The effect of mental stress on prostaglandin F$_{2\alpha}$ in patients with essential hypertension and in healthy subjects

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Summary

1. The influence of mental stress, 30 min Kraepelin's arithmetic test under noise on the plasma concentration and urinary excretion of prostaglandin (PG) F$_{2\alpha}$ was studied in patients with essential hypertension and in healthy subjects.

2. Before the arithmetic test the plasma PGF$_{2\alpha}$ in hypertensive patients was significantly higher than in healthy subjects. The mental stress produced a significant increase in plasma PGF$_{2\alpha}$ in healthy subjects but not in patients with essential hypertension.

3. Three hour urine excretion of PGF$_{2\alpha}$ before stress was about two times lower in hypertensive patients than in healthy subjects. After exposure to stress a significant decrease in urinary excretion of PGF$_{2\alpha}$ was found in healthy subjects, but not in hypertensive patients.

4. The stress-induced increase in plasma PGF$_{2\alpha}$ of healthy subjects may reflect elevated brain PGF$_{2\alpha}$ synthesis. The individual differences in response to stress in hypertensive patients may result from specific impairments in synthesis and/or prostaglandin turnover.

Key words: hypertension, stress, prostaglandin F$_{2\alpha}$.

Abbreviation: PG, prostaglandin.

Introduction

The functional significance of psychological factors in the onset and development of hypertension has been one of the areas of current research (Jansson & Hansson, 1977; Mustacchi, 1977). Environmental stimuli affect the endocrine regulation, and recent work demonstrates that stimulation enhances the release of brain prostaglandins of the F-group (Wolfe, Rostworowski & Marion, 1976; Holmes, 1970), which in turn contribute to the regulation of blood pressure (Heinemann & Lee, 1976). Therefore it seemed of interest to investigate mental stress-induced changes on prostaglandin release in hypertensive and healthy subjects.

Methods

Ten male patients with essential hypertension, aged 18–42 years (mean age 26.9 years) and eight healthy men, aged 26–43 years (mean age 31.1 years) participated in the study. All subjects were hospitalized and remained on a standard hospital diet with normal sodium intake. The patients did not receive any medication for at least 2 weeks before the study. All subjects gave their informed consent to participate in this study.

On the day of the investigation the subjects remained in a quiet room, and 30 ml of venous blood was withdrawn through an indwelling catheter after 3 h of rest in the sitting position. During this period urine was collected. The subjects performed a simple mental task, i.e. summing columns of four two-digit figures under continuous noise delivered through earphones for 30 min. The noise itself was from a specially prepared tape recording of superimposed sounds of urban traffic, unintelligible bits of speech and occasional bursts of noise produced by heavy machinery. This particular combination of sounds has been selected as an analogue of the spectrum of complex noises present in the urban environment. The tape was played at about 90dBA. After the test 30 ml of
venous blood was again taken. The subjects then collected the urine for another 3 h.

The blood samples were collected into ice-chilled plastic tubes containing EDTA and the plasma was separated immediately. The plasma concentration of \( \text{PGF}_{2\alpha} \) and its urinary excretion were determined by specific radioimmunoassay with antibody from Calbiochem after Amberlite XAD-2 ion-exchange extraction and silicic acid column chromatography. Intra-assay coefficient of variation was 10%. Losses were corrected by an internal standard of \(^3\text{H}\)-labelled \( \text{PGF}_{2\alpha} \).

Data were analysed by Student's \( t \)-test and are reported as the means ± SE.

Results

These are presented in Table 1. All healthy subjects responded to stress with an increase in plasma \( \text{PGF}_{2\alpha} \) (\( \Delta = 4 \) pg/ml, \( P < 0.01 \)). In contrast, the results for hypertensive subjects were less conclusive (\( \Delta = 1.4 \) pg/ml, N.S.).

Three-hour urine excretion of \( \text{PGF}_{2\alpha} \) before stress was about two times lower in hypertensive patients than in healthy subjects. After exposure to stress a significant decrease in urinary excretion of \( \text{PGF}_{2\alpha} \) was found in healthy subjects (\( \Delta = -201 \) ng/3 h, \( 0.02 < P < 0.05 \)), whereas in hypertensive patients the urinary excretion of \( \text{PGF}_{2\alpha} \) remained close to the control value (\( \Delta = -19 \) ng/3 h, N.S.).

Discussion

A uniform reaction pattern, manifested by the increase in plasma \( \text{PGF}_{2\alpha} \) and decrease in urine \( \text{PGF}_{2\alpha} \), was found in healthy subjects. The results in hypertensive patients were less clear, and neither plasma nor urine \( \text{PGF}_{2\alpha} \) changed significantly after stress.

The increase in plasma \( \text{PGF}_{2\alpha} \) after exposure to stress may reflect elevated synthesis in the brain. Several studies in vitro have demonstrated that brain prostaglandins are elevated in response to a variety of stimuli (Markelonis & Garbus, 1975; Wolfe, Pappius & Marion, 1976), and it has been found that brain prostaglandins can be transported to blood via the cerebrospinal fluid (Haggen, Gerber, Sweeney, White & Robertson, 1977). Therefore it has been argued that prostaglandins are a group of first mediators of cell response to stimulation (Hanukoglu, 1977a,b). This hypothesis is supported to some extent by Hedge (1977), who reported that indomethacin, an inhibitor of prostaglandin synthesis, inhibited stress-induced release of ACTH. Two aspects of the present results corroborate this hypothesis: (1) the magnitude of stress-induced changes in \( \text{PGF}_{2\alpha} \) in plasma of healthy subjects; (2) the elevated initial plasma concentration in hypertensive subjects. The former may be regarded as a direct response to stressful stimulation, and the latter is supposed to reflect the anticipation of stress. It is well established that prostaglandins contribute to blood pressure regulation, and prostaglandin deficiency is supposed to play an important role in hypertension. Thus the anticipation of stress must be taken into account in order to explain the strikingly high initial plasma \( \text{PGF}_{2\alpha} \) in this group. Irrespective of whether this preparedness is adequate or not, it affects the adaptive mechanisms.

The individual differences in response to stress in hypertensive patients may result from specific impairments in synthesis and/or turnover of prostaglandins. Exposure to stress had no effect on kidney prostaglandin synthesis in hypertensive subjects. The decrease in urinary excretion of \( \text{PGF}_{2\alpha} \) in healthy subjects might be due to circadian rhythm. If this is the case, both the low initial urinary \( \text{PGF}_{2\alpha} \) excretion as well as the lack of any change after exposure to stress in hypertension would suggest the existence of hypertension-related changes in the prostaglandin system.

<table>
<thead>
<tr>
<th>TABLE 1. Prostaglandin ( F_{2\alpha} ) in plasma and urine of healthy subjects and hypertensive patients</th>
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<tbody>
<tr>
<td>Mean values ± SEM are shown. *Hypertension vs controls: ( P &lt; 0.01 ). N.S., Not significant.</td>
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<tr>
<td>Hypertension (( n = 10 ))</td>
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<tr>
<td>Plasma concn. (pg/ml)</td>
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<tr>
<td>Before test</td>
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<td>18.9 ± 1.6*</td>
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<td>N.S.</td>
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Acknowledgments

We thank Dr John E. Pike of the Upjohn Company, Kalamazoo, Michigan, U.S.A. for kindly supplying the standard PGF\textsubscript{2\alpha} used in this study.

References


