THE EFFECT OF LABETALOL AND PROPRANOLOL ON THE PRESSOR RESPONSE TO SEXUAL AROUSAL IN WOMEN

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- 1 The effect of a single oral dose of labetalol (100 mg), propranolol (80 mg) and placebo on the pressor response to sexual autostimulation has been studied in six female volunteers.
- 2 Labetalol but not propranolol significantly reduced the increase in blood pressure that occurred at orgasm.
- 3 The subjective features of the sexual response were assessed by each subject using visual analogue scales.
- 4 Subjects reported a significant reduction in vaginal lubrication with labetalol compared to both placebo and propranolol.
- 5 No other effects were noted.

Introduction

Sexual arousal is associated with increase in blood pressure. Klumbies & Kleinsorge (1950) recorded blood pressure during psychogenically induced sexual arousal to orgasm in women and reported an increase of 50 mmHg in systolic pressure. Masters & Johnson (1966) reported increases of between 20 and 60 mmHg in blood pressure during the orgasmic phase of the female sexual response cycle. At orgasm during coitus, Fox & Fox (1969) demonstrated an increase in systolic blood pressure in a female subject from 100 mmHg to 200 mmHg. Littler, Honour & Sleight (1974) monitored intra-arterial blood pressure during coitus and reported increases in systolic and diastolic pressures of up to 100 mmHg and 48 mmHg respectively.

Fox (1970) investigated the effect of propranolol on blood pressure response to coitus in two normotensive subjects. He reported that 160 mg propranolol taken orally 90 minutes before the coitus reduced the usual rise in blood pressure occurring at orgasm. Since sexual arousal and in particular orgasm are associated with substantial increases in plasma nor-adrenaline concentration (Wiedeking *et al.*, 1977; Wiedeking, Ziegler & Lake, 1979), a drug possessing both α - and β -adrenoceptor antagonist activity might be more effective than a β -adrenoceptor blocker in reducing orgasm-induced increase in blood pressure. In the present study the effect of labetalol (an α - and β -adrenoceptor antagonist) and propranolol (a β -adrenoceptor antagonist) were compared with placebo control.

Methods

Six healthy women, aged 26–35 years (mean $\pm$ s.d.; 30 ± 3) took part in this study. All the subjects were known to be orgasmic by autostimulation and had taken part in previous investigations concerned with aspects of sexual function. None of the subjects was on medication including oral contraceptives and none was pregnant. Each subject was studied on three occasions at least three days apart between day 5 and day 16 of the menstrual cycle and within 24 to 36 h of their previous orgasmic experience.

Blood pressure was measured by a Bosomat II automatic sphygmomanometer and the subjects were instructed how to use it. The subject took a coded tablet. Ninety minutes later the sphygmomanometer cuff was applied to an arm. The same arm was used in each of the three experimental sessions. The subject rested supine for 30 min then she recorded her blood pressure by directly triggering the sphygmomanometer. She then proceeded to stimulate herself using a battery driven vibrator. At the onset of orgasm she switched on the sphygmomanometer which recorded her blood pressure and actuated the automatic facility of the instrument to repeat blood pressure measurement after an interval of 2 min. The subject was instructed to cease stimulation immediately after orgasm had occurred and to rest. The blood pressure was automatically recorded 2 min after the 'orgasmic' blood pressure recording. The subject then reported the subjective features of her experience on 10 cm analogue scales (Figure 1).

The drugs employed in the study were labetalol 100

1. *Sexual arousability*
Unable to become aroused Very easily aroused
2. *Vaginal lubrication*
No lubrication Excessive lubrication
3. *Speed of reaching orgasm*
Unable to reach orgasm Reach orgasm very quickly
4. *Sensation of orgasm*
No sensation Very much increased sensation
5. *Satisfaction*
Not satisfying Extremely satisfying

Figure 1 The analogue scales used in the study.

mg (Glaxo Group Research Limited), propranolol 80 mg (ICI Limited) and placebo (Glaxo Group Research Limited). The treatments were administered blindly as near-matching white tablets. Each subject took all the three treatments, the order of which was predetermined by a schedule based on a latin square randomisation.

The blood pressure recordings were read without knowledge of the treatment, and measurements were recorded to the nearest 5 mmHg. Statistical significance of differences in blood pressure were tested by Duncan's multiple comparison test (Duncan, 1955).

Data presented on the analogue scales were examined by Friedman rank sum analysis for statistical significance. P values larger than 0.05 were considered not significant.

Results

The results are shown in Figure 2. After placebo there was a mean rise in systolic and diastolic blood pressure of 31 and 38 mmHg respectively at the time of orgasm. Treatment with labetalol and propranolol did not affect the prestimulation systolic blood pressure but both drugs caused a significant reduction in diastolic blood pressure before stimulation ($F = 7.6$, $P < 0.01$). Labetalol but not propranolol treatment significantly reduced the orgasm-induced increase in systolic blood pressure ($F_{2,10} = 6.92$, $P < 0.05$). The between treatment group differences in diastolic blood pressure at the time of orgasm did not reach statistical significance. No drug-induced differences in post orgasmic blood pressure were observed.

