

POTENSI KHITOSAN DALAM MENGHAMBAT KELAINAN KONGENITAL EKSTERNAL FETUS DAN PENURUNAN KEMAMPUAN REPRODUKSI INDUK MENCIT (*Mus musculus*) AKIBAT PEMBERIAN ASAM RETINOAT

Sukarnah, Siti

Pembimbing : Dr. Bambang Poernomo S, Drh, MS

RETINOID ACID; CHITOSAN

KKA KK TKR 09/12 Suk p

Copyright © 2008 by Airlangga University Library Surabaya

RINGKASAN

Vitamin A dan hasil metabolit berupa Asam Retinoat (RA) dan retinoid yang lain mempunyai pengaruh yang sangat kuat pada morfogenesis embrio, pertumbuhan sel dan differensiasi, penglihatan dan reproduksi. RA adalah senyawa yang sangat banyak digunakan untuk terapi dari *acne cystic*, beberapa penyakit dermatologi dan penyakit maligna termasuk kanker dari ovarium, payudara, paru dan darah.

Tujuan penelitian ini untuk mengetahui kemampuan khitosan dalam menghambat kelainan kelainan kongenetal fetus dan penurunan kemampuan reproduksi pengaruh asam retinoat. Kemampuan reproduksi meliputi persentase berat badan fetus, implant, resorbsi, lahir mati, dan fetus lahir hidup. Kecacatan eksternal meliputi persentase *paloschisis, sindaktili, simpodia, talipes, pocomeli, ektradaktili, kilromilia, dan kinky tail*. Hewan coba yang digunakan dalam penelitian sebanyak 30 ekor mencit dara yang berumur 8 minggu dengan berat badan antara 20-25 gram kemudian dikawinkan untuk memperoleh kebuntingan. Mencit kemudian dibagi dalam 5 kelompok, yaitu kelompok kontrol negatif (Induk mencit bunting umur 10hari yang diinduksi asam retinoat 60 mg/kg berat badan), Induk mencit bunting umur 10hari yang diinduksi asam retinoat 60 mg/kg berat badan dan khitosaan 15 mg/kg berat badan, Induk mencit bunting umur 10hari yang diinduksi asam retinoat 60 mg/kg berat badan dan khitosaan 30 mg/kg berat badan, Induk mencit bunting umur 10hari yang diinduksi asam retinoat 60 mg/kg berat badan dan khitosaan 45 mg/kg berat badan, sehingga masing-masing kelompok terdiri dari 6 ekor.

Data hasil penelitian meliputi kemampuan reproduksi induk mencit yang tercermin oleh berat badan fetus, resorbsi, fetus hidup dianalisa menggunakan uji statistik *ANOVA ONE WAY* taraf signifikansi $p < 0.05$ yang dilanjutkan dengan uji *LSD* untuk mengetahui perbedaan antara perlakuan. Untuk fetus mati, dianalisa menggunakan uji beda statistik *Wilcoxon's Rank Tes* dengan nilai signifikansi $p < 0.05$. Kelainan eksternal terdiri dari *paloschisis, sindaktili, simpodia, talipes, pocomeli, ektradaktili, kilromilia, dan kinky tail* dianalisa menggunakan uji beda statistik *Wilcoxon's Rank Test*.

Hasil analisis statistik diskriptif menunjukkan nilai rerata persentase dan standar deviasi kemampuan reproduksi untuk berat badan fetus pada K_1 sampai dengan P_3 sebagai berikut ($1,02 \pm 0,19$, $1,00 \pm 0,31$, $0,64 \pm 0,51$, $1,04 \pm 2,84$, dan $1,19 \pm 0,14$). Rerata untuk Fetus resorbsi adalah (0 , $24,33 \pm 40,20$, $50,42 \pm 39,80$, $12,28 \pm 14,34$ dan $26,06 \pm 13,66$). Rerata untuk fetus mati adalah (0 , $18,05 \pm 30,91$, $3,36 \pm 30,91$, $3,36 \pm 5,24$, dan $17,17 \pm 9,32$). Rerata Fetus hidup adalah (100 ± 0 , $48,61 \pm 34,90$, $44,81 \pm 38,34$, $80,17 \pm 15,70$, dan $56,75 \pm 15,70$).

