

GW23-e2399

THE EFFECTS OF COMBINED AMLODIPINE AND ATORVASTATIN ON THE BALANCE OF ACTIVATED RANKL/RANK/OPG SYSTEM IN SHR

doi:10.1136/heartjnl-2012-302920a.102

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Objectives Introduction To explore the effect of amlodipine, atorvastatin, and their combination on the activated RANKL/RANK/OPG

system, by investigating the changes of RANKL, RANK and OPG expression in SHR.

Methods 36-week-old SHR were randomly allocated into four groups: a vehicle-treated control group; an amlodipine (10 mg/kg/day)-treated group; an atorvastatin (10 mg/kg/day)-treated group; and a group treated with a combination of amlodipine and atorvastatin (both at 10 mg/kg/day). In addition, WKY rat was chosen as control group of normal blood pressure. Drugs were administered by oral gavage every morning for a period of 12 weeks before hearts were harvested for analysis. Left ventricular mass index (LVMI) was assessed by morphology measurement. Western blot and RT-PCR was used to observe the protein and gene expression of RANKL, RANK and OPG.

Results LVMI in SHR was higher than that in WKY, and treatment with amlodipine or atorvastatin significantly decreased LVMI (each $p < 0.05$). Furthermore, combination therapy had the best lowering effect ($p < 0.05$). Western Blot and RT-PCR showed the protein and mRNA expression levels of RANKL and RANK as well as OPG in SHR control group were all obviously increased in contrast to that in WKY (each $p < 0.05$). The protein and mRNA expression levels of RANKL and RANK in either amlodipine or atorvastatin alone groups were obviously reduced compared with that in SHR control group (each $p < 0.05$). Furthermore, combination therapy reduced it further (each $p < 0.05$). The protein and mRNA expression levels of OPG in either amlodipine or atorvastatin alone groups were obviously reduced compared with that in SHR control group (each $P < 0.05$), but there was no difference among three different treatment ($p > 0.05$).

Conclusions Both protein and mRNA expression of RANKL, RANK, and OPG in SHR were significantly enhanced compared with WKY, suggesting that the pathologic changes of ventricular remodelling may be associated with the activation of RANKL/RANK/OPG system. Amlodipine and atorvastatin may obviously reverse advanced cardiac hypertrophy by way of down regulation of the activated RANKL/RANK/OPG system.