

Effect Of DLBS3233, Metformin, and Their Combination on the Expressions of VEGF and Endometriosis Implants in Endometriosis Mice (A Mouse Model in Endometriosis Study)

Pengaruh Pemberian Dlbs3233, Metformin Dan Kombinasi Keduanya Terhadap Ekspresi Vascular Endothelial Growth Factor Dan Luas Implan Endometriosis Pada Mencit Balb/C Model Endometriosis

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Abstract

Background: Endometriosis is a gynecological disorder characterized by the presence of endometrial tissue outside the uterine cavity. The process of angiogenesis is regulated by VEGF which plays an important role in the development of endometriosis implants. Metformin is an insulin sensitizer that is known to have a beneficial effect in the treatment of endometriosis and DLBS3233 is a PPAR γ agonist, it is hoped that it can reduce VEGF and reduce endometrial implants. The objective is to explore the effect of DLBS3233, metformin, and combination on VEGF expression and endometrial implant area of endometriosis-induced mice.

Methods: This experimental study used 3-months old 28 BALB/c mice of endometriosis that were randomly and equally divided into four groups (K, P1, P2, and P3). On the 15th day, the K group was given a placebo, the P1 group was given DLBS3233 0.25 mg/day for 14 days, the P2 group was given metformin 4 mg/day for 14 days and the P3 group was given a combination. The immunohistochemistry of VEGF expression was performed from the abdominal cavity and pelvic peritoneal tissues of the mice and measured by the Remmele Scale Index, while the extracted mice's endometrial implants were analyzed with a computer tracing method. All data normality tests were calculated with the Shapiro-Wilk test. The mean difference test of all groups was analyzed using the One-Way ANOVA test and the Kruskal-Wallis test.

Results: There were significant differences in the expressions of VEGF ($p=0.005$) and endometrial implants ($p=0.001$). Expression of VEGF in the P3 group was significantly lower compared to others and endometrial implant area in the P2 group was significantly lower compared to others.

Conclusion: DLBS3233 and Metformin may be a potentially effective drug treatments for endometriosis by decreasing VEGF expression and endometrial implants.

Keywords: DLBS3233, Metformin, VEGF, Endometriosis

Abstrak

Latar Belakang: Endometriosis adalah kelainan ginekologi yang ditandai dengan adanya jaringan endometrium di luar rongga rahim. Proses angiogenesis diatur oleh VEGF yang berperan penting dalam perkembangan implan endometriosis. Metformin adalah sensitizer insulin yang diketahui memiliki efek dalam pengobatan endometriosis dan DLBS3233 adalah agonis PPAR γ , diharapkan dapat menurunkan VEGF dan mengurangi implan endometrium. Tujuan penelitian ini untuk mengetahui efek DLBS3233, metformin dan kombinasi terhadap ekspresi VEGF dan luas implan endometrium mencit yang diinduksi endometriosis.

Metode: Penelitian ini bersifat eksperimental dengan menggunakan mencit endometriosis 28 BALB/c umur 3 bulan yang dibagi secara acak dan sama rata menjadi empat kelompok (K, P1, P2, dan P3). Pada hari ke-15 kelompok K diberikan plasebo, kelompok P1 diberikan DLBS3233 0,25 mg/hari selama 14 hari, kelompok P2 diberikan metformin 4 mg/hari selama 14 hari dan kelompok P3 diberikan kombinasi. Imunohistokimia ekspresi VEGF dilakukan dari jaringan rongga perut dan panggul tikus dan diukur dengan Remmele Scale Index, sedangkan implan endometrium tikus yang diekstraksi dianalisis dengan komputerisasi. Semua data dilakukan uji normalitas dengan uji Shapiro-Wilk. Uji beda rata-rata semua kelompok dianalisis menggunakan uji One-Way ANOVA dan uji Kruskal-wallis.

Hasil: terdapat perbedaan bermakna secara statistik pada ekspresi VEGF ($p=0,005$) dan luas implan endometrium ($p=0,001$). Ekspresi VEGF pada kelompok P2 secara signifikan lebih rendah dibandingkan kelompok lain dan luas implan endometriosis secara signifikan lebih rendah dibandingkan kelompok lain.

Simpulan: DLBS3233 dan Metformin mungkin merupakan pengobatan efektif yang potensial untuk endometriosis dengan mengurangi ekspresi VEGF dan implan endometrium.

Kata Kunci: DLBS3233, Metformin, VEGF, Endometriosis