

Title	Ketoconazole-induced estrogen deficiency causes transient decrease in placental blood flow associated with hypoxia and later placental weight gain in rats
Author(s)	Ichikawa, Aoi; Tamada, Hiromichi
Editor(s)	
Citation	Reproductive Toxicology. 2016, 63, p.62-69
Issue Date	2016-08
URL	http://hdl.handle.net/10466/15560
Rights	© 2016. This manuscript version is made available under the CC-BY-NC-ND 4.0 license http://creativecommons.org/licenses/by-nc-nd/4.0/

Table 1

Effects of KTZ treatment during various periods of pregnancy on the weight of fetuses and placentas.

	Control	Treatment period of KTZ (day of pregnancy)		
		9-11	12-14	15-17
No. of dams	6	5	7	7
No. of live fetuses per dam	11.5 ± 2.5	13.8 ± 0.8	13.0 ± 1.7	14.3 ± 1.8
Fetal weight (g)				
Male	3.57 ± 0.34	3.49 ± 0.17	3.60 ± 0.33	3.63 ± 0.24
Female	3.36 ± 0.22	3.35 ± 0.21	3.42 ± 0.26	3.48 ± 0.25
Placental weight (mg)				
Male	492 ± 59 ^a	458 ± 18 ^a	626 ± 88 ^b	516 ± 33 ^a
Female	476 ± 54 ^a	433 ± 36 ^a	614 ± 73 ^b	492 ± 49 ^a

Daily oral administration of KTZ (25 mg/kg) was given on Days 9 to 11, 12 to 14 or 15 to 17 of pregnancy and the fetuses and placentas were weighed on Day 20. Values are means ± SEM. ^{ab}Values of placental weights with different letters differ significantly at $p < 0.05$. There is no difference in the placental weights between male and female fetuses, while the values in the rats treated with KTZ on Days 12 to 14 are greater than the other groups regardless of fetal gender.

Table 2

Effects of KTZ and E₂ on percentage of sinusoid area per unit area in the labyrinth zone of placentas on Day 20 of pregnancy.

	Control	KTZ+0E ₂	KTZ+0.1E ₂	KTZ+1E ₂
Sinusoid area (%)	19.15 ± 1.63 ^a	46.16 ± 2.32 ^c	29.23 ± 2.93 ^b	27.62 ± 2.92 ^{ab}

KTZ (25 mg/kg/day) and E₂ (0, 0.1 or 1 µg/rat/day) were treated on Days 12 to 14 of pregnancy. Values are mean ± SEM (n=6). ^{abc}Values with different letters differ significantly at $p < 0.05$. The value in the KTZ+0E₂ group is greater than those in the other groups, and the value in the KTZ+0.1E₂ group is larger than that in controls.

Table 3

Effects of KTZ and E₂ on the number of erythrocytes and sinusoid area per unit area in the labyrinth zone of placentas on Day 14 of pregnancy.

	Control	KTZ+0E ₂	KTZ+1E ₂
No. of all erythrocytes	831.5 ± 75.5	838.0 ± 119.5	1100.0 ± 102.5
Ratio of fetal erythrocyte (%)	17.7 ± 4.0 ^a	45.2 ± 3.8 ^b	14.8 ± 2.8 ^a
Maternal sinusoid per unit area (%)	20.2 ± 3.2 ^a	11.9 ± 1.8 ^b	31.6 ± 1.4 ^c
Fetal sinusoid per unit area (%)	4.6 ± 0.6 ^a	10.8 ± 0.6 ^b	5.8 ± 0.9 ^a

KTZ (25 mg/kg/day) and E₂ (0 or 1 µg/rat/day) were administered on Days 12 to 14 of pregnancy. Values are mean ± SEM (n=6). ^{abc}Values with different letters within each row differ significantly at $p < 0.05$.