Lower folicular fluid levels of free vitamin A and E are associated with “poor response” to ovarian stimulation

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INTRODUCTION

Despite several advances in assisted reproductive technology (ART), there is still a considerable number of infertile couples that do not experience a successful pregnancy. According to the Bologna criteria, established by the European Society of Human Reproduction and Embryology (ESHRE) [1], low ovarian response is a diminished response to conventional ovarian stimulation, defined by the presence of at least two of the following features: i) advanced maternal age; ii) ≤ 3 oocytes follicles and iii) abnormal ovarian reserve test. Hence, women with poor ovarian response (POR) present a higher risk of cycle cancellation [2]. Moreover, sperm, oocyte and embryo quality are crucial to achieve fertilization. For instance, follicular fluid (FF) provides a nurturing environment for the development of oocytes and protects follicular cells from physical or oxidative damage. Exogenous antioxidants, obtained from dietary, play a prime role in cellular defense against oxidative stress and include fat-soluble vitamins like vitamin A and E.

OBJECTIVE

The present study evaluates the qualitative and quantitative pool of free antioxidants vitamin A, vitamin E, β-carotene, lutein and other carotenoids in the FF of infertile women who were submitted to ART procedures by normal phase HPLC-DAD/FLD.

MATERIAL AND METHODS

Follicular fluid from 200 follicles was carefully aspirated during oocyte retrieval. Only follicular fluid free of blood contamination as determined by visual inspection was processed by centrifuge at 300 × g for 10 minutes to remove cellular components, and the clear supernatant stored at −20°C for later analysis. Vitamin A, vitamin E (α, β, ɣ-tocopherol), β-carotene, lutein and other carotenoids concentration in follicular fluid were determined by HPLC-DAD/FLD. Student's t-test was used to compare FF antioxidant values. The level of significance was set at 95% (P<.05).

RESULTS

No association is identified between these antioxidants and body mass index or women' age. Similarly, no favorable associations are observed between FF antioxidants and fertilization success. However, there are differences in FF antioxidants profile and response to ovarian stimulation.

Table 1 - Characteristics of patients who underwent ART procedures.

Variable	Mean ± SD (n = 200)
Maternal age (years)	34.8 ± 3.4
Body mass index	23.9 ± 3.6
Duration of infertility (years)	3.7 ± 2.2
Follicle number	6.5 ± 4.0
Endometrial thickness (mm)	9.9 ± 2.5
Number of oocytes retrieved	9.6 ± 6.6
Number of embryos transferred	
0	26
1	91
2	65
Number of embryos implanted	
0	126
1	61
2	11
Causes of infertility	
Male + tubal factors	74
Endometriosis	25
Hormonal factors	34
Unexplained infertility	67
Serum	
FSH (ng/ml)	7.3 ± 2.7
LH (ng/ml)	6.1 ± 3.1
TSH (ng/ml)	1.9 ± 1.0
AMH (ng/ml)	23.5 ± 24.3
E2 (pg/ml)	57.7 ± 52.9

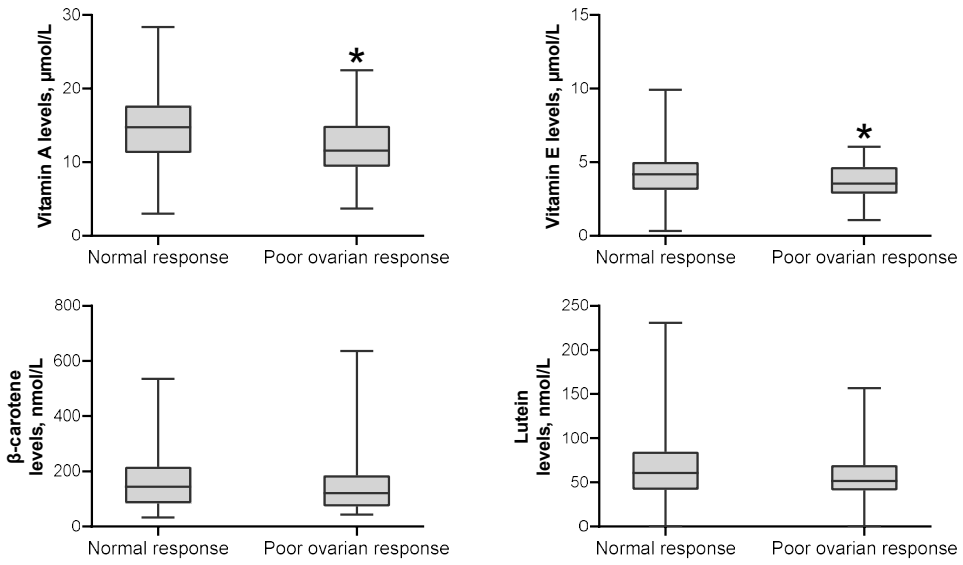

Figure 1 –Vitamin A, vitamin E (α, β, ɣ-tocopherol), β-carotene, lutein and other carotenoids concentrations in follicular fluid of infertile women. The poor ovarian response (POR) group presents lower FF vitamin A (12.138±3.854 µmol/L) and E (3.588±1.173 µmol/L) levels compared to women with normal/good response (14.471±4.902 and 4.079±1.537 µmol/L, respectively). There was no statistically significant difference in median β-carotene and lutein concentrations between groups. Significant differences between normal/good and poor ovarian response are denoted as *(p<0.05).

CONCLUSION

No association is identified between these antioxidants and body mass index or women' age. Similarly, no favorable associations are observed between FF antioxidants and fertilization success. However, there are differences in FF antioxidants profile and response to ovarian stimulation. This data indicate that antioxidant capacity of patients with infertility related to POR is slightly reduced at the follicular level suggesting that antioxidant profile may negatively impact ovarian response.

REFERENCES

[1] Guideline of the European Society of Human Reproduction and Embryology. 2019

[2] Ahmed Badawy, Alaa Wageah, Mohamed El Gharib, and Ezz Eldin Osman. Prediction and Diagnosis of Poor Ovarian Response: The Dilemma. J Reprod Infertil. 2011 Oct-Dec; 12(4): 241–248.

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