NOTE

Changes of Plasma Free Fatty Acids Levels after Oxytocin Administration in Man

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Synopsis

The effect of buccal administration of oxytocin tablet (100 u) on plasma FFA and TG was studied in healthy subjects. As a result, a decrease of plasma FFA ($101 \pm 27 \mu\text{Eq/l}$) in the male and an increase ($88 \pm 34 \mu\text{Eq/l}$) in the female were detected 60 min after the administration. Changes of plasma TG also suggested a similar tendency both in males and in females. Thus, sex differences in oxytocin effects on plasma FFA were observed after buccal administration, however the rate of change was rather small compared with the data obtained by intramuscular injection of oxytocin (5 u). The effect of oxytocin administration on plasma FFA was preliminarily investigated in female patients with simple obesity, and an increase of plasma FFA was found to be somewhat higher than in normal females.

The effect of neurohypophyseal hormones on plasma free fatty acids (FFA) has been reported by Mirsky (1963) in dogs, Goldman (1964) in man and Itoh *et al.* (1966) in rats. Despite the different species used in their experiments, the result unanimously indicated that neurohypophyseal hormones produced a decrease of plasma FFA concentration, and the mechanism of FFA-lowering action of Lys-vasopressin in rats was asserted as an inhibition of hormone sensitive lipase in the adipose tissue (Moriya and Itoh, 1969). On the other hand, an increase of plasma FFA after oxytocin administration to women was first reported by Burt and Leake (1962), and the sex differences in metabolic effects of oxytocin in man and dogs, that is, a decrease of plasma FFA in male and an increase in female, were clearly demonstrated by the sequential experiment (Burt, 1964).

In this paper, an attempt was made to see the effect of buccal administration of oxytocin

tablet (Sandoz), which became newly available in clinical use, on plasma FFA in normal subjects, and the result was compared with the data in the experiment of intravenous administration reported by Burt (1964) and with the data obtained by intramuscular injection of oxytocin (Syntocinon®, Sandoz). Furthermore, the FFA mobilizing effect of oxytocin was preliminarily examined in female patients with simple obesity. Changes of plasma triglycerides (TG) were also studied in normal subjects after buccal administration of oxytocin.

Methods

The effects of buccal administration of oxytocin tablet on plasma FFA and TG concentrations were observed in 5 healthy males and 4 healthy females. They had been fasted overnight and one tablet (100 u) of oxytocin was administered between 8 and 9 a.m. after control blood samples were taken. Blood samples were then taken 60 and 120 min after the administration, and plasma FFA was estimated by the

method of Dole (1956) and plasma TG by the method of Fletcher (1968).

The effect of 5 units of oxytocin i.m. on plasma FFA was studied by the same method in 3 of both healthy males and females and in 3 of female patients with simple obesity. In those cases blood samples were taken 30 and 60 min after the injection. In another female patient with simple obesity, effect on plasma FFA was also studied by single and double administration of oxytocin tablet and intravenous infusion of oxytocin (20 u of oxytocin in 300 ml of saline/120 min).

The ages of female subjects studied in this experiment were considerably divergent, however they had normal gonadal function, and their ovarian cycles were not taken into account when oxytocin was administered.

Results

The concentrations of plasma FFA and TG after buccal administration of oxytocin tablet in normal men are shown in Table 1. A

decrease of plasma FFA was observed in all 5 subjects investigated in this experiment, and in most of them the maximum effect of oxytocin was noticed by 60 min after the administration. There was a considerable individual variation in the effect on plasma TG, however a tendency to decrease was found 60 min after the administration, and the effect appeared to be remarkable in subjects with high plasma TG before the administration (S. S. and H. H.).

In contrast, plasma FFA increased 60 min after buccal administration of oxytocin in normal women, and plasma TG was also found to increase in 2 of them 120 min after the administration as shown in Table 2.

The results obtained by intramuscular administration of oxytocin are shown in Table 3 and 4. In normal subjects, almost the same effect of oxytocin was observed by intramuscular injection as by buccal administration,

Table 1. Plasma FFA and TG after buccal administration of oxytocin in normal men

Name	Age	FFA $\mu\text{Eq/l}$			TG mg/dl		
		0	60 min	120 min	0	60 min	120 min
S.S.	23	504	419	455	254	102	114
K.Y.	29	516	473	437	155	143	160
T.K.	48	650	577	613	126	105	109
H.H.	33	717	505	499	172	119	153
H.K.	37	599	498	555	—	—	—
ΔFFA or ΔTG^*			-101 ± 27	-85 ± 34		-60 ± 32	-43 ± 33

* Mean differences from pretest concentrations of FFA and TG.
(Mean $\pm$ S.E.)

