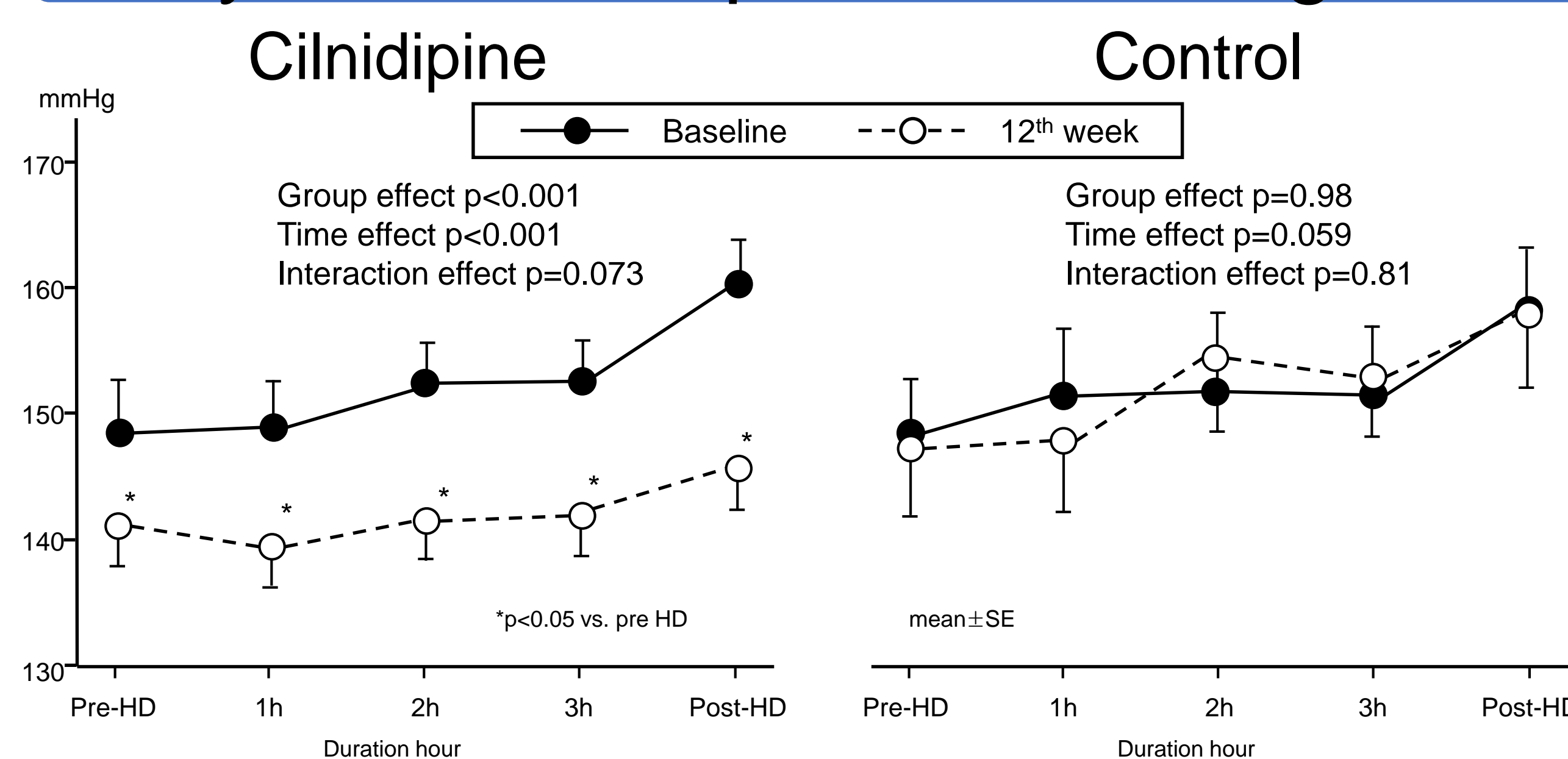


Result

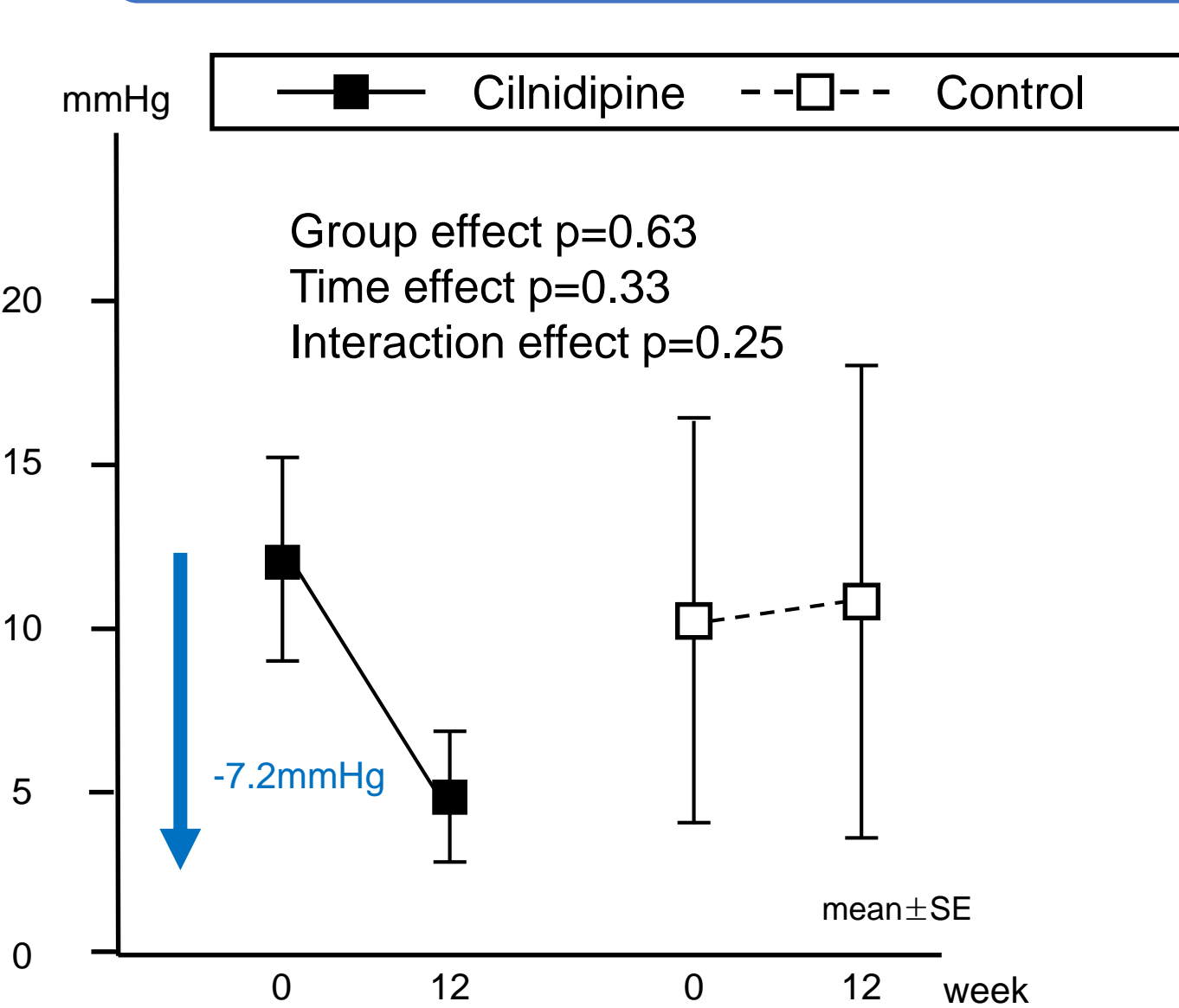
Table. Patient baseline characteristics

	Cilnidipine	Control	p
n	25	11	
Men, n (%)	16 (64.0%)	7 (63.6%)	0.68
Age (years)	69 ± 10	75 ± 9	0.10
Dialysis history (months)	87 ± 63	80 ± 54	0.76
Dialysis time (hours)	4.0 ± 0.4	3.9 ± 0.5	0.16
Pre HD SBP (mmHg)	148.3 ± 19.3	148.4 ± 12.9	0.99
Post HD SBP (mmHg)	160.3 ± 15.5	158.5 ± 15.0	0.75
ΔSBP (mmHg)	12.0 ± 15.4	10.1 ± 20.1	0.79
Kt/V	1.52 ± 0.22	1.39 ± 0.21	0.10
Access, n (%)			
AVF	24 (96.0%)	9 (100%)	0.33
AVG	1 (4.0%)	0	0.33
Medication, n (%)			
ACEI/ARB	18 (72.0%)	10 (90.9%)	0.15
CCB	21 (84.0%)	9 (81.8%)	0.88
