35. Altered gene expression of VEGF, IGFs and H19 lncRNA and epigenetic profile

of H19-DMR region in endometrial tissues of women with endometriosis

Sedigheh Kamrani, Elham Amirchaghmaghi, Firouzeh Ghaffari, Maryam

Shahhoseini, Kamran Ghaedi

Reprod Health. 2022 Apr 22;19(1):100.doi: 10.1186/s12978-022-01406-w.

Abstract

Background: Endometriosis, as chronic estrogen-dependent disease, is defined by the

presence of endometrial-like tissue outside the uterus. Proliferation of endometrial tissue and

neoangiogenesis are critical factors in development of endometriosis. Hence, vascular

endothelial growth factor (VEGF) as well as insulin-like growth factor 1 and 2 (IGF1, 2) may

be involved as inducers of cellular proliferation or neoangiogenesis. Imprinted long

noncoding RNA H19 (lncRNA H19) has been suggested to be involved in pathogenesis of

endometriosis via regulation of cellular proliferation and differentiation. Epigenetic

aberrations appear to play an important role in its pathogenesis. The present study was

designed to elucidate VEGF, IGF1, IGF2 and H19 lncRNA genes expression and epigenetic

alterations of differentially methylated region (DMR) of H19 (H19-DMR) regulatory region

in endometrial tissues of patients with endometriosis, in comparison with control women.

Methods: In this case-control study, 24 women with and without endometriosis were studied

for the relative expression of VEGF, IGF1, IGF2 and H19 lncRNA genes using real-time

polymerase chain reaction (PCR) technique. Occupancy of the MeCP2 on DMR region of

H19 gene was assessed using chromatin immunoprecipitation (ChIP), followed by real-time

PCR.

Results: Genes expression profile of H19, IGF1 and IGF2 was decreased in eutopic and

ectopic endometrial tissues of endometriosis group, compared to the control tissues.

Decreased expression of H19 in ectopic samples was significant in comparison with the

controls (P < 0.05). Gene expression of VEGF was increased in eutopic tissues of

endometriosis group, compared to control group. Whereas its expression level was lower in

ectopic lesions versus eutopic and control endometrial samples. ChIP analysis revealed

significant and nearly significant hypomethylation of H19-DMR region II in eutopic and

ectopic samples, compared to the control group respectively. This epigenetic change was

aligned with expression of IGF2. While methylation of H19-DMR region I was not

significantly different between the eutopic, ectopic and control endometrial samples.

Conclusion: These data showed that VEGF, IGF1, IGF2 and H19 lncRNA genes expression

and epigenetic alterations of H19 lncRNA have dynamic role in the pathogenesis of

endometriosis, specifically in the way that hypomethylation of H19-DMR region II can be

involved in IGF2 dysregulation in endometriosis.

Keywords: Endometriosis; Epigenetic; H19 long noncoding RNA; Insulin-like growth

factors; Vascular endothelial growth factor.