

ABSTRAK

**PENINGKATAN KADAR KORTIKOSTERON AKIBAT STRES KRONIS
TERHADAP EKSPRESI HBEGF SEBAGAI PENANDA GANGGUAN
RESEPTIVITAS ENDOMETRIUM
PADA *Rattus norvegicus***

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Latar belakang : Reseptivitas endometrium adalah keadaan fisiologis di mana endometrium memperoleh fenotip adhesif yang memungkinkan implantasi embrio memiliki peran terhadap kejadian kegagalan implantasi. Gangguan reseptivitas endometrium dapat disebabkan oleh adanya gangguan pada aksis Hipotalamus–Pituitari–Gonad (HPG) akibat aktivasi aksis Hipotalamus–Pituitary–Adrenal (HPA) oleh stres. HBEGF merupakan salah satu biomarker reseptivitas endometrium yang berperan dalam desidualisasi sel stroma endometrium untuk mencapai keadaan reseptif dan inisiasi implantasi. Kortikosteron merupakan hormon glukokortikoid yang dominan pada hewan pengerat, sama halnya seperti kortisol pada manusia. Tingginya hormon kortikosteron akibat stres kronis memicu gangguan homeostasis di endometrium oleh berakibat menurunnya kadar HBEGF.

Tujuan : Penelitian ini bertujuan untuk membuktikan pengaruh peningkatan kadar kortikosteron akibat stres kronis terhadap ekspresi HBEGF pada endometrium *Rattus norvegicus*.

Metode : Penelitian ini telah mendapatkan kelaikan etik dari Komisi Etik Penelitian Fakultas Kedokteran Universitas Airlangga. Sampel penelitian terdiri dari 34 *Rattus norvegicus* yang terbagi atas 2 kelompok, kelompok kontrol dan kelompok perlakuan stres menggunakan metode *Chronic Unpredictable Mild Stress* (CUMS). Kadar kortikosteron serum yang terdeteksi melalui ELISA dan ekspresi HBEGF endometrium pada fase diestrus dievaluasi dengan metode imunohistokimia.

Hasil : Kadar kortikosteron serum kelompok perlakuan stres lebih tinggi (72.84 ± 64.03) dibandingkan kelompok kontrol (23.29 ± 8.42). Ekspresi HBEGF kelompok perlakuan stres lebih rendah (82.06 ± 5.91) dibandingkan kelompok kontrol (118.76 ± 13.20). Uji statistik menunjukkan adanya perbedaan bermakna ekspresi HBEGF pada endometrium *Rattus norvegicus* $p = 0,000$ ($p < 0.05$).

Kesimpulan : Peningkatan kadar hormon kortikosteron akibat stres kronis dapat menurunkan ekspresi HBEGF pada endometrium *Rattus norvegicus*.

Kata kunci : kortikosteron, stres kronis, ekspresi HBEGF, reseptivitas endometrium

ABSTRACT

**ELEVATED CORTICOSTERONE LEVEL DUE TO CHRONIC STRESS
ON HBEGF EXPRESSION AS A MARKER OF ENDOMETRIAL
RECEPTIVITY DISORDER IN *Rattus norvegicus***

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Background : Endometrial receptivity is a physiological state in which the endometrium obtains an adhesive phenotype that allows embryo implantation and have a role in the problem of implantation failure. Endometrial receptivity disorders can be caused by interference with the Hypothalamus-Pituitary-Gonad (HPG) axis due to the activation of the Hypothalamus-Pituitary-Adrenal (HPA) axis by stress. HBEGF is a biomarker of endometrial receptivity that plays a role in the decidualization of endometrial stromal cells to reach the receptive state and initiation of implantation. Corticosterone is the dominant glucocorticoid hormone in rodents, as is cortisol in humans. High corticosterone due to chronic stress triggers disruption of homeostasis in the endometrium by resulting in decreased levels of HBEGF.

Objective : This study aims to find out the effect of increased corticosterone levels due to chronic stress on HBEGF expression in endometrium *Rattus norvegicus*

Materials and methods : This research has obtained ethical eligibility from the Research Ethics Commission of the Faculty of Medicine Airlangga University. The samples on this study were 34 rat (*Rattus norvegicus*) which were divided into 2 groups, the control group and the stress treatment group using the Chronic Unpredictable Mild Stress (CUMS) method. Corticosterone level were obtain from blood serum detected via ELISA and HBEGF expression was obtained from endometrial in diestrus phase was evaluated by immunohistochemical methods.

Results : Corticosterone levels in the stress treatment group were higher (72.84 ± 64.03) than in the control group (23.29 ± 8.42). HBEGF expression in the stress treatment group was lower (82.06 ± 5.91) than in the control group (118.76 ± 13.20). Statistical tests showed significant differences in HBEGF expression in endometrium *Rattus norvegicus* $p = 0,000$ ($p < 0.05$).

Conclusion : Elevated level of corticosterone due to chronic stress can decrease HBEGF expression in endometrium *Rattus norvegicus*.

Keywords : corticosterone, chronic stress, HBEGF expression, endometrial receptivity