Genetic variants of CYP2C9 and IL-6 on female infertility

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AIM

To study the polymorphic variants in CYP2C9*2*3 and the C-174G promoter polymorphism of the IL-6 gene on Infertile Women.

BACKGROUND

•Infertility affects 15–20% of couples worldwide. Within the past decades, there has been a steady rise in the treatment of female infertility with several drugs (Udell et al, CMAJ, 2017).

•The cytochrome P450 (CYP) genes are oxygenases involved in estrogen biosynthesis and metabolism, generation of DNA damaging procarcinogens, and response to anti-estrogen therapies (Blackburn et al, Cancer Causes and Control, 2015)

•IL6 Interleukin-6 (IL-6) is a pleiotropic cytokine expressed in many tissues. This cytokine is largely expressed in female urogenital tract as well as reproduction organs. Very high or very low levels of IL-6 are associated with estrogen metabolism imbalance (Prins et al, J Reprod Immunol, 2012).

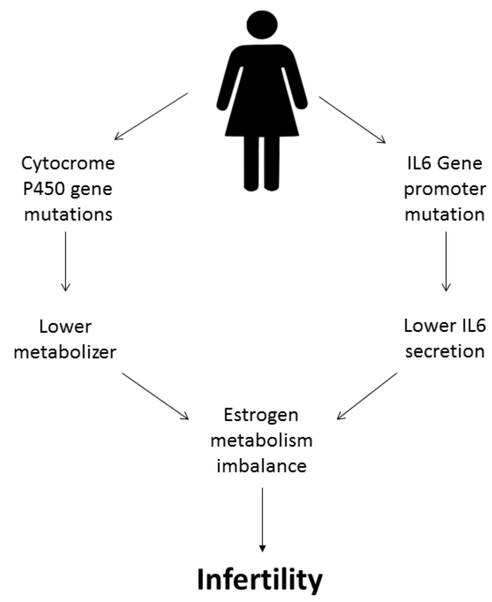

Fig. 1: Estrogen metabolism imbalance in infertility

METHODOLOGICAL STRATEGY

1. 10 infertile patients were targeted in this study.
2. DNA was extracted from urine sediments
3. LightMix Kit for the detection of CYP 2C9 alleles *2,and *3 and LightMix Kit for the detection of IL6 G-174C were used with LightCycler 2.0 Instrument.

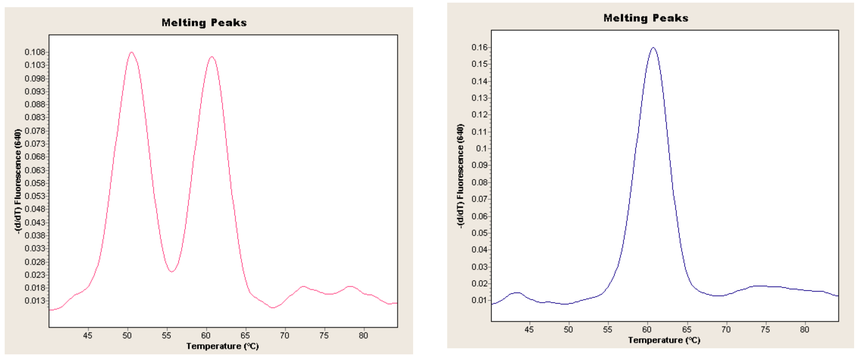

*Fig.2: Control samples melting peak for CYP2C9*3 (left panel heterozygote; right panel mutant)*

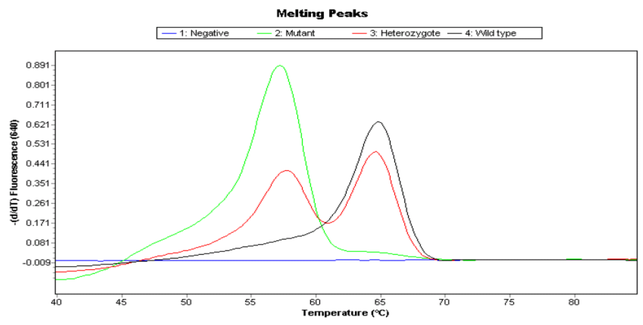

Fig. 3: Control sample melting peak for IL6 G-174C

RESULTS

1. Some samples did not amplified. To the CYP2C9*2 allele we got amplification in 8 samples. All of them were WildType genotype (80%) Vs 77.6% in a control population. To the CYP2C9*3 we got amplification in 5 samples. 60% were wildtype genotype (AA), 20% were heterozigotic (AC) and 20% were homozygous for the mutation (CC). The frequency of AC and CC genotypes in a control population are 12.1% and 0.45% respectively (Vasilyev, et al, Res Pharm Sci, 2016).

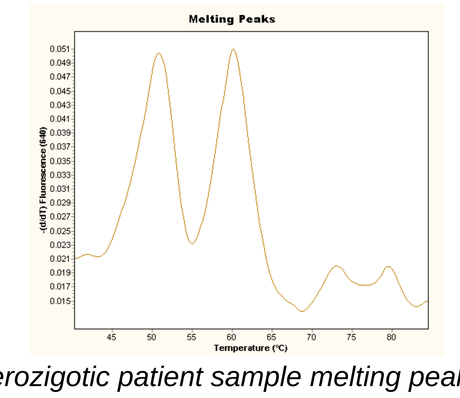

*Fig. 4: Heterozigotic patient sample melting peak for CYP2C9*3*

2. Some samples did not amplified. IL6 – CC genotype was not found, IL6 - 174C/G genotype that is known to be associated with lower IL6 secretion was 80%. The frequency of GC genotype in a Caucasian control population is 44% (Fishman et al, J Clin Invest, 1998).

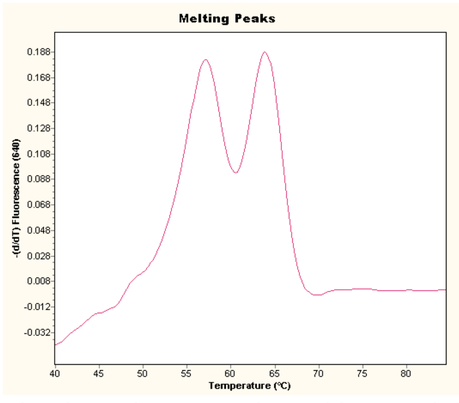

Fig. 5: Heterozigotic patient sample melting peak for IL6 -174G/C

CONCLUSIONS

• CYP2C9*3 C mutant and IL6-174C/G heterozygote genotypes may represent potential biomarkers for female infertility.

• On the other hand, they may have prognostic significance, namely regarding the metabolism of drugs used in infertility treatments, something which will need to be addressed in further studies.

•Their role in female infertility should be clarified using a larger group of infertile women.