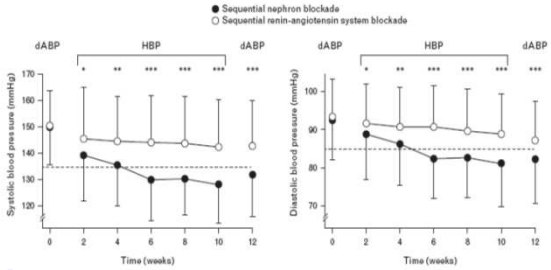
How to assess medication adherence among patients with resistant hypertension treated with two different pharmacological intensification strategies.

Beaussier H (1,6), Coudore F (5), Peyrard S (4), Bobrie G (2), Bezie Y (1), Azizi M (3), Boutouyrie P (5,6).
(1) CRC - Groupe Hospitalier Paris Saint-Joseph, (2) APHP, Hôpital Européen Georges Pompidou, Service d'Hypertension Artérielle, (3) APHP, HEGP, CIC - EC4 INSERM (4) URC - CIC HEGP, (5) APHP, HEGP, Service de Pharmacologie Clinique, (6) INSERM U 970 PARCC.

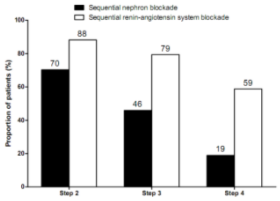
BACKGROUND

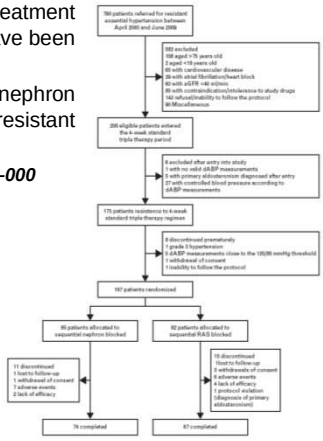
Non-adherence to medication (MA) and lifestyle measures is the main contributor to resistance to antihypertensive treatment (AHT). Various measures to assess medication adherence (MA) among patients (pts) with resistant hypertension (RH) have been proposed but none is fully effective.

We have previously shown that combined renin-angiotensin system (RAS) blockade was less efficacious than sequential nephron blockade (SNB), based on anti-aldosterone diuretic treatment for controlling blood pressure in patients with resistant hypertension.



Bobrie et al. Journal of Hypertension 2012, 30:000–000





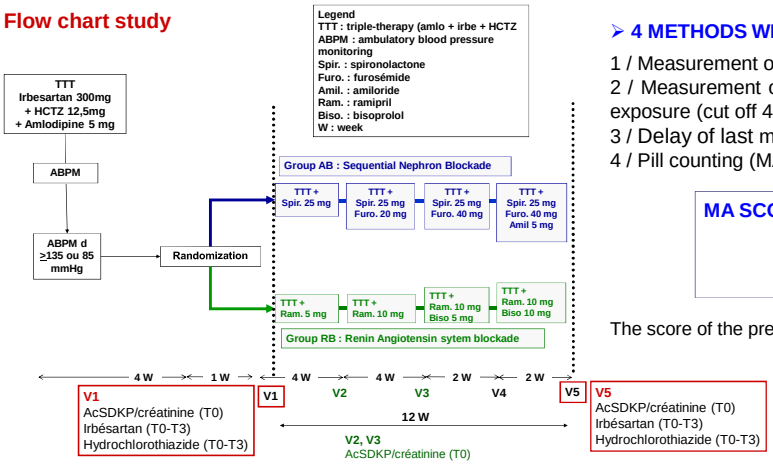
AIM

To assess MA with a new scoring system in RH patients included in a randomized controlled trial and the characteristics associated with low MA.

METHOD

Pts with RH to a 4 week-treatment with irbesartan 300 mg+ hydrocholorothiazide 12.5 mg+amlodipine 5 mg, were randomised to either reinforcement of sodium depletion by sequential administration of spironolactone and other diuretics (AB group, n=82) or reinforcement of renin angiotensin system blockade by sequential administration of ramipril 5-10 mg and bisoprolol 5-10 mg (RB group, n=82) for 12 weeks. Blood pressure was monitored monthly (and weekly by HBPM). Drugs were uptitrated and added if blood pressure remained uncontrolled at each monthly visit.

