Ovarian endometrioma is associated with increased AMH levels

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Background

It is believed that endometriosis has significant damaging effect on ovarian reserve. With regards to the effect of endometrioma on AMH levels, currently available evidence provides conflicting views: ranging significantly lower AMH measurements in smaller studies, to no association between AMH and endometrioma in more robust studies (Uncu et al. 2013, Hwu et al. 2013, Streuli et al. 2012).

Methods

Study design, size, duration

All women 20 to 45 years of age referred to the tertiary centre for management of infertility from 01.09.2008 to 16.11.2010 and had measurement of AMH (DSL assay) were included. Patients with polycystic ovaries were excluded.

All samples were processed and analysed strictly according to the assay kit insert. Serum samples were separated within two hours from venepuncture and frozen at -20C until analysed using the enzymatically amplified two-site immunoassay (DSL, Active MIS/AMH ELISA; Diagnostic Systems Laboratories, Webster, Texas).

Participants/materials, setting, methods

The AMH measurements of patients with endometrioma were compared to that of without disease using robust multivariable regression analysis following adjusting for relevant covariates such as age, ethnicity, BMI, endometriosis (with and without endometrioma), causes of infertility and reproductive surgery.

Results

In total of 2816 patients met inclusion criteria. 2627 women did not have endometriosis, whilst 189 were diagnosed with endometriosis and 46 of which had unilateral or bilateral endometrioma. The mean and median ages of patients were 32.9(±4.5) and 33.2(IQR: 29.5-36.5), respectively. Mean AMH measurement was 17.4(±5.0) pmol/L, median 14.2(IQR: 7.6-23.2) pmol/L.

Our study found that patients with endometrioma have in average 31% higher AMH compared to that of without which was statistically significant (p=0.034).

Contrary to widely accepted view, endometrioma does not appear to be associated with reduced AMH measurements.

Furthermore our study, which is based on a robust multivariable analysis, suggests that presence of endometrioma may be associated with higher AMH levels.

The study population is derived from the patients referred for management of infertility and hence these findings may not apply to general population. We recommend further studies should be conducted to understand this association further.


Discussion

Published evidence on the effect of endometrioma on AMH levels provides conflicting views. Using univariate analysis without controlling for confounders, Uncu et al reported that women with endometrioma (n=30) had significantly lower AMH and AFC measurements compared to control (n=30) group (Uncu et al 2013). Similarly, Hwu et al reported that women with endometrioma (n=141) had significantly lower AMH measurements compared to that of without pathology (n=1323) pathology (Hwu et al 2013). However, the study population appears to have disproportionately higher number of women with history of previous and current history of endometrioma (319/1642) compared to any surgery. Kim et al. reported lower AMH measurements in women with endometrioma (n=102) compared to control group (102), mean±SEM, 2.9±0.3 ng/mL vs. 3.3±0.3 ng/mL, although this did not reach statistical significance (P=0.28).

In contrast, more robust study conducted by Streuli et al. did not find any association between endometrioma and AMH measurements (Streuli et al. 2012). The study compared AMH levels of 313 women with laparoscopically and histologically confirmed endometriosis to 413 women without pathology. The group with endometriosis consisted of women with superficial peritoneal endometriosis (n=36), deep infiltrating endometriosis (n=183) and ovarian endometrioma (n=95). Importantly, relevant factors such as age, parity, smoking and previous ovarian surgery were adjusted for using multivariate regression analysis. The study demonstrated that, women with endometrioma did not have lower AMH levels; except the patients with previous history of surgery for endometrioma.

However, our study showed that the presence of endometrioma may be associated with significant increase in serum AMH levels. Given that an endometrioma is believed to cause significant damage to ovarian stroma this is unexpected finding. We hypothesize that increased AMH levels in the presence of endometrioma may be due to one of the factors a) acceleration in the rate of recruitment of primordial follicles, b) increased expression of AMH by granulosa cells in the presence of endometrioma and c) secretion of AMH by endometriotic cells.

Interestingly recent studies suggest that AMH is secreted by human endometrial cells. Wang et al. demonstrated that AMH is expressed in human endometrial cells in-vitro (Wang et al 2009), which has been confirmed by an independent group (Signorile et al. 2014). Furthermore increased expression of AMH in endometriotic cells have been demonstrated, suggesting AMH may play a role in pathogenesis of the disease (Carrarelli et al. 2014).

Summary

This study suggests that women with endometrioma may have higher AMH measurements compared to that of without pathology. Further studies to ascertain AMH measurements in women with endometrioma and the pathophysiology of this association should be conducted.

References

Carrarelli et al. Increased expression of antimullerian hormone and its receptor in endometriosis. (Fertil Steril 2015;103:1538-44)
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