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17-hydroxyprogesterone caproate for women with congenital uterine anomalies: does it impact the risk of recurrent preterm birth?

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OBJECTIVE:

Since 2003, the American College of Obstetricians and Gynecologists has recommended the administration of 17-hydroxyprogesterone caproate (17-OHPC) for preventing recurrent preterm birth (PTB).^{1,2} The Food and Drug Administration recently recommended its withdrawal from the market as clinical benefit could not be verified. However, women with congenital uterine anomalies (CUAs) were excluded from all trials; thus, the utility of 17-OHPC in this population is unknown. We sought to describe the impact of 17-OHPC on delivery timing in women with CUAs and previous PTB.

STUDY DESIGN:

This is a retrospective cohort study, including singleton, nonanomalous gestations in women with CUAs who delivered in 2 tertiary health systems between 2013 and 2019. During this period, weekly administration of 17-OHPC from 16 to 36 weeks' gestation was offered to

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all women with a history of spontaneous PTB between 16 and 36 weeks' gestation. Among women with CUAs, usage was based on shared decision making. Demographics, obstetrical history, and delivery outcomes were abstracted from the electronic medical record. All women with CUAs and previous PTB were included. The primary outcome was recurrent PTB. Secondary outcomes included a PTB at <34 weeks' gestation and median gestational age (GA) at delivery. Women with CUAs who received 17-OHPC were compared with those who did not using bivariate statistics. This study was found exempt by the Duke University and University of North Carolina institutional review boards.

RESULTS:

Of 48 women with CUAs and previous PTB, 11 (23%) received 17-OHPC and 37 (77%) did not. Demographics, including CUA type, initial cervical length, and rates of short cervix (<25 mm), did not differ between the groups (Table). The recurrent PTB rate was high (46%) but did not differ between the groups (46.0% for the 17-OHPC group vs 45.5% for the non-17-OHPC group; $P>.99$). Of the 22 women with recurrent PTB, 50% experienced spontaneous PTB. Another 32% delivered prematurely with preterm premature rupture of membranes. Placentally mediated etiologies (14%) and history of classical cesarean delivery (5%) made up the nonspontaneous PTBs. Rates of preterm delivery before 34 weeks' gestation were elevated but without differences between the groups (27.3% for the 17-OHPC group vs 27.0% for the non-17-OHPC group; $P>.99$). The median GA at delivery was equivalent between the groups (37.7 [interquartile range (IQR), 30.7–38.3] in the 17-OHPC group and 37.1 [IQR, 31.0–38.4] in the none17-OHPC group).

CONCLUSION:

The use of 17-OHPC was low in this cohort of women with CUAs and previous PTB, likely related to the perceived differences in the mechanism of PTB in these women. Recurrent PTB was common, and the administration of weekly 17-OHPC did not affect this risk. Our data are limited by a lack of information regarding the timing of initiation and adherence to 17-OHPC, which could influence its perceived utility. Because women with CUAs were excluded from the original trials and the recent multinational PROLONG trial (17-OHPC to prevent recurrent preterm birth in singleton gestations), the efficacy of this medication on PTB prevention in this population is unclear.³ However, our data suggest that 17-OHPC may also not be effective for preventing recurrent PTB in women with CUAs. Further research with a larger cohort is needed to confirm this finding

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TABLE
Demographics of women with CUAs who received and did not receive 17-OHPC

Characteristic	Received 17-OHPC (n=11)	No 17-OHPC (n=37)	P value
CUA type			.07
Arcuate	3 (75.0)	1 (25.0)	
Septate	1 (7.0)	13 (93.0)	
Bicornuate	4 (20.0)	16 (80.0)	
Didelphys	2 (29.0)	5 (71.0)	
Unicornuate	1 (33.0)	2 (67.0)	
Maternal age (y)	31.0 (21.1–38.0)	31.6 (28.5–36.3)	.98
Black race	0 (0.0)	5 (13.5)	.58
Prepregnancy BMI (kg/m ²)	28.9 (26.4–32.1)	27.2 (23.6–32.9)	.55
Initial TVCL (mm)	34.0 (23.0–43.0)	41.0 (37.0–43.0)	.29
Short TVCL<25 mm	3 (27.3)	2 (8.0)	.15
Received vaginal progesterone	2 (18.2)	6 (16.2)	>.99

Data are presented as number (percentage) or mean (interquartile range).

17-OHPC, 17-hydroxyprogesterone caproate; *BMI*, body mass index; *CUA*, congenital uterine anomaly; *TVCL*, transvaginal cervical length.
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