

Association between testicular aryl hydrocarbon receptor levels and idiopathic male infertility: A case-control study in Iran

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Background and Aims: Increased urinary concentrations of Polycyclic Aromatic Hydrocarbons (PAHs) and their metabolites are associated with increased risk of unexplained infertility in males. The toxicity of PAHs and dioxins are exclusively mediated through Aryl hydrocarbon Receptor (AhR). AhR overexpression contributes to the loss of normal ovarian function in polluted environments but its expression level in unexplained male infertility has remained unclear. This study aimed to compare the differential testicular levels of AhR and its interactions with other fundamental genes (ER, AR, PgR and MMP9) in a case control study.

Methods: To conduct the immunohistochemical studies, 29 unexplained infertile and 10 fertile males were selected retrospectively from Jihad pathology center of Tehran from 2007 to 2009. Differential expression of AhR in Leydig, Sertoli, spermatogonia, spermatocyte, spermatid, and spermatozoa cells was determined and AhR association with other genes was compared between cases and controls.

Results: Higher levels of AhR in Leydig cells ($p=0.024$), Sertoli cells ($p=0.041$) and spermatid cells ($p=0.028$) of infertile men have emphasized the susceptibility of these cells to environmental-induced impaired testicular functions. Moreover 85% of infertile cases showed coexpression of AhR and MMP9 in their Leydig cells ($p=0.02$).

Conclusions: Inactivation of ER, PgR and AR in AhR positive testicular cells suggests the antagonistic interactions between AhR ligands and sex steroid hormones receptors. It seems that unexplained male infertility could be originated from environmental AhR ligands which overexpress the AhR in Leydig cells, downregulate the expression of sex steroid receptors and upregulate the MMP9 in Leydig cells as the main testicular target cell of AhR ligands.

Keywords: AhR-MMP9-Male Infertility