Effects of a Histone Methyltransferase Inhibitor on Fertility on a Rat Model of Endometriosis

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Abstract

Endometriosis is an estrogen-dependent, inflammatory disease that affects 5-10% of women of reproductive age. It is defined as the growth of functioning endometrium outside the uterus that results in severe pelvic pain and often infertility. Currently, endometriosis has no cure, and available treatments have limited efficacy and side effects. Epigenetics play a key role in the etiology of this disease, and we have previously shown that treatment with histone methyltransferase inhibitors (HMTi) in an animal model of endometriosis significantly decreases vesicle development, suggesting the potential use of epigenetic drugs for endometriosis. The objective of this study was to investigate the effects of HMTi on fertility by analyzing the effects of the drug on expression of fertility genes in this model. Endometriosis induction was performed in female Sprague Dawley rats. Two weeks after, rats were treated intraperitoneally with HMTi for four weeks. At sacrifice, uterine tissues were collected and mRNA extracted to study fertility gene expression using a real-time polymerase chain reaction (RT²Profiler PCR Array). HMTi treatment modified the expression of a limited number of genes (2 out of 84), and increased the expression of key genes related to embryonic implantation and development of the ovary. These observations suggest that HMTi has a positive effect on fertility, a possibility that requires additional investigations in vivo.

KEYWORDS: Epigenetics, Endometriosis; Infertility; histone methylation; histone methyltransferase inhibitors

*The STEP-UP HS program is supported by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health, Grant number: R25DK098067. This study was funded by the Puerto Rico Science, Research, and Technology Trust and the PHSU RISE Program (NIGMS Grant R25GM082406).
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Endometriosis is an estrogen-dependent, inflammatory disease that affects 5-10% of women of reproductive age. It is defined as the growth of functioning endometrium outside the uterus that results in severe pelvic pain and often infertility. Currently, endometriosis has no cure, and available treatments have limited efficacy and side effects. Epigenetics play a key role in the etiology of this disease, and we have previously shown that treatment with histone methyltransferase inhibitors (HMTi) in an animal model of endometriosis significantly decreases vesicle development, suggesting the potential use of epigenetic drugs for endometriosis. The objective of this study was to investigate the effects of HMTi on fertility by analyzing the effects of the drug on expression of fertility genes in this model. Endometriosis induction was performed in female Sprague Dawley rats. Two weeks after, rats were treated intraperitoneally with HMTi for four weeks. At sacrifice, uterine tissues were collected and mRNA extracted to study fertility gene expression using a real-time polymerase chain reaction (RT² Profiler PCR Array). HMTi treatment modified the expression of a limited number of genes (2 out of 84), and increased the expression of key genes related to embryonic implantation and development of the ovary. These observations suggest that HMTi has a positive effect on fertility, a possibility that requires additional investigations in vivo.

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