Natural progesterone and antihypertensive action

P B RYLANCE, M BRINCAT, K LAFFERTY, J C DE TRAFFORD, S BRINCAT, V PARSONS, J W W STUDD

Abstract

In a placebo controlled, double blind crossover study natural progesterone was given by mouth, in increasing doses, to six men and four postmenopausal women with mild to moderate hypertension who were not receiving any other antihypertensive drugs. When compared with values recorded before treatment and during administration of placebo progesterone caused a significant reduction in blood pressure, suggesting that progesterone has an antihypertensive action rather than a hypertensive one as has been previously thought.

This possible protective effect of progesterone should be investigated further.

Introduction

Although oestrogen has been implicated as the factor that protects women against cardiovascular disease,[1] progesterone could equally be considered to have this protective role. Progesterone relaxes uterine smooth muscle by sequestering intracellular calcium[2] and reducing the number of α adrenoreceptors[3]; a similar action on peripheral vascular smooth muscle could contribute to the lower blood pressure in premenopausal women. This is contrary to traditional teaching, which suggests that progestogens cause hypertension.[4]

To test this hypothesis we carried out a double blind placebo controlled pilot study, using natural progesterone, in men and postmenopausal women with mild to moderate hypertension.

Patients and methods

We studied eight men (mean age 55·8 years, range 29-73) and four postmenopausal women (mean age 55·2 years, range 53-60). Nine were taking antihypertensive drugs. This treatment was stopped four weeks before entry into the study.

Supine and erect blood pressures were recorded three times at two weeks before and on the day of entry into the study, and the mean value of the six systolic and diastolic (phase V) readings was calculated. Subjects were then randomly allocated to receive either oral natural progesterone (Ultrogestan; Besins, Paris) 100 mg twice daily or placebo 100 mg twice daily for two weeks. Crossover was carried out at the end of the two weeks. This was repeated with the dose (active and placebo) being increased to 200 mg twice daily and 300 mg twice daily, the patients being crossed over every two weeks. Plasma concentrations achieved with 200 mg of progesterone are equivalent to concentrations seen during the luteal phase.[5]

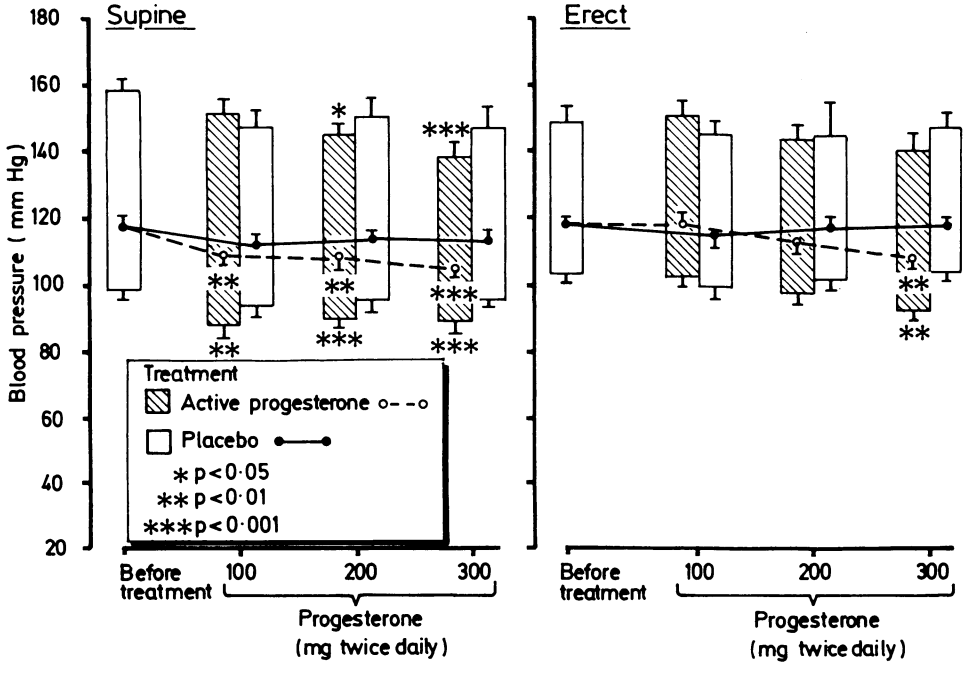
Two men were withdrawn from the study; one needed reintroduction of diuretics for recurrence of oedema before starting treatment with progesterone; the other needed combination treatment because of the severity of his hypertension.

Systolic, diastolic, and mean arterial blood pressures were analysed and comparisons, using the paired Student's *t* test, made between values recorded at the end of each period of two weeks and before treatment and also between those recorded during treatment with the active drug and while receiving the corresponding dose of placebo.

Departments of Renal Medicine, Medical Engineering and Physics, and Obstetrics and Gynaecology, Dulwich Hospital, London SE22

P B RYLANCE, BSC, MRCP, renal research fellow
M BRINCAT, MRCS, LRCP, registrar in gynaecology
K LAFFERTY, MB, FRCS, lecturer in surgery
J C DE TRAFFORD, BA, research assistant
S BRINCAT, MRCP, senior house officer
V PARSONS, DM, FRCP, consultant physician
J W W STUDD, MD, MRCOG, consultant in obstetrics and gynaecology

Correspondence to: Mr M Brincat.



