EFFECT OF NAPROXCINOD ON BLOOD PRESSURE AND VASCULAR RESPONSE TO ACETYLCHOLINE IN SPONTANEOUSLY HYPERTENSIVE RATS

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BACKGROUND

The use of non-steroidal anti-inflammatory drugs (NSAIDs) may increase blood pressure (BP), induce new onset and aggravate hypertension and predispose to cardiovascular events (Wilson & Poulter, 2006; McGgettigan & Henry, 2008).

Hypertension is a frequent comorbidity in patients with osteoarthritis (OA) (~ 50% of OA patients ≥ 65 years) (Singh et al., 2002).

Hypertension is associated to endothelial dysfunction, characterized by impaired nitric oxide (NO) production and activity (Munzel et al., 2008).

Cyclooxygenase-inhibiting nitric oxide donors (CINODs), by inhibiting both COX-1 and COX-2 while releasing NO, were originally designed to mitigate some of NSAIDs’ unwanted effects, such as gastrointestinal and cardiovascular adverse events (Wallace et al., 2009).

OBJECTIVE

To test the effects of the CINOD naproxcinod in comparison to naproxen on blood pressure and ex vivo endothelium-dependent vascular relaxation in spontaneously hypertensive rats (SHR).

CONCLUSION

Naproxinod provides a slight but significant reduction of systolic BP in SHR rats; naproxen does not cause any significant change. No effect is observed in normotensive animals.

Hypertensive rats show impaired endothelial function, evidenced by the reduced vasorelaxation of aortic rings to acetylcholine.

Seven-day treatment with naproxcinod improves ex vivo response to acetylcholine in aortic rings from hypertensive rats, suggesting a possible restoration of the vascular endothelial function.

REFERENCES


EXPERIMENTAL PROTOCOL

Normotensive and hypertensive rats treated with naproxcinod or naproxen show similar endothelial-independent response ex vivo.

Naproxinod increases plasma nitrites/nitrates (NOx) in both normotensive and hypertensive rats.

The ex vivo response to the NO-donor sodium nitroprusside (SNP) was used to test the relaxation potential of aortic rings from normotensive Wistar (left panel) or hypertensive SHR rats (right panel) treated with naproxcinod, naproxen or vehicle once a day for 7 days.

Plasma NOx concentrations were determined 3 hrs after the last treatment by the Griess reaction. *, p<0.05 vs. vehicle or naproxen.