PENGARUH KHITOSAN TERHADAP KELAINAN RANGKA JANIN MENCIT (*Mus musculus*) AKIBAT ASAM RETINOAT

PRIJATNI, IDA
PEMBIMBING : Dr. Bambang Poernomo S. drh. MS.
RETINOID ACID; CHITOSAN; MUS MUSCULUS

RINGKASAN

Vitamin A adalah zat gm esensial untuk penglihatan, reproduksi, pertumbuhan dan diferensiasi jaringan. Vitamin A yang sering menimbulkan efek teratogenik adalah Asam Retinoat dan hasil metabolismenya yaitu all-*tran*-retinoid acid, 13-*cis*-retinoid acid dan 13-*cis*-4-oxoetinoid acid. Fungsi asam retinoat adalah sebagai regulasi dan transkripsi gen.

Toksisitas umumnya terjadi bila konsumsi melebihi 10x *Recommended Dietary Allowance* (RDA). Asam retinoat dengan dosis berlebih dapat menyebabkan kelainan rangka, pemendekan tulang rawan, penurunan jumlah jari-jari dan gangguan ossifikasi.

Khitosan yang disebut juga dengan β-1,4-2amino-dioksi-D-glukosamin, adalah senyawa turunan khitin yang diisolasi dari kulit udang dengan cara kimia atau enzimatis. Khitosan mempunyai kemampuan memperbaiki jaringan kondrosit dan tulang yang mengalami kerusakan dan juga merangsang pembentukan matrik protein extra seluler dari osteoklas dan kondrosit.

Tujuan dari penelitian ini adalah untuk membuktikan bahwa khitosan dengan dosis berbeda (15 mg/kg/BB, 30 mg/kg/BB, 45 mg/kg/BB) dapat mengurangi kelainan morfologi rangka dan kelambatan penulangan pada fetus mencit setelah diberi asam retinoat dengan dosis 60 mg/kg/BB pada usia kebuntingan induk mencit 10 hari.

Penelitian ini menggunakan rancangan *The Post Test Only Control Group Design* dengan hewan coba mencit (*Mus musculus*) umur 8-10 minggu dengan berat badan 20-25 gr, sebanyak 28 ekor mencit.

Khitosan diberikan dengan dosis 15 mg/kg/BB, 30 mg/kg/BB, 45 mg/kg/BB satu jam setelah induk mencit diberi asam retinoat dengan dosis tunggal 60 mg/kg/BB. Pada hari ke-18 dikorbankan, diwarnai dengan Alizarin Red S. dan diidentifikasi kelainan morfologi dan kelainan penulangannya.

Kelainan morfologi rangka fetus mencit dianalisa dengan *Wilcoxon Signed Ranks Test*, sedangkan untuk kelambatan penulangan rangka fetus mencit di analisa dengan Uji Anova Satu Arah dan bila ada beda dilanjutkan dengan *Least Significant Difference* (LSD).

Penelitian ini dapat disimpulkan bahwa tidak ada pengaruh pemberian khitosan dengan dosis berbeda terhadap kelainan morfologi rangka fetus mencit. Sedangkan pada kelambatan penulangan rangka fetus mencit dengan pemberian khitosan dengan dosis 15 mg/kg/BB, 30 mg/kg/BB dan 45 mg/kg/BB berbeda signifikan ($p < 0,05$) pada tulang sakrokaudalis, falanks distal anggota depan dan falanks distal anggota belakang.

SUMMARY

Vitamin A is essential nutrient for vision, reproduction, growth and tissue differentiation. Vitamin A that is often creates teratogenic effect is Retinoat acid and its metabolic result are all-tran-retinoid acid, 13-cis-retinoid-acid and 13-cis-4-oxoretinoid acid. The function of retinoat acid is regulator and transcription of gen.

Generally, toxicity occurred when consumption is more than 10x Recommended Dietary Allowance (RDA). Retinoat acid with excessive dosage will causes morphology malformation, shortening of cartilage, decreasing of limb amount and ossification disorder.

Chitosan or β-1,4-2amine-dioxy-D-Glucosamine, is hereditary of chitin compound that is chemically isolated from shrimp skin or enzymatic. has ability to repair chondrocyte tissue and damaged bone and stimulate the performing of extra cellular matrix protein of osteoblast and chondrocyte.

This research has aimed to prove that with different dosage (15 mg/kg of the weight, 30 mg/kg of the weight, 45 mg/kg of the weight) will decrease skeleton morphology malformation and delay ossification on mice fetus after treated by retinoat acid with dose 60 mg/kg of the weight on 18^{th} gestation days.

This research used The Post Test Only Control Group Design with 28 experimental mice (*Mus musculus*) with age 8-10 weeks, with weight 20-25 gr.

Chitosan was given with dosage 15 mg/kg of the weight, 30 mg/kg of the weight, 45 mg/kg of the weight on one hour after retinoid acid was given with single dose 60 mg/kg of the weight. On 18^{th} day, then mice was slaughtered and colored by Alizarin Red S and then morphology malformation and delay ossification was identified.

The morphology malformation of mice fetus was analyzed by Wilcoxon Signed Ranks Test, meanwhile, the delay ossification of mice fetus was analyzed by one way ANOVA and continued by Least Significance Differences (LSD).

The result of this research can be concluded that chitosan with different dosage are not influenced to morphology malformation of mice fetus. Meanwhile, the late ossification of mice fetus with treatment on dosage 15 mg/kg of the weight, 30 mg/kg of the weight and 45 mg/kg of the weight are different significantly ($p < 0.05$) on sacrum and caudal bone, phalanges distal of forelimb and phalanges distal of hindlimb.

ABSTRACT

The function of retinoid acid is regulator and transcription of gene, but on excessive dosage, that is more than 10x Recommended Dietary Allowance (RDA), Retinoat acid and its metabolic result, they are all-tran-retinoid acid, 13-cis-retinoid acid and 13-cis-4-oxoretinoid acid have teratogenic characteristic on mice fetus (disorder of skeleton, shortening of cartilage, decreasing of limb amount and ossification disorder).

Chitosan or β-1,4-2amine-dioxy-D-glucosamine, has ability to repair chondrocyte tissue and damaged bone and to stimulate the performing of extra cellular matrix protein of osteoblast and chondrocyte.

This research used The Post Test Only Control Group Design with 28 experimental mice (*Mus musculus*) age 8-10 weeks with weight 20-25 gr.

Chitosan was given on dosages 15 mg/kg of the weight, 30 mg/kg of the weight, 45 mg/kg of the weight on one hour after retinoid acid was given with single dose 60 mg/kg of the weight to mice mother. On the 18th days, experimental mice was slaughtered and colored by Alizarin Red S and then morphology malformation and delay ossification retardation was identified.
The data of skeleton morphology malformation of mice fetus was analyzed by Wilcoxon Signed Ranks Test. Meanwhile, ossification retardation of mice fetus was analyzed by one way ANOVA and continued by Least Significance Differences (LSD).
The result of this research can be concluded that chitosan with different dosage are not to skeleton morphology malformation of mice fetus. Meanwhile, the delay ossification of mice fetus with chitosan treatment on dosage 15 mg/kg of the weight, 30 mg/kg of the weight and 45 mg/kg of the weight was different significantly ($p < 0,05$) on sacrum and caudal bone, phalanges distal of forelimb and phalanges distal of hindlimb.

Keywords: retinoid acid, chitosan, malformation, ossification