Supine and erect systolic and diastolic blood pressures together with mean arterial pressures represented by continuous and broken lines. (Vertical bars represent standard error of the mean.) p Values refer to significance of difference between values recorded before and during treatment.

Results

Before treatment mean blood pressure was 158·0/98·4 mm Hg supine and 148·7/103·2 mm Hg erect and the mean arterial blood pressure was 118·3 mm Hg (supine and erect) (figure). Blood pressures recorded while subjects were receiving any of the three doses of placebo were not significantly different from those recorded before treatment.

Supine blood pressure was significantly reduced with all three doses of natural progesterone when compared with pretreatment readings. The maximum fall was with 300 mg twice daily, the mean being 19·7 mm Hg systolic and 9·6 mm Hg diastolic. Supine blood pressure was always lower during treatment with progesterone than with placebo, but the difference did not always reach significance (100 mg diastolic, $p < 0.05$; 200 mg mean arterial pressure, $p < 0.05$). Erect blood pressure with progesterone was also reduced when compared with pretreatment readings, the difference reaching significance with 300 mg twice daily in the diastolic and mean arterial blood pressure readings. When compared with placebo, there was a significant reduction in erect diastolic ($p < 0.001$) and mean arterial blood pressures ($p < 0.002$) with the 300 mg dose.

No significant changes were observed in pulse rate or weight during the trial. Two men reported slight light headedness about one hour after ingestion of the two higher doses.

Discussion

Blood concentrations of progesterone in premenopausal women are high in the luteal phase of each ovulatory menstrual cycle but fall to 30% of the follicular phase in postmenopausal women. Men have similarly low blood concentrations of progesterone. The results of this pilot study suggest that natural progesterone produces a significant reduction in blood pressure at doses which give plasma concentrations that are just above luteal phase concentrations.

The physiology of progesterone suggests that its antihypertensive action is peripheral, although an additional central action cannot be excluded. In this study the less predictable reduction of erect blood pressure could have been due to the presumed vasodilation action of natural progesterone being overridden by reflex sympathetic vasoconstrictor activity.

We suggest that progesterone is a "protective" female hormone. The low blood progesterone concentrations present after the menopause could account for the finding that the prevalence of high blood pressure and incidence of cardiovascular disease in women tend to catch up with those in men.[1 3] This property would recommend the use of natural progesterone in combined oral contraceptives instead of synthetic gestagens.

References

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Impaired antipneumococcal antibody production in patients without spleens

FRANCO DI PADOVA, MICHAEL DÜRIG, FELIX HARDER, CARLO DI PADOVA, CARLO ZANUSSI

Abstract

Fifteen splenectomised and 15 normal subjects were studied, in absence of any intentional immunisation, for pokeweed mitogen induced synthesis of antipneumococcal capsular polysaccharide antibodies in vitro by peripheral blood mononuclear cells. Results showed that removal of the spleen had caused a persistent immune deficiency of circulating B cells capable of synthesising IgM antipneumococcal capsular polysaccharide. In vitro synthesis of polyclonal IgM and IgG by peripheral blood mononuclear cells of subjects without spleens was also depressed. These defects were due to an abnormality of the B cell compartment.

These data are evidence of the major role of the spleen in the control and production of a consistent part of pokeweed mitogen responsive circulating B cells and add another facet to the complex immune dysfunction of splenectomised subjects. The findings, moreover, may help in understanding the susceptibility of splenectomised people to pneumococcal sepsis and the delayed and impaired antibody response to pneumococcal vaccine.

Department of Clinical Immunology, University of Milan, School of Medicine, I-20122, Milan, Italy
FRANCO DI PADOVA, MD, assistant professor

Department of Surgery, University of Basel, Kantonspital, CH-4031, Basel, Switzerland
MICHAEL DÜRIG, MD, senior registrar
FELIX HARDER, MD, professor and chairman, department of surgery

3rd Medical Clinic, University of Milan, School of Medicine, I-20122, Milan, Italy
CARLO DI PADOVA, MD, assistant professor

2nd Medical Clinic, University of Milan, School of Medicine, I-20122, Milan, Italy
CARLO ZANUSSI, MD, professor and chairman, 2nd medical clinic

Correspondence and requests for reprints to: Dr Franco Di Padova, Department of Clinical Immunology, 2nd Medical Clinic, University of Milan, School of Medicine, via F Sforza 35, I-20122 Milan, Italy.

Introduction

Despite the wide range of antibiotics available pneumococcal infections remain a substantial cause of morbidity and mortality.[1] In asplenic children and patients whose spleens have been removed for therapeutic reasons or after trauma overwhelming pneumococcal sepsis and an increased incidence of pneumococcal infections have been described.[2] The association between absence of the spleen and infections has stimulated a great number of clinical and experimental investigations that have shown the relevant role of the spleen in the defence against