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ORIGINAL ARTICLE

Effect of 24, 25-dihydroxycholecalciferol on the placental immunoreactive calcitonin

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Abstract

OBJECTIVES: Calcitonin (CT) has a regulative function in calcium (Ca) transfer from mother to the fetus. There are indications that cholecalciferol can play a role in this process. With this background, the effect of 24, 25-dihydroxycholecalciferol (24, 25-DHC) on immunoreactive CT by human placenta at term was studied in vitro.
METHODS: Placental tissue samples were incubated in culture medium with normal total Ca (1.3 mM) concentrations during 6 hours at 37°C. 24, 25-DHC was added to the samples.
RESULTS: Addition of 24, 25-DHC in concentrations of 25, 75 and 150 pg/ml was followed by a significant decrease of CT levels in medium. The concentrations decreased from 100% (basis value after 2 hours) to 31%, 46% and 49% respectively.
CONCLUSION: Probably 24, 25-DHC has a modulating effect on the regulation of placental Ca transfer by CT.

Introduction

Recently it was demonstrated that CT is produced, secreted as well as degraded by human placenta at term, in vitro [1, 2, 3]. These facts suggest that the hormone is involved in regulation of Ca transfer from mother to the fetus. There are also indications that human placenta can metabolize cholecalciferol and has target sites for 24, 25-DHC too. Raising the question as to the biological significance of 24-, 25-DHC, it was investigated if there is a correlation between this metabolite and CT.

Material and Methods

Human placentae at term were obtained immediately after delivery from five healthy mothers. An informed maternal consent was present. Separate placental tissue samples (1 g) were washed with 0.9% NaCl, cut in slices of about 1 mm and incubated in flask with 5 ml Hank's solution with 1.3 mM Ca and 0.8 mM magnesium, for 6 h in an atmosphere of 95% air and 5% CO_2. In three parallel incubations, 2 h after the start of the experiments, 24, 25-DHC in concentrations of 25, 75 and 150 pg/ml was added to the media, and incubated as above. The CT concentrations into the media were determined hourly. The secretion during the first 2 h was fixed as basic value (100%). The change of concentrations during the following hours was set in reference.

The CT concentrations in the medium were determined by radioimmunoassay (Institut National des Radioelements, Belgium). The standard was human synthetic CT. An antibody with titer 1: 25,000, raised in rabbit, was used. The lower limit of detection was 15 pg/ml. The nonspecific binding of the assay and the incubation media, without and with tissue samples, were 152 counts per minute (cpm), 158 cpm and 150 cpm respectively. The cross reactions with ACTH, CT, TSH, T3, T4, leucine- and methionine-encephalin were below 0.1%. The intra- and interassay coefficients of variation were 9.8% (n = 11) and 11.2% (n = 38). The Ca concentrations were measured by complexometric titration.

Results

The CT concentrations in the medium without 24, 25-DHC increased up to 109% during the 6 h-incubation. After addition of 25, 75 and 150 pg/ml 24, 25-DHC in the parallel incubations, the CT levels decreased significantly to 31%, 46% and 49% respectively (Wilcoxon test). The results are given in the table below.

Discussion

The present results indicated a decrease of placental CT after addition of 24, 25-DHC to the medium. Generally, the major significance of CT is the prevention of hypercalcemia. During pregnancy the hormone regulates also the Ca transfer from mother to the fetus and protects the skeleton against excessive demineralization by inhibition of bone Ca release [4, 5, 6].

CT exerts also central analgesic effects [7, 8, 9, 10]. These effects, based on a Ca ion reduction in the target cells, are related only to the specific aminoacid sequences with hypocalcemic action [10].

As previously mentioned, degradation of CT by placental tissue up to 35%, in vitro, was observed. The process is localized in the mitochondrial fraction of placenta and temperature dependent [3].

The mechanism of the CT decrease as observed in the present study is not clarified. In mammal placenta target sites for 1,25- and 24, 25-DHC were found [11, 12, 13]. It is accepted that the mammal placenta can convert 25-dihydroxycholecalciferol (25-DHC) to 1,25-dihydroxycholecalciferol (1,25-DHC) and 24, 25-DHC in vivo and in vitro [14,

CT concentrations in medium (Mean values in % ± SD)

Incubation time (h)	Without 24, 25-DHC	With 24, 25-DHC		
2.	100	100	100	100
3.	99 ± 9	50 ± 22	52 ± 10	63 ± 18
4.	96 ± 15	38 ± 7	50 ± 15	63 ± 21
5.	104 ± 17	35 ± 14	43 ± 11	65 ± 25
6.	109 ± 14	31 ± 10	46 ± 19	49 ± 24

Table. CT concentration in % ± SD (mean values of 5 placentae) as to basal value (100%, 2h) in media without and with 25 pg/ml, 75 pg/ml and 150 pg/ml 24, 25-DHC, respectively.

15, 16, 17, 18, 19, 20]. It is possible that 24, 25-DHC has a direct inhibitory effect on the placental CT synthesis. Such an inhibitory effect of 1,25-DHC on placental CT synthesis was observed. It is also conceivable that 24, 25-DHC stimulates the CT degrading enzymes. Probably 1,25- and 24, 25-DHC have a modulating effect on regulation of placental Ca transfer by CT. In general, 1,25-DHC regulates its own synthesis by feedback inhibition of 1-alpha-hydroxylase and stimulates in this way the transformation of 25-DHC to 24, 25-DHC. It is significant here that also 24, 25-DHC can effect a decrease of CT. Probably this process is induced in the last analysis by a relative Ca deficiency in the placenta. In this case, the role of hormones like parathyroid hormone, estrogen, prolactin and growth hormone is unknown.

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