Alpha-blockers	6 (24.0%)	0	0.01
Beta-blockers	6 (24.0%)	1 (9.1%)	0.25
Diuretics	8 (32.0%)	4 (36.4%)	0.81
Statin	8 (32.0%)	4 (36.4%)	0.81
ESA	21 (84.0%)	10 (90.9%)	0.56
Comorbidity, n (%)			
Diabetes mellitus	12 (48.0%)	8 (72.7%)	0.17
History of CVD	4 (16.0%)	3 (27.3%)	0.49
Stroke	1 (4.0%)	1 (9.1%)	0.62
Hemoglobin (g/dl)	11.0 ± 1.1	11.0 ± 1.4	0.92
Albumin (g/dl)	3.8 ± 0.3	3.9 ± 0.3	0.59
Urea nitrogen (mg/dl)	65.9 ± 17.2	66.6 ± 12.3	0.90
Creatinine (mg/dl)	10.6 ± 2.7	9.8 ± 1.7	0.31
Sodium (mEq/l)	138.8 ± 2.9	137.8 ± 3.9	0.45
Potassium (mEq/l)	4.9 ± 0.9	4.9 ± 0.8	0.94
Calcium (mg/dl)	9.0 ± 0.8	8.8 ± 0.6	0.37
Phosphate (mg/dl)	5.8 ± 2.1	5.2 ± 0.8	0.21
Total cholesterol (mg/dl)	150.3 ± 31.5	157.7 ± 44.6	0.62
Triglyceride (mg/dl)	86.1 ± 30.7	98.7 ± 56.5	0.50
Glycoalbumin (%)	17.4 ± 3.6	19.4 ± 6.3	0.36
Cardiothoracic ratio (%)	50.2 ± 4.3	49.9 ± 3.8	0.84
Brain natriuretic peptide (pg/ml)	218.6 ± 188.0	171.6 ± 122.2	0.96
Atrial natriuretic peptide (pg/ml)	78.7 ± 44.4	74 ± 52.5	0.42
Plasma renin activity (ng/ml/h)	2.3 ± 2.6	2.0 ± 2.2	0.31
Plasma aldosterone concentration (pg/ml)	90.6 ± 109.4	62.2 ± 20.6	0.18
Noradrenaline (ng/ml)	414.4 ± 200.4	467.9 ± 137.7	0.99
Adrenaline (ng/ml)	41.6 ± 26.0	54.4 ± 39.4	0.39
Dopamine (ng/ml)	17.4 ± 12.9	26.0 ± 16.2	0.22
Intact parathyroid hormone (pg/ml)	122.3 ± 73.9	162.9 ± 64.3	0.053