Table 2. Plasma FFA and TG after buccal administration of oxytocin in normal women

Name	Age	FFA $\mu\text{Eq/l}$			TG mg/dl		
		0	60 min	120 min	0	60 min	120 min
K.K.	21	672	692	698	78	86	174
T.A.	50	783	868	850	85	132	176
S.S.	40	751	930	959	74	78	—
T.N.	29	763	832	883	114	106	101
ΔFFA or ΔTG^*			$+88 \pm 34$	$+105 \pm 39$		$+13 \pm 12$	$+58 \pm 36$

* Mean differences from pretest concentrations of FFA and TG.
(Mean $\pm$ S.E.)

however the rate of increase in plasma FFA in the female was prominent compared with the rate of increase by buccal administration. In 3 female patients with simple obesity, a mean increase of plasma FFA 30 after the administration was found to be somewhat higher than in the normal women, but such a difference was not noticed 60 min after the administration.

In Figure 1, changes of plasma FFA after buccal and intravenous administration of oxytocin in a female patient with simple obesity were depicted. No marked difference was detected in the maximum increase of plasma FFA among 3 kinds of administration, but the increase of plasma FFA after buccal administration in this case was higher than in the normal female.

Table 3. Plasma FFA after intramuscular administration of oxytocin in normal subjects

Name	Sex	Age	FFA μ Eq/l		
			0	30 min	60 min
A.M.	M.	24	416	384	290
T.T.	M.	24	576	477	408
S.Y.	M.	42	334	315	208
Δ FFA(mean $\pm$ SE)*				-50 ± 25	-140 ± 14
M.M.	F.	21	545	725	868
K.M.	F.	37	786	1060	1083
F.M.	F.	30	525	611	744
Δ FFA(mean $\pm$ SE)*				$+180\pm 54$	$+279\pm 31$

* Mean differences from pretest concentration of FFA.

Discussion

The efficacy of buccal administration of oxytocin has been well recognized in the field of obstetrics. The results presented in this paper have shown that buccal administration of oxytocin also has a similar effect on plasma FFA as observed by intravenous or intramuscular administration. Compared with the data reported by Burt (1964) who used rapid infusion, changes of plasma FFA after buccal administration were rather small and the changes after intramuscular injection were about the same. The smaller changes after buccal administration were thought to be caused by slow and poor absorption of oxytocin through the mucous membrane. Nevertheless, sex differences in the effects of oxytocin on plasma FFA were clearly demonstrated by buccal administration.

Precise mechanism of sex differences in the oxytocin effect was not elucidated yet, although the plasma FFA-elevating effect of oxytocin in women was shown to be dependent on gonadal function (Burt 1964). In normal rats, oxytocin did not produce any effects on plasmal FFA, but this hormone increased plasma FFA concentration in the dehydrated female rat and did not show any significant change in the dehydrated male (Yano *et al.* 1971). Those results indicated that the female adipose tissue of rat was also sensitive to oxytocin in FFA mobilization, even though the same pattern of sex differ-

Table 4. Effect of oxytocin administration i.m. on plasma FFA in female patients with simple obesity

Name	Age	Height (cm)	Weight (kg)	FFA μ Eq/l		
				0	30 min	60 min
J.U.	18	154	88.5	685	936	1040
T.Y.	43	156	79.0	860	1130	1165
R.W.	27	150	85.0	521	914	794
Δ FFA (mean $\pm$ S.E.)*					$+287\pm 27$	$+311\pm 24$

* Mean differences from pretest concentration of FFA.

Fig. 1. Effect of oxytocin administration on plasma FFA in a patient with simple obesity.
(K.O. 14 yrs., female. Height 157 cm, weight 70 kg)

ences as in man and dogs was not clearly demonstrated.

The effect on plasma TG concentration was also investigated in this experiment. It was difficult to draw a conclusion from the small number of subjects, but the similar tendency of sex differences in the oxytocin effect was conjectured. Those results might suggest that FFA mobilized from the female adipose tissue was partially converted to TG in the liver and consequently released to the blood as TG. On the contrary, an inhibited release of FFA from the male adipose tissue after oxytocin administration was thought to bring a decrease in plasma TG concentration.

In addition, it was of interest to find an accentuated increase of plasma FFA concentration after oxytocin administration in the female patients with simple obesity. Since this result was only preliminary, further study must be conducted to obtain a definite conclusion.

References

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