



# Recurrent Preterm Labor After Treatment with 17 Alpha-Hydroxyprogesterone Caproate (17-P) Therapy in Hispanic Females Living in Puerto Rico

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## ABSTRACT

Preterm delivery (PTD) continues to be the leading cause of infant mortality worldwide. A major risk factor is a prior spontaneous PTD (SPTD). Several studies have been conducted to evaluate the efficacy of 17-P in preventing recurrent PTD (RPTD) with conflicting results. In Puerto Rico (PR) the prevalence of PTD which was 19.8% in 2008 has decreased to 11% in 2019. In 2009, an island wide program of homecare administration of 17-P was instituted. The purpose of this study is to determine the efficacy of 17-P in preventing RPTD in patients with prior SPTD. A retrospective review of Hispanic women with singleton pregnancy and history of previous SPTD <37 weeks (n=3,344) treated between 2015 to 12/2019 was performed. The patients received 17-P 250mg IM weekly starting ideally at 16-20 weeks until 36 weeks. Most data was prospectively collected with retrospective record review for missing information. Institutional IRB approval was obtained. Results show that previous preterm deliveries: I=81%; ≥II=19%. Mean doses administered: 15.7 and mean GA at start of treatment: 18.6 weeks. PTD <37 weeks: 33.8%. Prolongation of pregnancy compared to earliest PTD was 6.2 weeks (95% CI 6.1-6.5) and last PTD was 5.6 weeks (95% CI 5.4-5.8). No correlation of the incidence of PTD with maternal age or weight found. This preliminary data shows that treatment with 17-P led to prolongation of pregnancy of at least 5 weeks when comparing patients to their own previous PTD. Although data on neonatal outcome was not available, 5-6 weeks prolongation of pregnancy can be expected to significantly decrease morbidity and mortality.

## BACKGROUND

- Despite improvement in pediatric and perinatal care for premature babies and the overall reduction of perinatal mortality, preterm delivery has an increasing trend and continues to be a leading cause of perinatal mortality
- Pregnancy history is important as ratio of previous term or preterm delivery affects the risk of subsequent PTD
- Multiple studies have been done to evaluate the efficacy of 17 alpha hydroxyprogesterone caproate (17-P) in preventing preterm delivery in different stances, all with conflicting results
- A study in 2003 showed that patients with singleton pregnancies and previous PTD that received weekly injections of 250mg 17-P starting at 16-20 weeks of gestational age until 37 weeks, had reduced risk of PTD by 30-40% and reduced risks of NEC, IVH and need for supplemental oxygen
- In 2009, an initiative for 17-P was implemented in Puerto Rico. However, no studies have been made in Puerto Rico regarding the use of 17-P and the prevention of preterm deliveries
- In 2019 a similar study: *17-OHPC to Prevent Recurrent Preterm Birth in Singleton Gestations (PROLONG Study): A Multicenter, International, Randomized Double-Blind Trial*, was conducted and found that 17-OHPC did not decrease recurrent PTB and was not associated with increased fetal/early infant death. The study lacked a distinct population which could explain findings

## METHODS

### 1. Data Collection

- Retrospective review of 3,809 patients
- Hispanic women with singleton pregnancy and history of prior SPTD treated with 17-P from 2015-2019
- Treatment consisted of 17-P IM weekly ideally starting at 16-20 WGA

### 2. Variables

- Record review to obtain information concerning prior SPTD and gestational age, when patient started 17-P, when she gave birth, and how many doses were administered

### 3. Statistical Evaluation

- Wilcoxon Matched-Pairs Signed rank test
- Chi Squar test
- Performed by Stephanie Rodriguez-Gali, Biostatistics Expert

## RESULTS

- Since there are no control groups, patients were compared against themselves
- WGA was subdivided into 5 categories to show the prolongation in weeks of Gestational Age at delivery as compared to the lowest birth date as seen in Table 1
- Previous pregnancies were divided into 3 main categories as can be seen in Table 2. The results had a statistically significant effect on Gestational Age at delivery in weeks of prolongation
- Mean doses of 17-P administered was 15.7
- Mean Gestational Age at start of treatment was 16.6 weeks
- 81% of patients had 1 previous PTD while 19% had 2 or more PTD's

**Table 1. Pregnancy prolongation in weeks by Weeks Gestational Age of lowest birth date**

Weeks Gestational Age of lowest birth date	n	Average in weeks	SD	CI 95%
16 to 20 weeks	283	16.33	0.361	15.619, 17.039
21 to 24 weeks	405	13.30	0.251	12.803, 13.790
25 to 28 weeks	422	9.897	0.200	9.503, 10.291
29 to 32 weeks	587	5.435	0.160	5.120, 5.749
33 to 36 weeks	1,604	2.004	0.073	1.860, 2.147

**Table 2. Prolongation of pregnancy in weeks**

	n	Average in weeks	SD	CI 95%
Under treatment vs. Most recent	3,301	5.65	0.110	5.433, 5.863
Under treatment vs. Lowest	3,301	6.24	0.111	6.019, 6.454
Under treatment vs. Highest	3,301	5.25	0.108	5.035, 5.460
Under treatment vs Average	3,301	5.74	0.107	5.527, 5.946

- No correlation was found between the time treatment was started and the GA at delivery as illustrated on Table 3
- Although we can't say duration of treatment is correlated to GA at birth, we saw that almost 2/3 of patients reached 37 weeks as evidenced by Table 4
- While most patients started treatment between 16-20 weeks and received an average of 16-21 doses of 17-P there was no correlation found between number of doses and GA at birth

## RESULTS

**Table 3. Gestational Age at birth vs. Gestational age at treatment start**

Gestational Age at beginning of treatment	< 37 weeks		37 weeks or more	
	Frequency	Percentage	Frequency	Percentage
16 a 20 weeks	856	34.63%	1,616	65.37%
21 a 30 weeks	239	32.34%	500	67.66%
<b>Total</b>	<b>1,095</b>		<b>2,116</b>	

**Table 4. Gestational Age at birth**

Gestational Age	Frequency	Percentage
< 32 weeks	253	7.57%
< 35 weeks	533	15.94%
< 37 weeks	1,130	33.79%
37 – 42 weeks	2,214	66.21%

## CONCLUSIONS

- Preliminary data shows that treatment with 17-P led to prolongation of pregnancy of at least 5 weeks when comparing patients to their own previous PTD
- Although data on neonatal outcome was not available, 5-6 weeks prolongation of pregnancy can be expected to significantly decrease morbidity and mortality
- Approximately 80% of patients started treatment at recommended GA, however, there was no relation seen on statistical evaluation of GA at the beginning of treatment when compared to GA at the moment of delivery
- It's important to consider that PTD conditions are unknown and medically indicated delivery should be considered as a factor in some patients
- Further studies are warranted which take into account medically indicated PTD and data showing patient's comorbidities which are risk factors for PTD

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