The analogue scale measurements median and range are shown in Table 1. The only significant effect revealed by subjecting this data to statistical analysis was a reduction in vaginal lubrication with labetalol compared to placebo and propranolol treatment.

No subject complained of side effects during any of the treatment periods.

Discussion

A variable amount of physical effort normally occurs during coitus. The elevation of blood pressure recorded during coitus therefore results from the com-

Figure 2 The effect of labetalol (□), propranolol (▨) and placebo (■) on blood pressure response to sexual arousal (mean ± s.e. mean, $n=6$). * $P < 0.05$.

Table 1 Results of subjects subjective assessment of sexual response on 10 cm analogue scales expressed as median (range)

	Placebo	Labetalol	Propranolol
Arousability	55 (25-72)	52 (47-61)	60 (29-83)
Vaginal lubrication	60 (27-82)	14 (4-23)*	54 (39-71)
Speed of reaching orgasm	51 (33-65)	54 (27-70)	36 (16-75)
Sensation of orgasm	50 (35-72)	53 (22-66)	48 (41-77)
Satisfaction	45 (1-86)	43 (21-78)	41 (11-53)

* significantly different from placebo and propranolol

bined effect of sexual arousal and physical work. In the present study we aimed at studying the effect of adrenoceptor antagonists on the pressor response to sexual arousal. Autostimulation by means of a vibrator involves negligible physical work. This would explain why the increases in blood pressure observed were smaller than those reported to occur during coitus by Fox & Fox (1969) and Littler *et al.* (1974), but they are within the range reported by Masters & Johnson (1966) who also employed masturbation or artificial coitus in their experiments.

An important methodological weakness in the design of this study is the measurement of the 'orgasmic' blood pressure. The subject triggered the sphygmomanometer at the onset of orgasm, hence the blood pressure recording was made relative to this point in time. The pressure recorded may therefore not be the peak pressure that occurred during the orgasm which could only have been recorded by means of continuous monitoring. It is unfortunate that the pulse rate was not recorded. It was not possible to compute the pulse rate accurately from the blood pressure recordings.

In the early stages of sexual arousal, Littler *et al.* (1974) reported a relative slowing of the heart at a time when the blood pressure was rising. Such cardiovascular events occur when noradrenaline is infused into healthy volunteers (Richards, Prichard & Hernandez, 1979). In both males and females plasma noradrenaline levels increase during sexual arousal and a significant correlation has been reported between the subjective level of sexual arousal and plasma noradrenaline concentration (Wiedeking *et al.*, 1977, 1979).

Tachycardia accompanies the later stages of sexual arousal. The increase in blood pressure seen at orgasm results from the combined effect of increased peripheral resistance (α -adrenoceptor response) and increased cardiac output (predominantly a β -adrenoceptor response). As Fox (1970) demonstrated, the increase in blood pressure induced by sexual arousal can be partially inhibited by the β -adrenoceptor blocking drug, propranolol. In the present study half the dose of propranolol that Fox (1970) used caused a

statistically insignificant reduction in orgasm-induced increased blood pressure.

Labetalol is between four and six times less potent than propranolol with respect to antagonist activity at β -adrenergic receptors (Richards, Prichard & Dobbs, 1978), and yet treatment with 100 mg labetalol produced a significant reduction in the pressor response to orgasm whereas 80 mg propranolol did not. Labetalol has been shown to competitively antagonise the systolic and diastolic pressor effects of noradrenaline (Richards *et al.*, 1979). Labetalol but not propranolol inhibits the pressor response to cold, another situation where there is increased noradrenergic activity (Maconochie, Richards & Woodings, 1977). The α -adrenoceptor blocking activity of labetalol therefore makes the drug more effective than β -adrenoceptor blockade alone in reducing the diffuse sympathetic nervous activity that is a feature of sexual arousal.

The assessment of the effect of drugs upon the subjective elements of sexual function is difficult. The use of analogue scales for the assessment of subjective phenomenon is controversial. Whilst they are simple for the subject to use, the data is difficult to analyse. This difficulty is intensified by the small number of subjects included in the present study. However, using the Friedman rank sum analysis the only significant effect demonstrated was a reduction in vaginal lubrication with labetalol compared to both placebo and propranolol. This may be caused by a direct pharmacological effect of labetalol on the vascular or cellular mechanisms of vaginal lubrication or indirectly by decreased perfusion pressure through the genital blood vessels secondary to the inhibition of sexual-arousal-induced pressor response. We are currently investigating the effect of labetalol and other drugs on vaginal blood flow using infrared photoplethysmography and the results will be presented later.

This study has shown that a single dose of labetalol (100 mg) is more effective than propranolol (80 mg) in inhibiting the rise in blood pressure that occurs at orgasm induced by effortless autostimulation. Oral labetalol has previously been shown to inhibit in-

creases in systolic blood pressure induced by exercise in normotensive subjects (Richards *et al.*, 1974) and hypertensive subjects (Edwards & Raftery, 1976) and therefore should be effective in minimising the pressor response to coitus.

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