Critical Periods for TCDD-Induced Cleft Palate in Mice (*Mus musculus* L.)

Kerentanan Palatogenesis Mencit (*Mus musculus* L.) terhadap Induksi Cleft Palate TCDD

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Abstract

An experiment was conducted in order to test the susceptibility of mice palatogenesis to the effects of 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD). The experiments were designed according to Completely Randomized Design with a 4 X 3 factorial experiment. Forty-eight pregnant mice were given TCDD at a dose of 0 (control), 5, 10 or 20 µg / kg bw on gestation days (GD) 9–10, 11–12, or 13–14. TCDD was solubilized in DMSO, diluted in sesame oil to appropriate volume and administered to mice orally by gavage; control group received the vehicle only (98.5% sesame oil + 1.5% DMSO). On GD 18 mice were anesthetized and then killed by cervical dislocation. Fetuses with cleft palate (cp) were calculated (%), degree of palatal closure were scored, and the feature of cleft palate were observed in 6 µm craniofacial microsections. Result showed, TCDD treatment on GD 9 to 12 induced cp; the highest induction was on GD 9–10 treatment. TCDD dose of 10 or 20 µg / kg bw when given on GD 9–10 or on GD 11–12 induced cp in more than 90% of the offspring. The percentages of cp were still high when the treatments were given on GD 11–12, especially with dose of 20 µg / kg bw (87.3%). The lowest dose of TCDD (5 µg / kg bw) induced cp which was dominated by narrow-gap feature, indicating that fusion stage was disturbed; dose of 10 or 20 µg / kg bw induced cp with intermediate-gap or wide-gap feature, suggested that there has been a disruption in initiation or elevation stage. In conclusion, all stages of palatogenesis were susceptible to TCDD effects, but the most susceptible was fusion stage.

Key words: TCDD, palatogenesis, *cleft palate*

Abstrak

Telah dilakukan percobaan untuk menentukan tahapan palatogenesis pada mencit (*Mus musculus* L.) yang rentan terhadap efek polutan 2,3,7,8-Tetraklorodibenzo-*p*-dioksin (TCDD). Percobaan dirancang mengikuti Rancangan Acak Lengkap dengan pola faktorial (4X3). Empat puluh delapan ekor mencit bunting dicekok TCDD dengan dosis 0 (kontrol), 5, 10, atau 20 µg/kg bb. Perlakuan diberikan pada hari kebuntingan (Hk) 9−10, 11−12, atau 13−14. Mencit kontrol dicekok pelarut saja (98,5% minyak wijen + 1,5% DMSO). Pada Hk 18 mencit dibius lalu dibunuh dengan teknik *cervical dislocation*, persentase fetus *cleft palate* (cp) dihitung, derajat penutupan palatum diberi skor, preparat dengan ketebalan 6 µm dibuat, dan mikrostruktur kraniofasial diamati. Hasil menunjukkan, pemberian TCDD antara hari ke 9 dan 12 menginduksi cacat cp, dengan kecenderungan hasil tertinggi pada pemberian Hk 9–10. Perlakuan TCDD dosis 10 atau 20 µg/kg bb pada Hk 9–10 menghasilkan fetus cacat cp >90%. Persentase fetus cp tetap tinggi pada pemberian Hk 11–12, khususnya pada kelompok dosis 20 µg/kg bb (87,3%). TCDD dosis terendah (5 µg/kg bb) menginduksi cp dominan bercelah sempit, menunjukkan adanya hambatan pada tahap fusi. Dosis 10 dan 20 µg/kg bb menginduksi cp bercelah sedang atau lebar, mengisyaratkan terjadi hambatan pada tahap inisiasi atau elevasi. Disimpulkan, seluruh tahapan palatogenesis rentan terhadap efek TCDD, namun tahap paling rentan adalah tahap fusi palatum.

Kata kunci: TCDD, palatogenesis, *cleft palate*