Hasil analisis statistik diskriptif menunjukkan nilai rerata persentase dan standar deviasi untuk kelainan eksternal fetus *Palatosisis* pada K₁ sampai dengan P₃ sebagai berikut (0, 65,0±27,38, 16,66±40,82, 16,66±40,82, dan 0). Rerata untuk kelainan eksternal fetus *Simpodia* adalah (0, 22,22±25,09, 0, 0 dan 0). Rerata untuk kelainan eksternal fetus *Talipes* adalah (0, 19,99±26,66, 0, 3,33±8,16, dan 0). Rerata untuk kelainan eksternal fetus *Pocomelia* adalah (0, 27,77±40,36, 0, 0, dan 0). Rerata untuk kelainan eksternal fetus *Ektrodaktili* adalah (0, 0, 66,66±51,63, 0 dan 0). Rerata untuk kelainan eksternal fetus *Kinky tail* adalah (0, 33,33±51,64, 33,33±51,64, 0 dan 0). Rerata untuk kelainan eksternal fetus *Syndaktily* adalah (0, 14,58±22,93, 10,14±15,82, 0 dan 0).

Berdasarkan hasil analisis statistik diatas dapat disimpulkan bahwa pemberian khitosan dosis 15 mg/kg BB, 30mg/kg BB, dan 45mg/kg BB mencit secara *gavage* pada umur kebuntingan 10 hari pada induk mencit yang telah diinduksi asam retinoat dosis 60 mg/kg berat badan 1 jam sebelumnya mampu menghambat penurunan kemampuan reproduksi induk mencit. Peningkatan dosis khitosan dari 15 mg/kg BB hingga 45 mg/kg BB menurunkan kecacatan eksternal fetus mencit, tetapi masih ada kelainan yang muncul pada kelompok perlakuan yaitu *ektrodaktili* dan *mikromelia*. Ada perbedaan antara pemberian chitosan secara *gavage* dengan dosis 15mg/kg BB, 30mg/kg BB, dan 45mg/kg BB mencit pada induk mencit bunting usia kebuntingan 10 hari 1 jam setelah pemberian asam retinoat dalam menghambat kecacatan eksternal fetus dan penurunan kemampuan reproduksi induk mencit.

SUMMARY

Chitosan potency to blockes external malformation and decreases of outcome reproduction resalted by administer retinoid acid into female mus musculus

Vitamin A and the result of metabolism that is Retinoid Acid (RA) and retinoid have a significant influence in the embryos morphogenesis, the growth and differentiation of cell, eyes and reproductive organ. RA is a substance that mainly used for acne cystic therapy, some of many dermatology problems and malignant diseases including ovarian, breast, lungs and blood cancer.

The aim of this research is to understand the ability of chitosan in blocking of fetus congenital malformation and reducing the ability of reproductive organ because of retinoid acid effect. The outcome reproduction are weight fetus percentages, implantation of placenta, fetus reabsorbing, fetal death and fetus. The external malformation resulted by retinoid acid are including palatoschisis, syndactyly, simphodia, talipes, pocomely, ectrodactily, mikromyilia and kinky tail.

The number of samples used in this research are 30 female mus musculus in the age of 8 weeks and their weight are 20-25 gram approximately. These female mus musculus are made to be pregnant. The mus musculus are divided into 5 groups. There are 6 mus musculus in every group. The first group is the positive control group (10th days pregnant female mus musculus induced by sesame oil). The second group is the negative control group (10th days pregnant female mus musculus induced by retinoid acid 60mg/kg BW). The third is the 10th days pregnant female mus musculus which are induced by retinoid

acid 60mg/kg BW plus Chitosan 15 mg/Kg BW. The fourth group is 10th days pregnant female mus musculus which are inducted by retinoid acid 60mg/kg BW plus Chitosan 30 mg/Kg BW. The last group including 10th days pregnant female mus musculus which are inducted by retinoid acid 60mg/kg BW plus Chitosan 45 mg/Kg BW

