Effects of 5-Hydroxymethylfurfural on Pubertal Development of Female Wistar Rats

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Introduction

5-Hydroxymethylfurfural (HMF) is formed when sugars like glucose and fructose are heated in the presence of amino acids. HMF is naturally present in many foods and we are exposed to HMF in daily life. There are conflicting data on potential genotoxic, mutagenic, carcinogenic, DNA-damaging, organotoxic and enzyme inhibitory effects of HMF and its metabolites. We aimed to investigate toxic effects of HMF on reproductive system in peripubertal rats.

Method

In the study, 24 immature Wistar rats were divided into control and HMF groups fed 750 mg/kg/day and 1500 mg/kg/day for 3 weeks from postnatal day 21. They were controlled for vaginal opening (VO) daily and necropsied on postnatal day 44. Blood samples were collected with cardiac puncture on termination day. Follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), progesterone (P) and anti-Müllerian hormone (AMH) levels in blood serum were measured using rat-specific enzyme-linked immunosorbent assay kits. Hormone levels, reproductive organ weights and ovarian follicle counts were compared.

Results

High dosege HMF group had earlier VO with higher LH and E2 levels. High dosege HMF group also had increased number of secondary atrophic follicles and decreased AMH levels (Table 1, 2).

Table 1 Vaginal opening time (in days) in different experimental groups

Parameter	Control Group								Low Dosage Group								High Dosage Group						
Subject	1	2	3	4	5	6	7	8	1	2	3	4	5	6	7	8	1	2	3	4	5	6	7
PND	34	37	40	40	40	43	43	43	33	37	40	44	44	-	-	-	33	33	33	37	37	37	40

Table 2: Measurements of serum hormone levels, weight of reproductive organs and follicle counts of the study groups

Parameter (mean ± SD)	Control (n=8)	Low Dosage (n=8)	High Dosage (n=7)
FSH level (ng/ml)	9.4 ± 1.9	10.1 ± 3.1	13.7± 3.6
LH level (mlU/ml)	1.3 ± 0.3	2.2 ± 1.5	2.9 ± 1.2*
E2 level (pg/ml)	21.2 ± 3.9	20.1 ± 8.6	34.7 ± 8.8*,**
P level (ng/ml)	10.1 ± 1.8	9.7 ± 1.6	11.2 ± 2.4
AMH level (ng/ml)	4.7 ± 0.7	4.1 ± 0.8	2.7 ± 0.5*,**
Relative weight of ovaries (mg/%)	59.4 ± 12.6	51.9 ± 9.0	57.4 ± 10.0
Relative weight of uterus (mg/%)	214.0 ± 77.4	242.5 ± 125.1	339.0 ±141.0*
Healthy secondary follicles (n)	53.0 ± 16.4	77.8 ± 24.4	70.5 ± 21.3
Atrophic secondary follicles (n)	4 ± 1.6	6.1 ± 1.8*	8.0 ± 4.0*
Healthy tertiary follicles (n)	6.6 ± 2.6	8.5 ± 3.5	7.8 ± 3.8
Atrophic tertiary follicles (n)	2.1 ± 1.8	2.8 ± 1.2	2.8 ± 0.8
Atrophic/total follicle (%)	10.3 ± 7.0	9.8 ±2.9	11.9 ±3.8

*Significantly different ($p \leq 0.05$) from the control group
** Significantly different ($p \leq 0.05$) from low dosage group

Conclusion

These results indicate that peripubertal exposure to HMF in high doses result in precocious puberty and decreased AMH levels in female Wistar rats.