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Clinical And Laboratory Findings Of 17α -Hydroxy-Progesterone In Women At Risk For Preterm Delivery

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Progesterone (P) and 17α -hydroxy-progesterone caproate (17P) have long been considered important agents in maintaining uterine quiescence. The effectiveness of 17P in reducing preterm delivery firstly reported in the seventies has been further confirmed in a recent multi-centre, randomized trial, in women presenting with a previous preterm birth. However, very little is known about the mechanism(s) of action of P and 17P in prolonging gestation.

It seems possible that 17P increases the tocolytic effectiveness of endogenous substances accounting for uterine quiescence, such an effect being mediated by both genomic (receptor-mediated) and non-genomic mechanisms. Moreover, progesterone derivatives have been demonstrated to inhibit the activation of immune receptors which normally mediate inflammatory response in the uterus, cervix and placenta.

The pivotal role exerted by cervical maturation in the processes allowing spontaneous preterm delivery (PTD) has been acknowledged only in the recent years. It is generally accepted now that cervical remodeling, softening and effacement, is a multifactorial phenomenon accompanied by neutrophilic granulocytes invasion. Such an apyretic, inflammatory reaction is extensively mediated through the local release of cytokines.

In a recent trial we reported the treatment with high-dose 17P (341mg of i.m. Lentogest, AMSA, Italy, every 4 days, until 36th week) of women remaining undelivered after preterm labour. Cervical length was measured by transvaginal ultrasound at discharge, and at 7th and 21st day post discharge. The 17P treatment was associated with both a lower shortening of the cervix and a reduced rate of PTD.

In another study while confirming the above clinical findings, we collected a cervical swab for Interleukin (IL)- 1β , IL-6, IL-8, Tumor necrosis factor α (TNF α), and for Nitrates/Nitrites (NO x) assays. It was demonstrated that 17P action is associated with a decrease of cervical concentrations of IL- 1β .

The suppression of IL- 1β in the cervix seems a specific effect since the remnant pro-inflammatory cytokines we checked for remained unaffected, in both treated and untreated patients.

In humans, IL- 1β levels has consistently been found elevated in cervico-vaginal and/or cervical fluids, thus predicting those women destined to undergo spontaneous PTD. IL- 1β is an early marker of host-response to infection and seem to play a main role in host reaction, namely if PTD is associated with amniotic fluid infections. Indeed, IL- 1β initiate a cascade of paracrine events activating several cytokines. Thus, the observation that 17P induce a selective inhibition of cervical IL- 1β is a key phenomenon and possibly has a pivotal role in mediating the protective effect on PTD.

In conclusion, these findings reinforce the notion that high-dose 17P treatment represents a maintenance therapy in women remaining undelivered after a successful acute tocolysis. We speculate that preterm cervical ripening is a driver of PTD and the cervical inflammation is the main target of the inhibition exerted by 17P.