Dates resulted from this research that includes outcome reproduction of mice is reflected by the implantation, the weight of fetus, the reabsorbing of fetus and fetus is analyzed using ANOVA One Way statistic test with the level significance $p < 0.05$ and followed by LSD test to understand the differences between the treatment. The fetal death is analyzed using Wilcoxon Range's Test with the level significance $p < 0.05$. The external malformation including palatoschisis, sindactily, simphodia, talipes, pocomely, ectrodactily, mikromyilia and kinky tail are analyzed using Wilcoxon Range's Test as well.

The research descriptive statistic analysis reveals percentile mean and standard deviation of outcome reproduction of body weigh for first group up to third administered as (1,02±0,19, 1,00±0,31, 0,64±0,51, 1,04±2,84, and 1,19±0,14). The mean reabsorbing of fetus as (0, 24,33±40,20, 50,42±39,80, 12,28±14,34 and 26,06±13,66). The mean of fetal death as (0, 18,05 ± 3 0,91, 3,36±30,91, 3,36±5,24, and 17,17±9,32). The mean of fetus as (100±0, 48,61 ± 34,90, 44,81±38,34, 80,17±15,70, and 56,75±15,70).

The research descriptive statistic analysis reveals percentile mean and standard deviation of palatoschisis external malformation for first group up to third administered as (0, 65,0±27,38, 16,66±40,82, 16,66±40,82, and 0). The mean and standard deviation of Simphodia external malformation as (0, 22,22 ± 25,09, 0, 0 and 0). The mean and standard deviation of Talipes external malformation were followed (0, 19,99 ± 26.66, 0, 3,33±8,16, and 0). The mean and standard deviation of Pocomelia external malformation as (0, 27,77 ± 40,36 , 0, 0, and 0). The mean and standard deviation of Ektrodaktily external malformation as (0, 0, 66,66 ± 51,63, 0 and 0). The mean and standard deviation of Kinky tail external malformation as (0, 33,33 ± 51,64, 33,33±51,64 , 0 and 0). The mean and standard deviation of Syndaktily external malformation were as (0, 14,58 ±22,93, 10,14±15,82, 0 and 0).

Resulted of research that the increasing of chitosan dose from 15 mg/Kg BW to 45 mg/Kg BW can increase the outcome of mice reproduction when it is compared with the control group. Furthermore it reduces the number of external malformation in the fetus, even though the external malformation is still found in the treatment group which are ectrodactily and mikromyilia.

This research also result in a fact that the reproductive outcome which increases with the significance of < 0.05 is happened at the fetus weight, reabsorbing and fetus. Decreasing of significance happened in the external malformation of palatoschisis. On the other hand there is a reduction the number of other external malformations but this reduction is not significant.

ABSTRACT

The aim of the administration of retinoid acid at dose of 60mg/kg into female *mus musculus* is to know the teratogenic effect of vitamin A in the growth of fetus (number of fetus, number of fetus resorption ,weighth of fetus ,and presentage of external malformation) .

The teratogenic and toxic effect are results of administration of one dose oral retinoid acid. The number of fetus ,the number of fetus resorbtion ,the weighth of fetus ,and the percentage of of normality external are calculated to know the teratogenic effect.

The teratogenic and toxic effect which is resulted by the administration of retinoid acid are blocked by chitosan that is administered one hour after induction of retinoid acid.

The result of macroscopic study shows that the administration of chitosan after induction of retinoid acid in the 10th days of pregnancy resulted in increasing the fetus weight, fetus, implantation of fetus and decreasing the number of fetus resorbtion ($p < 0.05$). Chitosan that is administered on the highest dose in the research (third group) increases number of weight fetus, fetus, implantation fetus and decreases the number of fetus resorbtion ($p < 0.05$). When chitosan was administered on the highest dose in the resech (third group), it reduces external malformation, except on the extromelia and micromelia. They remain in the previous number.

Key word : Retinoid acid, chitosan, external malformation, the growth of fetus.