

Epidermal Growth Factor Plasma Concentrations in Healthy Control Persons, Acute and Chronic Stress and During Pregnancy

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Summary

Plasma concentrations of Epidermal Growth Factor (EGF) in healthy control persons do not change significantly during adult lifetime and no diurnal changes could be detected. In addition, no alterations of plasma EGF concentrations occur during acute and chronic stress and in all three trimesters of pregnancy. Thus, the previously suggested theories that EGF might play a causative role in the activation of the hypothalamic-pituitary adrenal axis during the stress reaction and in the prevention of peptic ulcers in pregnancy could not be confirmed by the present data.

Key words

Epidermal Growth Factor (EGF) – Stress – Pregnancy

Introduction

Epidermal Growth Factor is a 6000 dalton polypeptide that had already been isolated in 1975 (Gregory 1975). Immunocytochemical studies showed a high concentration of EGF in the submandibular gland (Hirata and Orth 1979). Since then, numerous studies have been conducted to determine the physiologic and/or pathophysiologic relevance for EGF. A potential role of EGF has been postulated in wound healing (Niall, Ryan and O'Brien 1982), the low incidence of peptic ulceration during pregnancy (Gregory 1975), spermatogenesis (Tsutsumi, Kurachi and Oka 1986) and the stress reaction (Luger, Calogero, Kalogeras, Gallucci, Gold, Loriaux and Chrousos 1988). Tsutsumi et al. describe a marked decrease in sperm content of the epididymis in mice after sialadenectomy when EGF plasma concentrations are undetectable. After daily administration of EGF a dose dependent increase of sperm count could be detected. In addition Luger et al. demonstrated that EGF stimulates the hypothalamic-pituitary-adrenal axis in a dose dependent manner in rhesus monkeys. Because of these observations made after alteration of EGF plasma concentrations, it seemed of interest to determine plasma EGF concentrations in humans under different pathophysiologic conditions.

The aim of the present study was to test whether alterations of EGF plasma concentrations can be found during the stress reaction and during pregnancy to support the postulated involvement of EGF under these conditions.

Materials and Methods

EGF plasma concentrations were measured with the radioimmunoassay from Amersham, modified as described previously (Svoboda, Woloszczuk, Horzemska and Luger 1989).

A normal range was evaluated in 43 healthy control persons (33 male, 10 female, aged between 22 and 74 years) (range: 700–1700 pg/ml, mean: 1287 ± 39.7). Plasma samples were drawn between 8 and 9 a.m. in heparinized tubes, centrifuged immediately and deep frozen.

In order to detect whether EGF plasma concentrations change with age, EGF plasma concentrations in 7 healthy volunteers, all older than 60 years (mean 75 ± 3.2) were compared to those in 12 younger control persons (mean 26 ± 0.6). In order to detect any potential diurnal rhythm EGF plasma concentrations were measured in 6 healthy control persons at 8 a.m., 4 p.m. and 10 p.m.

Stress reaction

To test for a potential role of EGF in stress reactions, EGF plasma concentrations were measured in 13 critically ill patients whose condition was regarded as typically inducing chronic stress (characteristics of these patients are given in Table 1) and in 14 male healthy volunteers before, during, immediately after and thirty minutes after bicycle ergometry to exhaustion, representing acute stress.

EGF during pregnancy

Plasma concentrations of EGF were measured in 57 pregnant women (17 in the first, 21 in the second and 19 in the third trimester of pregnancy).

All results are given as mean \pm SEM. For statistical evaluation the Kruskal-Wallis test was used.

Results

Mean EGF plasma concentrations in subjects older than 60 years (mean 1395 ± 141.5 pg/ml) did not differ significantly from those in younger control persons (mean 1233 ± 103.6 pg/ml).

Table 1 Characteristics of the chronically stressed patients.

Patient	Age	Sex	Disease	EGF pg/ml
1	77	m	cerebral haemorrhage	800
2	54	m	sepsis	880
3	16	m	system. lupus erythematosus, sepsis	1100
4	60	m	terminal metastatic prostatic cancer	1010
5	60	m	terminal metastatic prostatic cancer	890
6	19	f	system. lupus erythematosus, sepsis	1340
7	32	m	hairy cell leucaemia, sepsis	948
8	40	f	terminal metastatic thyroid cancer	1197
9	64	m	terminal metastatic prostatic cancer	1307
10	70	m	terminal metastatic prostatic cancer	1396
11	64	f	terminal metastatic cancer of the breast	1121
12	60	m	myeloma	807
13	18	f	systematic lupus erythematosus, sepsis	1280

Table 2 EGF plasma concentrations during the day at 8 a.m., 4 p.m. and 10 p.m.