Flow chart study



➢ 4 METHODS WERE USED TO EVALUATE MA

1 / Measurement of plasma irbesartan concentration (HPLC) (Irb), (cut off 20 ng/ml) : V1,V5
2 / Measurement of urinary AcSDKP/creatinine ratio (UR) to evaluate ACE inhibitor (ramipril) exposure (cut off 4 nmol/mmol) : V1, V2,V3,V5
3 / Delay of last medication intake before visit :V2,V3,V5
4 / Pill counting (MA ratio=real/theoretical intakes):V2, V3, V5

MA SCORE
+1 : UR >4nmol/mmol
+1 : Irb >20ng/ml
+1 : Delay of last medication intake before visit <24h
+1 : MA ratio >80%.

The score of the present item was doubled in case of missing data, i.e in the SNB group without UR.

Three MA levels has been deduced :
- **Low MA (L) (score<2),**
- **Intermediate MA (I) (score=3)**
- **Sufficient MA (S) (score=4).**

RESULTS

Variable	Low MA	Intermediate MA	Sufficient MA	*P*
AB	13 (43.3%)	23 (44.2%)	46 (56.1%)	0.2945
RB	17 (56.7%)	29 (55.8%)	36 (43.9%)	
Gender (F/M)	11/19	11/41	18/64	0.2218
Age (years)	50.2 +/- 11.0	56.6 +/- 8.5	56.1 +/- 10.5	0.0114
Weight (kg)	85.7 +/- 15.9	87.6 +/- 12.5	82.6 +/- 13.0	0.1007
BMI (kg/m²)	29.3 +/- 4.7	29.6 +/- 3.9	28.2 +/- 4.5	0.1715
D2T (O/N)	6 (20.0%)	11 (21.2%)	13 (15.9%)	
Tabac (Jamais)	17 (56.7%)	22 (42.3%)	38 (46.3%)	
Cholestérolémie (mmol/L)	4.8 +/- 1.1	4.6 +/- 0.9	4.6 +/- 1.0	0.5523
Triglicéridémie (mmol/L)	1.6 +/- 1.0	1.3 +/- 0.6	1.4 +/- 1.0	0.3973
DFG (Cockcroft)	107.4 +/- 28.5	107.7 +/- 25.3	95.4 +/- 25.3	0.0119

Variable	Low MA	Intermediate MA	Sufficient MA	*p*
Office BP , mmHg				
Office SBP (mmHg)	153.0 +/- 26.7	154.0 +/- 18.7	149.8 +/- 17.8	0.4556
Office DBP (mmHg)	93.5 +/- 13.4	91.4 +/- 9.4	89.7 +/- 10.3	0.2436
Office Fc (bpm)	60.6 +/- 18.6	62.6 +/- 16.3	60.2 +/- 13.6	0.6573
Ambulatory BPM, mmHg				
SBP Diurne	152 +/- 15	152 +/- 14	148 +/- 12	0.1673
DBP Diurne	94 +/- 12	94 +/- 9	91 +/- 10	0.2533
Fc Diurne	82 +/- 9	82 +/- 11	79 +/- 10	0.0653
SBP Nocturne	141 +/- 19	138 +/- 17	136 +/- 13	0.3283
DBP Nocturne	84 +/- 14	82 +/- 11	80 +/- 9	0.2710
Fc Nocturne	73 +/- 8	71 +/- 11	68 +/- 9	0.0669
SBP 24h	148 +/- 16	147 +/- 14	144 +/- 12	0.2304
DBP 24h	91 +/- 12	90 +/- 9	87 +/- 9	0.2253
Fc 24h	79 +/- 8	78 +/- 10	75 +/- 9	0.0334

4 METHODS USED TO EVALUATE MA:

➢ **82** pts had **sufficient MA**
46 versus 36 pts among AB and RB groups, respectively;
➢ **52** had **Intermediate MA**
23 versus 29 pts among AB and RB groups, respectively;
➢ **30** had **Low MA**
13 versus 17 pts among AB and RB groups, respectively;
inter-groups difference NS.

Pts low MA are younger than sufficient MA pts (50±11 vs. 56±10 yrs, p<0.011); no difference of gender neither daily ambulatory SBP (152±14 vs. 148±12 mmHg, p=0.16) was observed.
Other clinical characteristics did not differ except the glomerular filtration rate: lower among sufficient MA pts than low MA pts (95±25 vs. 107±28 ml/min, p<0.02).

DISCUSSION/CONCLUSION

We propose a score of 3 MA levels (low, intermediate, sufficient) based on 4 complementary methods, either quantitative or qualitative. A combination approach is essential to balance imprecision of observance data.

No major clinical characteristics differ between groups. Further comparisons into each groups of treatment and longer duration of treatment might be necessary to observe significant differential effect among MA groups.

However, we could suppose that therapeutic education sessions could be useful for this specific population that undertake complex and heavy therapy.

CPC-065 18th EAHP Congress Paris, France, 13-15 March 2013