

RINGKASAN

PENGARUH PEMBERIAN KOMPLEKS *INSULIN LIKE GROWTH FACTOR-1* DAN *INSULIN LIKE GROWTH FACTOR BINDING PROTEIN-3* TERHADAP PERBAIKAN REPRODUKSI MENCIT BETINA (*Mus musculus*)

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Dalam bidang reproduksi waktu timbulnya dewasa kelamin yang lambat serta adanya gangguan perkembangan ovarium pada hewan betina yang meliputi gagalnya perkembangan proses pembentukan dan pertumbuhan folikel merupakan faktor utama yang menghambat tingkat reproduktivitas.

Beberapa upaya yang dilakukan untuk meningkatkan reproduktivitas yang tinggi adalah dengan melakukan perbaikan pengelolaan reproduksi melalui perbaikan kesehatan alat reproduksi betina baik melalui perbaikan pengelolaan pakan, pengobatan dan pencegahan penyakit kelamin menular, perangsangan dengan hormonal atau pemakaian bahan-bahan bioaktif yang mendukung perbaikan dan perkembangan organ reproduksi betina khususnya ovarium.

FSH dan LH merupakan hormon glikoprotein yang dapat merangsang pertumbuhan folikel dalam ovarium (folikulogenesis) dan juga merangsang sintesa steroid (steroidogenesis) pada sel granulosa di ovarium. Hormon LH sangat berpengaruh terhadap terjadinya ovulasi. Ada berbagai faktor yang dapat mempengaruhi kandungan hormon FSH dan LH. Salah satu diantaranya adalah kompleks *Insulin like Growth Factor-1* (IGF-1) dan *Insulin like Growth Factor Binding Protein 3* (IGFBP-3).

Insulin Like Growth Factor-1 (IGF-I) adalah peptida dasar yang disekresikan sebagian besar oleh hati dan diedarkan kedalam pembuluh darah sebagai rangsangan dari *growth hormone*. IGF-1 yang berikatan dengan IGFBP 3 dalam darah berfungsi mengatur pertumbuhan, seperti insulin (insulin-like) dan bersifat mitogenik. IGF-I pada sel granulosa dan sel theca dari folikel ovarium merangsang sel-sel reseptor tipe I. Yang selanjutnya secara autokrin, IGF merangsang proliferasi dan diferensiasi sel granulosa. Sedangkan secara parakrin, infusi IGF-I akan menstimulasi sekresi hormon steroid (steroidogenesis) dari ovarium yaitu meningkatkan produksi androstendion dan estradiol. Hal ini dapat memberikan petunjuk bahwa IGF-I dapat bekerja mempengaruhi produksi hormon steroid oleh sel granulosa dan sel theca pada folikel dari ovarium. Peningkatan produksi androstendione dan estradiol mempengaruhi hipofisa anterior untuk meningkatkan pengeluaran hormon LH (feedback positif). Peningkatan produksi hormon LH (LH membanjir) ini menyebabkan peningkatan aliran darah kedalam ovarium dan dengan bantuan enzim (ovulatory lytic enzim) folikel menjadi pecah dan terjadilah ovulasi.

Penelitian ini merupakan penelitian eksperimental laboratorium yang telah dilakukan melalui pemanfaatan isolat kompleks protein *Insulin like Growth Factor-1* (IGF-1) dan *Insulin Growth Factor Binding Protein-3* (IGFBP-3) dari cairan folikel sapi. Tujuan dari penelitian ini adalah untuk membuktikan bahwa pemberian isolat kompleks protein *Insulin like Growth Factor-1* (IGF-1) dan *Insulin Growth Factor Binding*

Protein-3 (IGFBP-3) dapat meningkatkan perolehan jumlah folikel, jumlah anak sekelahiran dan percepatan umur pubertas pada mencit betina.

Tahapan dalam penelitian ini meliputi isolasi, identifikasi, penentuan kadar protein serta pengujian pada hewan coba. Hewan coba yang digunakan dalam penelitian ini adalah mencit strain Balb/C yang dibagi dalam tiga kelompok perlakuan dengan tujuh ulangan.

Isolat kompleks protein didapatkan melalui aspirasi pada folikel sapi yang selanjutnya diisolasi dan identifikasi dengan metode SDS-PAGE dan ELUSI. Sedangkan untuk menentukan berat total proteinnya dipergunakan metode BIURET.

Rancangan yang dipergunakan dalam penelitian ini adalah rancangan acak lengkap. Data jumlah pertumbuhan folikel, jumlah anak sekelahiran serta percepatan umur pubertas mencit dianalisis dengan ANOVA (*analysis of varians*) dan apabila ada perbedaan dilanjutkan dengan uji BNJ 5 %.

Hasil penelitian ini menunjukkan terdapat perbedaan yang nyata ($P < 0.05$) terhadap perolehan jumlah folikel, jumlah anak dan percepatan umur pubertas. Dengan demikian penggunaan kompleks protein *Insulin like Growth Factor-1* (IGF-1) dan *Insulin Growth Factor Binding Protein-3* (IGFBP-3) dalam penelitian ini diharapkan dapat dijadikan sebagai salah satu alternatif penanggulangan kasus gangguan reproduksi karena kurangnya atau ketidakseimbangan hormonal maupun upaya meningkatkan produktivitas hewan.

SUMMARY

THE EFFECT OF INSULIN-LIKE GROWTH FACTOR-1 AND INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-3 COMPLEX ADMINISTRATION ON REPRODUCTIVE IMPROVEMENT IN FEMALE MICE (*Mus musculus*)

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In reproduction, major factors hampering the reproductive rate are delayed genital maturation and disordered ovarian development in female animals, which include the failure in follicular formation and growth process. One of several efforts to increase reproductivity is by improving reproductive management with the improvement in the health of female reproductive organs, through the improvement in feeding management, medication and prevention of sexually transmitted disease, hormonal stimulation or the use of bioactive agents that support improvement and development of female reproductive organs, particularly the ovary.

