# PROSTAGLANDIN $E_2$-INDUCED INHIBITING EFFECT ON HUMAN PLASMA PROLACTIN IN EARLY PUERPERIUM

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SUMMARY

On the fourth day after delivery $PGE_2$ was given orally in a dose schedule of 2 mg every 30 minutes for a total dose of 8 mg to twelve puerperal women. Serum prolactin showed a significant decrease in comparison to basal levels and to those of controls during the control times. The authors suggest that $PGE_2$-induced prolactin decrease could be mediated by hypothalamic dopaminergic neurons or by an hypothetic prostaglandin-receptor in the brain.

## INTRODUCTION

One might expect that prostaglandins contributed to hypothalamo-pituitary function because they are widely distributed in the central nervous system, including the hypothalamus ([1]). In recent years evidence has arisen concerning the existence of dopaminergic control on prolactin secretion from experiments carried out on animals and humans ([2, 3, 4, 5]). Several studies have been made on prostaglandins and prolactin secretion: Tucker et al. ([6]) have reported that prostaglandin $F_2\alpha$($PGF_2\alpha$) induces prolactin release in cows; Vermouth ([7]) and Yue ([8]) have referred $PGF_2\alpha$-induced prolactin release in early pregnancy. Ojeda ([9]) and Warberg ([10]) did not see any change in prolactin plasma values after the prostaglandins' injection in cerebral ventricles. The present study was designed to evaluate the prolactin plasma levels changes induced by orally administered prostaglandin $E_2$ ($PGE_2$) during the early puerperium.

## MATERIAL AND METHODS

Oral $PGE_2$ (0.5 mg tablets) — in a dose schedule of 2 mg every 30 minutes for a total dose of 8 mg — was given to twelve puerperal women, who did not want to nurse, on the fourth day after delivery.

Twelve control puerperae received placebo by the same schedule. The drug was administered in the morning (9 a.m.). Blood samples were collected before and then at 30, 60, 90, 120 and 240 minutes after the onset of the treatment.

Heparinized plasma was stored at — 20 °C until the assay. Concentrations of prolactin in the serum were measured by radioimmunoassay (Biodata, Italy), which have a coefficient of variation of 5 % (within assay) and 9 % (between assay). Data were statistically analysed by Student's test.

## RESULTS

Both the $PGE_2$-treated and control patients showed similar average basal levels of prolactin, according to normal puerpe-

