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Inhibitory Effects of PGE_1 and E_2 on Glucose Induced Insulin Release

Evidences in the literature describe PGs as being both, stimulatory and inhibitory to insulin secretion, depending on variables such as the *in vitro* or *in vivo* preparations and animal species studied (4). Virtually, all of the *in vivo* data indicate that PGE_1 and E_2 inhibit insulin secretion independently of α-adrenergic activity (3, 5).

No information is available on the effect of PGE_1 and E_2 on insulin secretion at different glucose concentrations *in vivo*, and in order to establish this effect we have administered PGE_1 or E_2 intraarterially, with and without glucose.

Female Wistar rats, weighing between 200-250 g were fasted for 24 h and anesthetized with pentobarbital (50 mg/kg) intraperitoneally. PGE_1, PGE_2 —prepared as described by BARLET (1)— or glucose, was administered in the abdominal aorta at caeliac artery level, using a procedure described in detail by GARCÍA CASARRUBIOS *et al.* (2).

Blood samples (0,6 ml) were collected from the jugular at different times: 0, 15, 30, 45 and 60 min after PGs or/and glucose administration. Only three samples were collected of each animal. Glycemia and insulinemia were determined in: a) untreated rats (receiving an equal volume of NaCl 9‰); b) rats with a PGE_1 injection (100 μg/kg body weight); c) rats with a PGE_2 injection (100 μg/kg); d) rats with a glucose dose (500 mg/kg); e) rats treated with PGE_1 (100 μg/kg) and glucose (500 mg/kg), and f) rats treated with PGE_2 (100 μg/kg) and glucose (500 mg/kg).

Insulin was determined in the plasma samples by a rat insulin radioimmunoassay kit (Novo, Denmark) and glucose, by a glucose-oxidase kit (Boehringer-Manheim). Statistical analysis was performed by Student's t test.

When PGE_1 and E_2 were administered together with a glucose pulse, the inhibitory effect on glucose induced insulin release confirms previous reports (2, 4) and the results are not significantly higher than those obtained with PGE_1 or E_2 without glucose (table I).

These data demonstrate that, intraaortic PGE_1 and E_2 injection inhibits insulin release independently of glucose administration. This inhibition was accompanied by a increase on glycemia (table II) suggesting that, the reduction in insulin release was physiologically significant.

Our results have clearly shown that under PGs influence, the pancreatic activity is characterized by an apparent inability to respond to glucose signals, and the secretory response is the same at high or low glucose concentration. This secretory pathway is similar in adult-onset diabetics, where lacks an acute insulin response to an intravenous glucose challenge, thus, the possibility that PGs have an interesting role in the pathogenesis of diabetes mellitus could be considered.

WAITZMAN and RUDMAN (6) found a higher concentration of PGs in blood

Table I. *Effect of PGE_1 and E_2 on basal or glucose stimulated insulin release.*
Values are means (ng/ml) ± S.E.M.; number of experiences in parentheses.

TIME (min):	0	15	30	45	60
BASAL CONTROL	0.610 ± 0.063 (6)	0.523 ± 0.066 (6)	0.532 ± 0.052 (6)	0.480 ± 0.039 (6)	0.552 ± 0.048 (6)
PGE_1	0.602 ± 0.077 (6)	0.501 ± 0.043 (6)	0.512 ± 0.073 (8)	0.457 ± 0.074 (6)	0.544 ± 0.122 (6)
PGE_2	0.599 ± 0.063 (6)	0.238 ± 0.060* (6)	0.243 ± 0.045* (6)	0.342 ± 0.054 (6)	0.331 ± 0.089 (6)
GLUCOSE CONTROL	0.593 ± 0.053 (6)	1.041 ± 0.131 (6)	0.897 ± 0.153 (6)	0.724 ± 0.054 (6)	0.681 ± 0.063 (6)
PGE_1 + GLUCOSE	0.608 ± 0.064 (6)	0.539 ± 0.118* (6)	0.445 ± 0.111* (6)	0.430 ± 0.072* (6)	0.654 ± 0.148 (6)
PGE_2 + GLUCOSE	0.592 ± 0.048 (6)	0.303 ± 0.072* (6)	0.370 ± 0.074* (6)	0.313 ± 0.090* (6)	0.364 ± 0.066* (6)

* Significant difference ($p < 0.05$) from basal or glucose control (Student's t test).

Table II. *Effect of PGE_1 and E_2 on plasma glucose concentration with and without glucose administration.*
Values are means (mg/100 ml) ± S.E.M.; number of experiences in parentheses.

TIME (min):	0	15	30	45	60
BASAL CONTROL	86.7 ± 5.6 (9)	86.9 ± 6.4 (9)	86.0 ± 4.4 (9)	85.2 ± 4.7 (9)	85.1 ± 7.1 (8)
PGE_1	85.8 ± 2.8 (7)	126.7 ± 10.0* (7)	132.0 ± 4.5* (6)	141.9 ± 11.6* (9)	124.4 ± 13.8* (6)
PGE_2	86.7 ± 5.6 (9)	120.2 ± 6.9* (9)	118.5 ± 5.0* (9)	121.1 ± 8.4* (9)	123.8 ± 7.6* (9)
GLUCOSE CONTROL	86.6 ± 2.3 (20)	198.4 ± 12.9 (10)	162.2 ± 11.9 (10)	143.4 ± 6.8 (10)	127.2 ± 8.9 (9)
GLUCOSE + PGE_1	85.7 ± 1.4 (10)	186.9 ± 10.9 (10)	177.7 ± 10.5 (10)	171.9 ± 3.7* (9)	171.3 ± 8.7* (8)
GLUCOSE + PGE_2	85.9 ± 2.7 (15)	201.7 ± 9.9 (11)	187.7 ± 8.3 (11)	185.2 ± 6.7* (11)	182.6 ± 7.6* (10)

* Significant difference ($p < 0.05$) from basal or glucose control (Student's t test).

from diabetic patients, compared with blood from non diabetics, these evidences and our results suggest that defects on insulin release in diabetes, could therefore be due in part, to an excessive production of PGs. Our failure to demonstrate an augmentation on insulin release by a high concentration of glucose in presence of PGs, indicates that both compounds interact in a not competitive and complex manner, in order to modify the β cell secretory process.

Key words: PGsE, Insulin inhibition.

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A. VILLAR DEL FRESNO, M. P. D'OCON, M. D. IVORRA and E. ANSELMI

Departamento de Farmacognosia
y Farmacodinamia
Facultad de Farmacia
Valencia-10 (Spain)

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