

Effects of Oestrogen on Haemodynamic and Vascular Reactivity
A study in animal models and humans

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This thesis is based on the following papers:

- I Brandin L, Gustafsson H. 17beta-estradiol relaxes precontracted mesenteric arteries from male and female rats; a transient effect which is lost after a short incubation period.
In manuscript
- II Brandin L, Bergstrom G, Manhem K, Gustafsson H. Oestrogen modulates vascular adrenergic reactivity of the spontaneously hypertensive rat.
J Hypertension 2003;21:1695-1702
- III Brandin L, Bergstrom G, Manhem K, Gustafsson H. Estrogen attenuates ambulatory pressure and heart rate in hypertensive rats with small effects on hemodynamic responses to stress.
Submitted
- IV Manhem K, Brandin L, Ghanoum B, Rosengren A, Gustafsson H. Acute effects of transdermal estrogen on hemodynamic and vascular reactivity in elderly postmenopausal healthy women.
J Hypertension 2003;21:387-394
- V Brandin L, Gustafsson H, Ghanoum B, Milsom I, Manhem K. Chronic effects of conjugated equine estrogen on hemodynamic and vascular reactivity in hypertensive postmenopausal women
Submitted



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Abstract

Previous studies have shown that oestrogen, the female sex hormone, plays a protective role in the cardiovascular system. However the site of action remains incompletely understood. Large clinical interventional trials have not proven that longer treatment with oestrogen plus progesterone yields lower incidence of cardiovascular outcomes, suggesting that hormone replacement therapy (HRT) might protect only a selective group of postmenopausal women.

The present study treated normo- and hypertensive female rats and postmenopausal women with oestrogen for short and longer time periods. We also investigated the acute effect of 17β -estradiol on isolated small resistance arteries and the effects of oestrogen treatment on vascular reactivity and endothelial function in a wire-myograph. Further, we recorded haemodynamic parameters during daily life and stress, and evaluated the effect of HRT on the autonomic nervous systems of hypertensive women by evaluating heart rate variability (HRV) with 24 h analysis.

Blood pressure (BP) was attenuated after 24 hour treatment with 17β -estradiol in normotensive postmenopausal women and normo- and hypertensive rats. In hypertensive rats a lowered BP sustained after 10 days of treatment. Although we observed an attenuated heart rate (HR), haemodynamic responses to stress remained largely unaffected. Six months of HRT did not affect BP, HR, HRV, or haemodynamic responses to stress in hypertensive postmenopausal women but did result in reduced sensitivity to noradrenaline, a stress hormone, in subcutaneous arteries. Lower adrenergic response occurred in the resistance arteries of hypertensive rats but not in normotensive rats or women. 17β -estradiol relaxed precontracted mesenteric arteries, due mainly to endothelial release of nitric oxide. We also observed a modulated endothelial response to acetylcholine following 17β -estradiol treatment in normotensive women and hypertensive rats and HRT in hypertensive women.

In conclusion, the effects of oestrogen on vascular reactivity and haemodynamics differed between hypertensive and nonhypertensive subjects and also according to the type of oestrogen used. Decreased BP and HR with 17β -estradiol treatment but not with HRT suggests that 17β -estradiol participates selectively in the haemodynamic system. However, the attenuated adrenergic vascular response observed in hypertensive subjects independent of oestrogen type may contribute to improved blood flow to peripheral tissue even though BP remains unchanged. The clinical importance of the reinforced acetylcholine induced response in normotensive and hypertensive women and rats after oestrogen treatment requires further evaluation.

Key words: adrenergic reactivity, endothelium, haemodynamic, hypertension, oestrogen, postmenopausal women, resistance arteries, spontaneously hypertensive rats, stress