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Evaluating influence of the genotypes in the follicle-stimulating hormone receptor (FSHR) Ser680Asn (rs6166) polymorphism on poor and hyper-responders to ovarian stimulation: a meta-analysis

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Abstract

Background/aims: Reported associations of controlled ovarian hyperstimulation response (COH) with genotypes of the Ser680Asn (N680S) polymorphism in the follicle stimulating hormone receptor (FSHR) gene have conflicting results.

Methods: PubMed and Embase databases were searched for studies that investigated the N680S polymorphism in the FSHR gene in COH. Parameters used to examine ovarian response were poor and hyper-responses to COH. Using the meta-analytic approach, we estimated ovarian response risk (odds ratio [OR] with 95% confidence intervals) according to genotype.

Results: Our findings showed that SS genotype carriers were most likely to be poor responders (OR 1.61, $p = 0.08$) compared to the NN and NS genotypes which showed no associations (OR 0.93-0.95, $p = 0.75-0.78$). Heterogeneity of these pooled ORs warranted examining its sources. We detected outlying studies in each of the three N680S genotypes. Omitting these outliers erased the heterogeneity of the recalculated pooled outcomes. It also materially altered the SS effects where carriers became slightly unlikely to be poor responders (OR 0.90, $p = 0.52$). The S allele carrier effect was modulated for poor responders (OR 1.24, $p = 0.39$) in the Non-Hispanic Caucasian (NHC) subgroup. The likelihood of the S allele carriers (OR 1.47, $p = 0.02$) and the unlikelihood of the N allele carriers (OR 0.64, $p = 0.007$) were significant in our hyper-response findings. Confined to NHC retained significance of the S allele effects (OR 1.57, $p = 0.01$) but not among the N allele carriers (OR 0.68, $p = 0.18$).

Conclusions: In summary, this is a meta-analytical confirmation of the FSHR SS genotype role in COH response. Hyper-responder analysis strengths lie on the non-heterogeneity and robustness of its results. Non-robustness and heterogeneity of the poor-responder results compose its limitations. Thus, poor response findings probably require caution as to the interpretation as a susceptibility marker for ovarian response.

Keywords: Follicle-stimulating hormone receptor, FSHR, Polymorphisms, Ovarian response, Meta-analysis

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