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# EXPRESSION AND HORMONAL REGULATION OF AQUAPORINS IN THE UTERUS

Av

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# ABSTRACT

## BACKGROUND

*Aquaporins* (AQPs) are water channels present in the cell wall, allowing water – and occasionally other molecules – to pass the cell membrane. So far 13 AQPs have been found in humans. Their function is to maintain the cell internal milieu by regulating water and ion equilibrium. AQPs can be found in virtually all cell types and tissues and are essential to the normal function of cells and organs. Malfunction of the water channels can cause disease.

*The uterine wall* consists of three layers of which the endometrium is the innermost portion, facing the uterine cavity. The endometrium undergoes structural changes during the menstrual cycle, influenced by the hormones estrogen (E) and progesterone (P), as a preparation for implantation of a fertilized egg.

*Angiogenesis* is the formation of new blood vessels from existing ones. This process is essential for regeneration of the endometrium after shedding during menstruation.

*Excessive uterine bleeding*, also called menorrhagia, is a common gynecological disorder, presenting with large menstrual bleedings and reduced quality of life for those affected. Several organic diseases can lead to excessive uterine bleeding, but in most of the cases the cause is unknown.

*Mifepristone* is a synthetic steroid which has the ability to bind to P-receptors, thereby mainly blocking the effect of P. Mifepristone treatment improves menstrual bleeding pattern and has an effect on endometrial vessels.

## OBJECTIVES OF THE STUDIES

The general objective of the studies was to gain knowledge about the expression and hormonal regulation of AQPs in the uterus as well as to investigate the connection between AQPs and uterine function in healthy subjects and patients diagnosed with excessive uterine bleeding.

## RESULTS AND CONCLUSIONS

AQP1 and AQP2 are present in human endometrium; AQP1 in endothelial cells (lining the interior surface of blood vessels) and AQP2 in epithelial cells (lining cavities, surface structures, and glands). They can be assumed to be involved in events where water transport is essential, e.g. menstruation and reduction of uterine fluid volume at the time of implantation. AQP1 levels in the endometrium are reduced in women with excessive uterine bleeding, indicating that an impaired expression of AQP1 could be a cause to this condition. Mifepristone treatment increases AQP1 expression in human endometrium, which could imply a regulation by P. In cell culture, it was possible to show a hormonal regulation of certain AQPs: AQP1 protein-expression was up-regulated in endothelial cells when exposed to E, as well as to P; AQP2 mRNA levels increased after exposure to E + IC, and P combined with mifepristone, and AQP7 protein-expression increased after treatment with E + IC, and E + P, suggesting a role for these AQPs in increased endometrial secretion after ovulation.