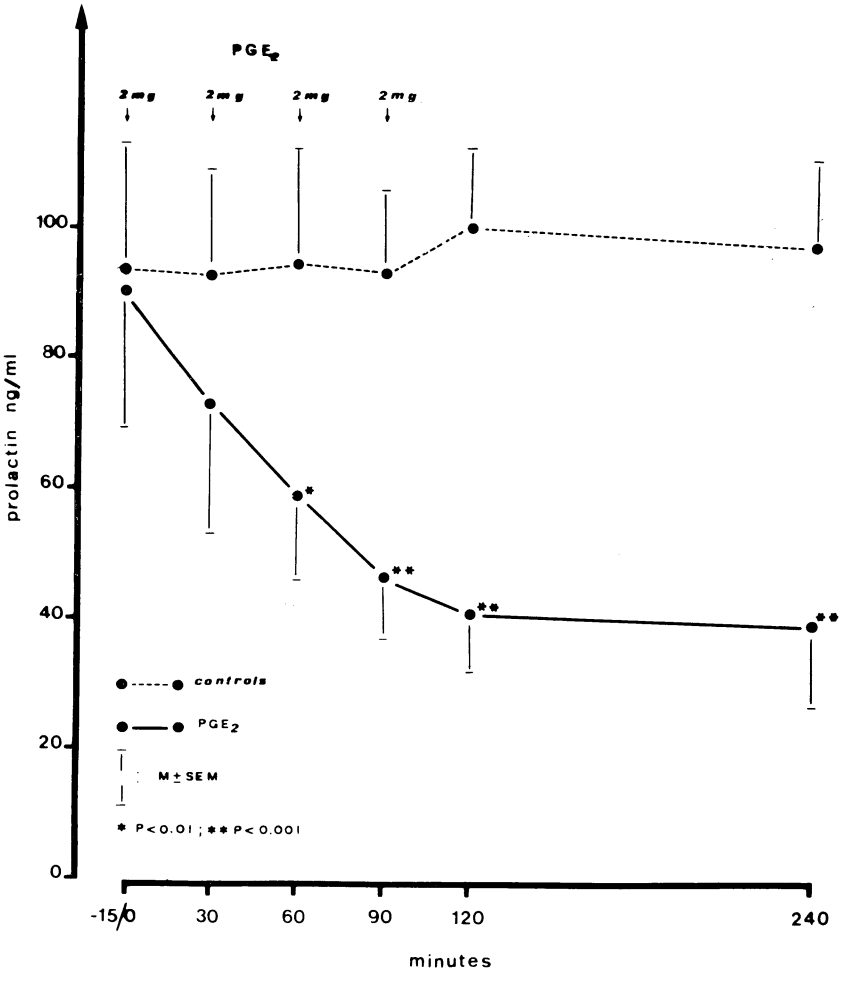


Fig. 1. — Serum prolactin decrease induced by oral prostaglandin $E_2$ in twelve puerperal women on the fourth day after delivery.

rium ([11]). In the $PGE_2$- treated women serum prolactin dropped from 91.4±23.5 ng/ml at 0 time to 73.7±20.0 ng/ml at 30 minutes, 58.8±12.3 ng/ml at 60 minutes, 47.2±9.1 ng/ml at 90 minutes, remaining constantly low at 120 (42.5± 7.9 ng/ml) and 240 minutes (46.4±8.1 ng/ml) (fig. 1).

The plasma prolactin of control patients (mean of basal levels 94.2±26.1 ng/ml) remained unchanged at all control times. When compared with initial values and control levels the drop of plasma prolactin was statistically significant at 60 ($P<0.01$), 90, 120 and 240 minutes ($P<0.001$).

## DISCUSSION

Prolactin secretion is regulated by a tonic inhibition secondary to a hypothalamic factor known as prolactin inhibiting factor (PIF) ([12]). Interruption of the hypothalamic-pituitary portal system results in a rapid elevation of serum prolactin confirming the findings relative to a hypothalamic control of prolactin secretion ([13]). Hypothalamic PIF is controlled by dopaminergic neurons, which, when stimulated, produce PIF ([12]). Although dopamine appears mainly to affect prolactin secretion, recent studies have hypothesized that also serotonin could modulate prolactin secretion by stimulating prolactin releasing factor (PRF) ([14]). It is conceivable, however, that the regulation of prolactin is a results of a balance between PIF and PRF. Recent evidence suggests that prostaglandins may act as mediators of the hypothalamic function ([15, 16]) by mediating or modulating the action of synaptic transmitters such as dopamine ([17]) which has been shown to release the PIF. From our data there is evidence that $PGE_2$ induces a decrease of prolactin secretion, but it is still unclear if this effect is exerted directly on the pituitary or mediated by some hypothalamic site. We believe it unlikely that $PGE_2$ could act directly on the pituitary, because as previously reported by us([18]) $PGE_2$ administration seems ineffective to modify pituitary adenoma-induced hyperprolactinemia, while significantly suppressing prolactin secretion in functional hyperprolactinemia. $PGE_2$ could inhibit prolactin secretion indirectly by acting on the hypothalamic median eminence, presumably via dopamina, as referred to by Fioretti et al. ([19]). They observed a dopamine increase in median eminence followed by prolactin plasma decrease after $PGF_2\alpha$ administration in nursing rats. Since the presence of prostaglandin receptors has been reported in several tissues ([20, 21, 22]), it is probable that a prostaglandin receptor in the brain is activated for $PGE_2$-induced prolactin decrease, as suggested by Warberg et al. ([10]) for prostaglandin-induced LH release. Moreover, since it has been demonstrated in the human that $PGE_2$ can be converted into prostaglandin F derivatives ([23]), it is possible that the prolactin decrease is not a direct effect of $PGE_2$ but may be mediated by its F derivatives. However, further investigations are needed to validate these hypotheses.

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