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Long-term Thyroxine Administration Protects the Heart in a Similar Pattern as Ischaemic Preconditioning

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AIM

We have previously shown that long-term thyroxine administration can protect the heart against ischaemia. In the present study, we investigated whether thyroxine induced cardioprotection can mimic the pattern of protection that is afforded by a well-established cardioprotective means such as ischaemic preconditioning.

METHODS

Hyperthyroidism was induced in Wistar rats by L-thyroxine administration (25μg/100g body weight) for 14 days (THYR), while normal animals treated with normal saline served as controls (NORM). Isolated rat hearts were perfused in a Langendorff mode. After an initial stabilization period, hearts were subjected to 20 min of zero-flow global ischaemia (I) followed by 45 min of reperfusion (R), NORM(I/R), n=6 and THYR(I/R), n=6. Normal hearts were also were also subjected to 4 cycles of ischemic preconditioning (3I/5R, 5I/5R, 5I/5R and 5I/5R) prior to 20min I and 45min R, NORM(Pc+I/R), n=6. Postischaemic recovery of left ventricular developed (LVDP) pressure was expressed as % of the initial value (LVDP%). Ischemic contracture was estimated by the time to peak contracture (Tmax) in min. Phosphorylated and total p38 MAP kinase was measured by Western blot analysis in normal, hyperthyroid and preconditioned hearts that were subjected to stabilization and 20 min I alone, NORM(I), n=4, THYR(I), n=5, and NORM(Pc+I), n=5. Phosphorylated and total PKCδ were measured by Western blot analysis in normal and hyperthyroid hearts that were not subjected to any ischemic stress.

RESULTS

LVDP% was higher in THYR(I/R) as compared to NORM(I/R) [61.5 (6.6) vs 42.8 (4.9)], $p<0.05$. In addition, LVDP% was higher in NORM(Pc+I/R) as compared to NORM(I/R) [59.2 (4.6) vs 42.8 (4.9)], $p<0.05$. Tmax was 14.3 (0.7) for THYR(I/R) hearts, 12.8 (1.8) for NORM(Pc+I/R) hearts, while did not reach a plateau during 20 min of I in NORM(I/R) hearts.

Phosphorylated p38 MAPK was 1.9 fold more in NORM(I) as compared to THYR(I) hearts, $p<0.05$ and 3.5 fold more in NORM(I) as compared to NORM(Pc+I) hearts, $p<0.05$. Total PKCδ was 2.8 fold higher in THYR as compared to NORM hearts, $p<0.05$, while phosphorylated PKCδ was 3 fold higher in THYR as compared to NORM hearts, $p<0.05$.

CONCLUSION

Long term thyroxine administration protects the heart against ischemia in a similar pattern as ischemic preconditioning.