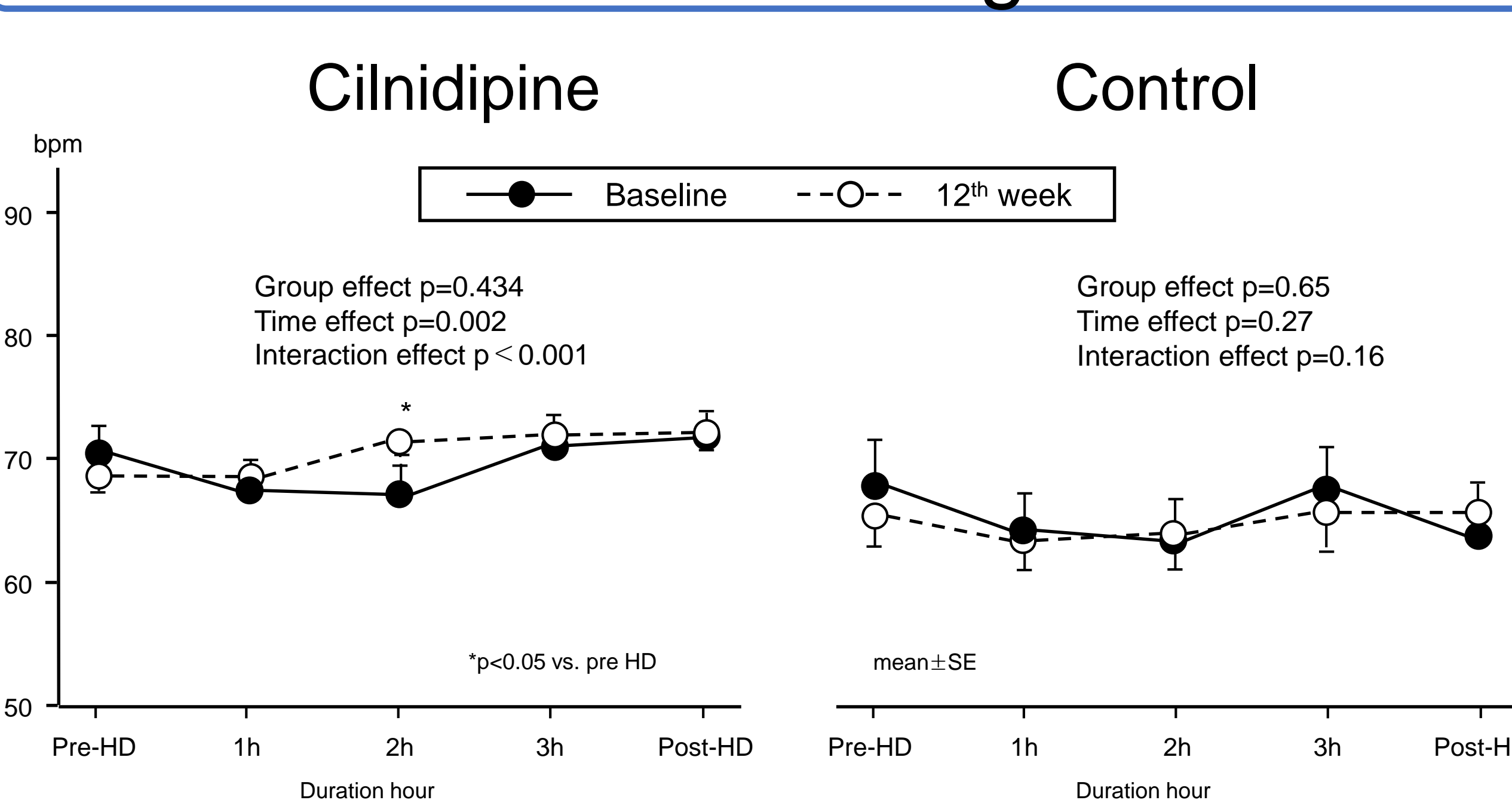
Systolic blood pressure during HD



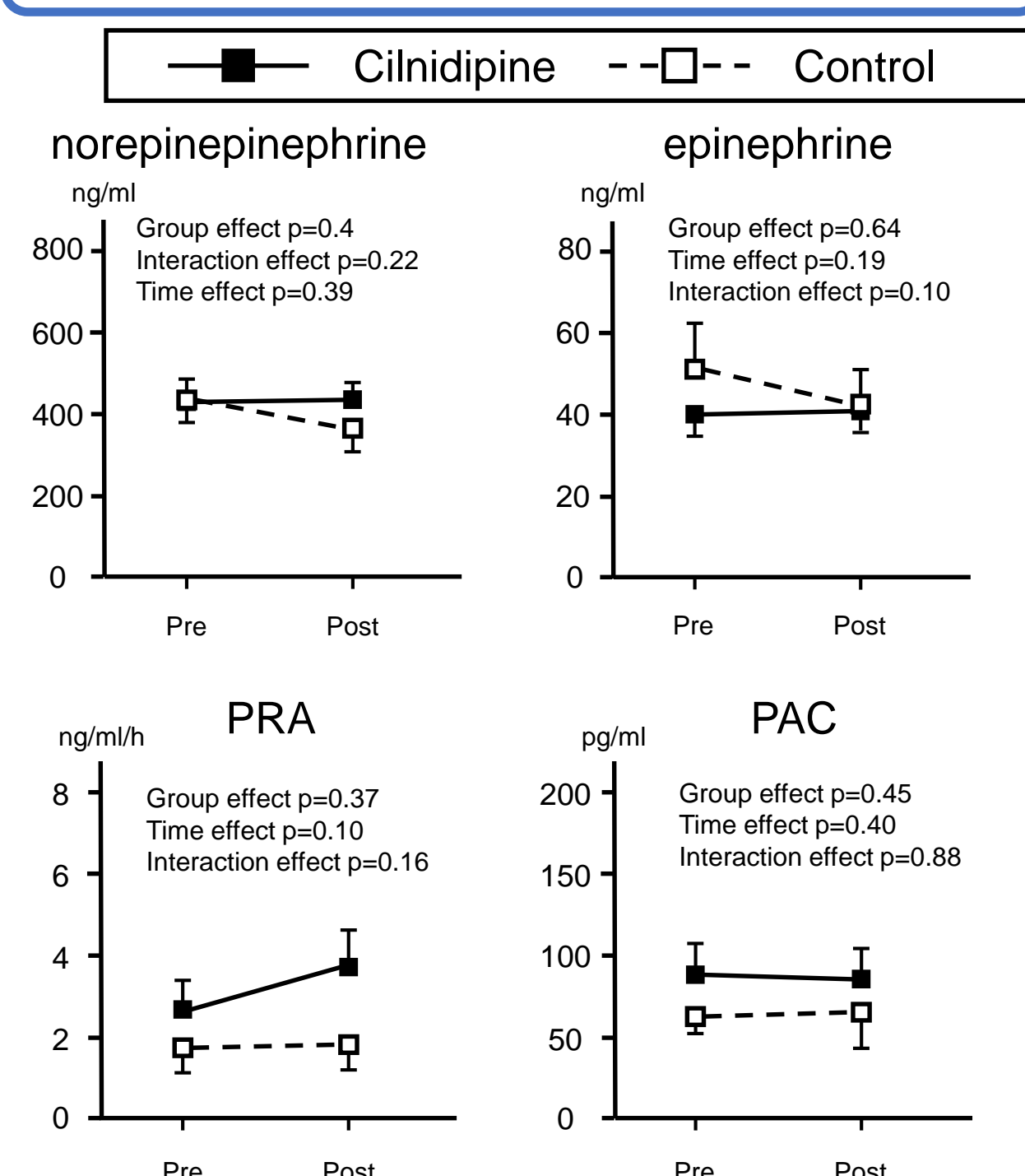
Intradialytic SBP elevation



Heart Rate during HD



Humoral factors



Summary

- The delta of SBP during HD appeared to be decreased in cilnidipine group.
- Cilnidipine significantly decreased SBP during HD at 12th week compared with baseline.
- Cilnidipine significantly increased HR at 2 hours after the initiation of HD.
- No significant changes were observed in catecholamines, PRA and PAC in both groups.

Conclusion

- Although cilnidipine failed to attenuate intradialytic SBP elevation in patients with intradialytic HTN, cilnidipine decreased both pre- and post-dialytic SBP.
- Cilnidipine may be effective to lower SBP during HD in patients with intradialytic HTN.