	8 a.m.	4 p.m.	10 p.m.
EGF pg/ml	1215.8 ± 83.2	1068 ± 131	1049 ± 116

In addition no diurnal changes in plasma EGF concentrations could be observed (Table 2).

Stress reaction

EGF plasma levels in 13 critically ill persons (Table 1) representing chronic stress lay well within normal range (mean 1080 ± 113 pg/ml) (Figure 1). In addition EGF plasma levels in 14 male healthy volunteers before and after bicycle ergometry were measured. As in chronically stressed patients, also acute stress induced no significant increases in EGF plasma levels (Figure 1).

EGF during pregnancy

In all three trimesters of pregnancy EGF plasma concentrations were within normal range (Figure 2).

Discussion

In the present study the postulated involvement of EGF in the stress reaction and in the prevention of peptic

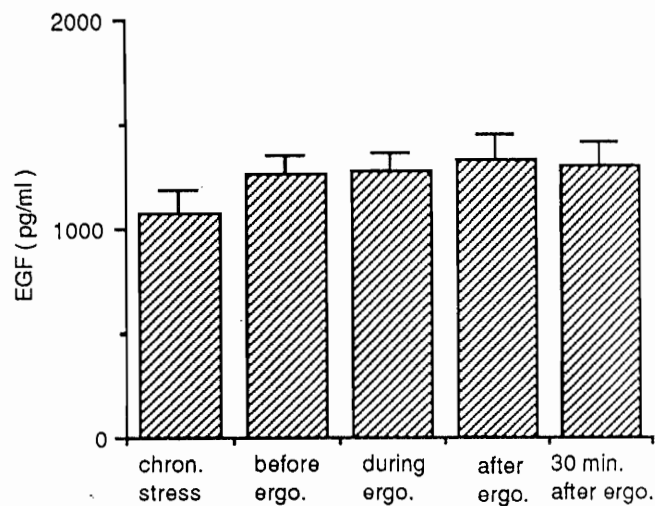


Fig. 1 Plasma levels of EGF in chronic stress, before, during, after and 30 min after ergometry (normal range 700–1700 pg/ml).

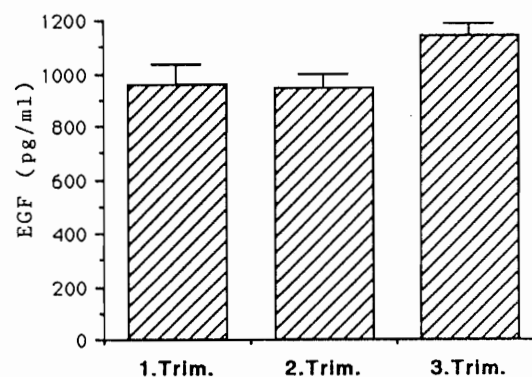


Fig. 2 Plasma levels of EGF during the three trimesters of pregnancy (normal range 700–1700 pg/ml).

ulceration during pregnancy could not be confirmed. Although it has been reported that EGF is able to elevate ACTH and cortisol concentrations in a dose dependent manner, this does not seem to be one of the physiologic mechanisms in the stress reaction, since plasma levels of EGF were found to be normal in acute and chronic stress.

Since no elevation of plasma EGF concentrations during pregnancy could be observed, the importance of circulating EGF in the protection of the gastric mucosa during pregnancy can be discarded, whereas a direct effect of EGF on the gastric mucosa cannot be excluded. However direct measurement of EGF concentrations in the gastric juices can hardly be performed in pregnancy and salivary EGF concentrations vary over a wide range (Svoboda, Woloszczuk, Horzemsky and Luger 1988). Furthermore one would have also to consider saliva production in nonpregnant and pregnant women and thus no definite conclusion on the role of EGF in the prevention of peptic ulcers during pregnancy can be drawn.

In summary the physiologic and/or pathophysiologic role of EGF remains unclear.

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