FSH and LH are glycoprotein hormones that may stimulate follicular growth (folliculogenesis) in the ovary and also stimulate steroid synthesis (steroidogenesis) in ovarian granulose cells. The hormone LH has a high effect on the occurrence of ovulation. There are several factors that may affect the content of FSH and LH hormones. Two of those factors are the complex of Insulin like Growth Factor-1 (IGF-1) and Insulin like Growth Factor Binding Protein 3 (IGFBP-3).

Insulin-Like Growth Factor-1 (IGF-I) is the basic peptide mostly secreted by the liver and circulated in blood vessels as a result of stimulation by growth hormone. IGF-1 bound to IGFBP 3 in the circulation has a function to regulate growth, have characteristics like insulin (insulin-like) and mitogenic. IGF-I in granulose and theca cells from ovarian follicles stimulate type I receptor cells. Autocrinally, IGF stimulates proliferation and differentiation of granulose cells, while paracrinally, IGF-I infusion stimulates steroid hormone secretion (steroidogenesis) from the ovary by increasing androstendion and estradiol production. This indicates that IGF-I may act to affect steroid hormone production by granulose and theca cells in ovarian follicles. The increase of androstendion and estradiol affect anterior pituitary to enhance LH release (positive feedback). The increasing LH production (LH surge) results in blood flow into the ovary and, with the presence of enzyme (ovulatory lytic enzyme), follicles break down and the ovulation occurs.

This was a laboratory experimental study conducted by using isolates of Insulin-like Growth Factor-1 (IGF-1) and Insulin Growth Factor Binding Protein-3 (IGFBP-3) protein complexes from bovine follicular fluid. The purpose was to prove that the administration of these proteins could increase obtainable follicular count, the number of offspring in one delivery, and to accelerate pubertal age in female mice.

Stages in this study consisted of isolation, identification, determination of protein level and examination in experimental animals. This study used female Balb/C strain mice, divided into 3 tests, each comprised three treatments and seven repetitions. Bovine follicular fluid was collected by means of follicular aspiration. Isolation and identification were done using SDS-PAGE and ELUSI methods, while the weight of total protein was determined using BIURET method. This study used complete randomized design. Obtained data on follicular growth, the number of offspring in one delivery, and accelerated pubertal age in mice were analyzed with ANOVA (analysis of variance) and, if difference was found, 5% BNT test was carried out.

The results showed significant difference ($p < 0.05$) in obtained follicular count, the number of offspring in one delivery, and accelerated pubertal age. In short, the use of Insulin like Growth Factor-1 (IGF-1) and Insulin like Growth Factor Binding Protein 3 (IGFBP-3) can be used as one alternative to overcome reproductive problems due to hormonal shortage or imbalance as well as to improve animal reproductivity.

ABSTRACT**THE EFFECT OF INSULIN-LIKE GROWTH FACTOR-1 AND INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-3 COMPLEX ADMINISTRATION ON REPRODUCTIVE IMPROVEMENT IN FEMALE MICE (*Mus musculus*)****GRACIA ANGELINA HENDARTI**

Insulin-Like Growth Factor-1 (IGF-I) is the basic peptide mostly secreted by the liver and circulated in blood vessels as a result of stimulation by growth hormone. Circulating IGF-1 binds to protein complexes, such as Insulin like Growth Factor Binding Protein 3 (IGFBP-3). The functions of these IGF-1 and IGFBP-3 protein complexes are to stimulate proliferation and differentiation of granulosa cells as well as to stimulate theca cells of the follicle to increase androstendion and estradiol production.

This was a laboratory experimental study conducted by using isolates of IGF-1 and IGFBP-3 protein complexes from bovine follicular fluid. The purpose was to increase obtainable follicular count, the number of offspring in one delivery, and to accelerate pubertal age in female mice.

Stages in this study consisted of isolation, identification, determination of protein level and examination in experimental animals. First, bovine follicular fluid was collected by means of follicular aspiration. Isolation and identification were subsequently done using SDS-PAGE and ELUSI methods. The weight of total protein was determined using BIURET method. This study used complete randomized design. Collected data were analyzed by using ANOVA (Analysis of Variance) and, if significant difference was found, 5% BNT test was carried out.

Sixty three female Balb strain mice were divided into 3 experimental group, each group consisted of 28 mice. The first experimental was intended to find the effect of isolated IGF-1 and IGFBP-3 complex on the increase number of follicular on the ovary count in female mice. The results showed increasing follicular count in three treatments ($P < 0.05$). The highest was found in third treatment (P3), in which the dose of isolated IGF-1 and IGFBP-3 complexes was 50 :g, with average follicular count of 23.14 ± 2.41 . The experimental of the effect of isolated IGF-1 and IGFBP-3 complexes on the number of offspring showed significant difference in P2 and P3 among the three treatments ($p < 0.05$) with average offspring of 9.57 ± 0.78 and 9.85 ± 1.34 , while the effect on accelerated pubertal age in female mice showed significant difference between control and the three treatments ($p < 0.05$). However, the difference was not found among treatment groups.

Conclusion can be drawn that administration of isolated IGF-1 and IGFBP-3 complexes can be used to increase follicular count, the number of offspring, and accelerate pubertal age in female mice.

Keywords: Insulin Like Growth Factor-1 (IGF-I), Insulin like Growth Factor Binding Protein 3 (IGFBP-3)