

Is it time to consider patients suffering from endometriosis-related infertility as “novel candidates” for targeted peri-conceptual D-chiro inositol supplementation? Hypothesis, rationale and some considerations

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Dear Editor,

We read with great pleasure the interesting data reported by Piomboni et al. concerning several advantages patients affected by polycystic ovarian syndrome (PCOS) and undergoing controlled ovarian hyperstimulation (COH) with pre-treatment supplementation by D-chiro inositol and/or metformin treatment. [1] The demonstrated D-chiro inositol supplementation and metformin treatment were both shown to significantly improve the follicular fluid (FF) milieu by decreasing the oxidative damage (measured as free-SH groups levels) on FF proteins and, as a consequence, significantly increase the number of good quality MII oocytes.

Although for many years it was known that the oxidative stress could have a negative effect on the FF environment, recent evidence has suggested that good quality oocytes require a correct balance in FF pro-oxidative and anti-oxidative factors, [2] since an excess in pro-oxidative status is associated with poor quality oocytes, low fertilization and implantation rates while a deficit may be responsible for follicular atresia. [3, 4]

Interestingly, several studies reported that women suffering from endometriosis frequently experience infertility and poor IVF outcomes (poor qualitative and quantitative ovarian response, low implantation rate), particularly when they have an imbalance in thiol-redox and oxidative status. [5–8]

It is known that, frequently, abnormalities in oxidative status balance may reflect alterations in glucose and lipid metabolism. Similarly to PCOS patients, several studies noticed that patients suffering from endometriosis have abnor-

malities in both glucose and lipid metabolism. For example, McKinnon et al. found that in endometriotic lesions GLUT4 (glucose transporter-4) protein expression was enhanced, probably due to increased glucose availability in the growing lesions. [8] In contrast, Melo et al. report that patients affected by endometriosis frequently show “unfavourable” lipid profile (increase in low-density and reduction in high-density lipoprotein), potentially favouring oxidative stress (via lipid peroxidation) typically increased in this cohort of women. [9–11]

D-chiro inositol is a “dietary supplement” of Inositol, an essential component of the phospholipids that make up cellular membranes, detectable in every cell of the body. The available formulations for oral administration show good bio-availability, safe pharmacologic profiles and beneficial effects in improving spontaneous fertility (or success rate of ARTs) also after short-term treatment, particularly in patients affected by PCOS and anovulation. [11]

Basically, oral formulations of D-chiro inositol appear to significantly reduce oxidative status as a result of its antioxidant properties that in turn lead to improvements in glucose metabolism (insulin-sensitizing effect mainly fulfilled by D-chiro inositol phosphoglycan via glycogen synthase activity) and a reduction in circulating levels of LDL and triglycerides in addition to BMI reduction. [12]

The properties of D-chiro inositol in reducing the “unbalanced” oxidative status of PCOS patients without significant adverse effects prompts speculation as to whether patients suffering from endometriosis in association with hypo/infertility should be considered as “novel candidates” who may potentially benefit from this supplementation in a pre-conception period (or pre-treatment period when referred to ARTs).

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Our proposal warrants further investigation. Much effort is being made to improve the fertility of patients suffering from endometriosis, and more and more therapeutic strategies are targeted to oxidative stress reduction. [11, 12] In fact, several Authors [13] recently showed that pre-treatment administration of ultra-long GnRH agonist (1.8 mg s.c. every 28 days for three courses) was effective in balancing intra follicular oxidative stress (checked by 8-hydroxy-2-deoxyguanosine reduction and increase in melatonin levels) and in improving ARTs outcomes of women affected by endometriosis. Others [14] have proposed the use of statins for endometriosis targeted treatment. Despite the beneficial effects, potential adverse effects should not be underestimated.

In the future both scientists and clinicians must join forces in seeking novel approaches to improve fertility in patients suffering from endometriosis reducing their “over” oxidative status. It is our opinion that the time has arrived to shift attention towards potential efficacy and safety of D-chiro inositol supplementation to balance the oxidative status of patients suffering from endometriosis, evaluating by appropriate studies the real cost-efficacy of peri-conceptual D-chiro inositol supplementation in this potential “novel candidate” cohort of patients.

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