

Association of ABO Blood Type and Ovarian Stimulation Response in Oocyte Donors

Nigel Pereira^{1*}, Anne P Hutchinson², Jovana P Lekovich¹, Rony T Elias¹, Zev Rosenwaks¹ and Steven D Spandorfer¹

¹Ronald O Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medical Center, USA

²Department of Obstetrics and Gynecology, Weill Cornell Medical College, USA

***Corresponding Author:** Nigel Pereira, Weill Cornell Medical Center, The Ronald O Perelman and Claudia Cohen Center for Reproductive Medicine, 1305 York Ave., New York 10021, USA.

Received: August 02, 2015; **Published:** August 19, 2015

Synopsis: Our study suggests no association between ABO blood type and ovarian stimulation response or oocyte yield in oocyte donors.

Abstract

Introduction: Recent studies have explored the relationship between ABO blood type and ovarian reserve. While some have suggested that certain blood types may be associated with diminished ovarian reserve, others have failed to show such a relationship.

Objective: To investigate the association between ABO blood type and oocyte yield in oocyte donors.

Methods: Retrospective cohort study of oocyte donors undergoing controlled ovarian stimulation (COS) and oocyte retrieval between January 2010 and June 2013. Patients were sub-grouped based on ABO blood types. Within each blood type group, baseline demographic and COS response parameters were compared. Donors with known polycystic ovarian syndrome were excluded. The primary outcome was the number of mature oocytes retrieved. Chi-square and analysis of variance (ANOVA) tests were used to compare percentages and means between ABO blood types.

Results: Five hundred and four donors met inclusion criteria. The distribution of ABO blood types in the cohort was as follows: 32.7% (A), 4.37% (AB), 14.9% (B), and 48.0% (O). The mean (\pm standard deviation) age of the study cohort was 27.5 (\pm 3.70) years. The demographics and baseline IVF characteristics among patients with blood types A, AB, B, and O were comparable. Within each blood type group, no difference was found in the total days of COS, total gonadotropins administered, peak estradiol level, peak endometrial stripe, or the number of mature oocytes retrieved.

Conclusions: Our study suggests no association between ABO blood type and oocyte yield in oocyte donors undergoing ovarian stimulation. Therefore, the value of ABO blood type in predicting ovarian stimulation response in oocyte donors is currently limited.

Keywords: ABO; blood type; ovarian reserve; ovarian stimulation; oocyte donation

Introduction

The association of ABO blood type with ovarian reserve has been the focus of a growing body of recent literature. The results of initial studies have largely been contradictory; some have suggested that certain blood types may be associated with diminished ovarian reserve [1,2], while others have failed to show such a relationship [3-6]. Currently, there is minimal data regarding the association between ABO blood type and ovarian stimulation response or oocyte yield. Oocyte donation, the process by which oocytes are collected from a donor for use in assisted reproductive technology (ART), is a viable alternative for the treatment of infertility in women with poor ovarian reserve, certain types of genetic disease and idiopathic infertility. In 2013, there were approximately 8921 fresh donor oocyte cycles in the

Citation: Nigel Pereira, *et al.* "Association of ABO Blood Type and Ovarian Stimulation Response in Oocyte Donors". *EC Gynaecology* 2.1 (2015): 126-131.

United States [7]. As donor oocyte cycles have become common, there has been an increasing interest in identifying parameters that may affect ovarian stimulation response in oocyte donors. As a woman's ovarian reserve usually determines response to ovarian stimulation and oocyte yield, and is therefore paramount to the success of donor oocyte cycles, we sought to investigate the association between ABO blood type and oocyte yield in oocyte donors. Because oocyte donors represent the majority of normal responders, our investigation also assesses the relationship between ABO blood type and oocyte yield in women with normal ovarian reserve testing.

Methods and Materials

Inclusion Criteria

The institutional review board at Weill Cornell Medical College approved our study protocol. All oocyte donors initiating ovarian stimulation at the Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine between January 2010 and June 2013 resulting in oocyte retrieval were analyzed for potential inclusion. Patients with polycystic ovarian syndrome or adrenal disease were excluded. Cycles cancelled prior to oocyte retrieval or with incomplete records were also excluded. A single serum anti-müllerian hormone (AMH) level was measured per patient prior to initiating ovarian stimulation. Donors were not taking hormonal contraception at the time of AMH determination. All serum AMH measurements were performed at our center's laboratory using the GenII Beckman ELISA (Beckman Coulter, Inc).

Clinical and Laboratory Protocols

Ovarian stimulation was aimed at maximizing follicular response while minimizing the risk of ovarian hyper stimulation syndrome (OHSS). Controlled ovarian stimulation (COS), human chorionic gonadotropin (hCG) trigger and oocyte retrieval were performed per our center's standard protocols [8]. Patients were down-regulated in the preceding luteal phase with oral contraceptive pills (Ortho-Novum, Janssen Pharmaceuticals) followed by ovarian stimulation with gonadotropins (Follistim, Merck; Gonal-F, EMD-Serono; and/or Menopur, Ferring). Ovulation was suppressed using a gonadotropin releasing hormone (GnRH) antagonist (Ganirelix Acetate, 0.25 mg [Organon]; or Cetrotide, 0.25 mg [EMD-Serono]) after ovarian stimulation was initiated. The initial gonadotropin dosages were based on patient age, weight, antral follicle count, serum AMH levels, and previous response to stimulation.

hCG was used as the ovulation trigger in the majority of cycles. Ovidrel (EMDSerono), Novarel (Ferring Pharmaceuticals) or Pregnyl (Schering-Plough) was administered according to a sliding scale [10,000 IU for E_2 (Estradiol) < 1,500 pg/mL, 5,000 IU for E_2 1,501-2,500 pg/mL, 4,000 IU for E_2 2,501-3,000 pg/mL, and 3,300 IU for E_2 > 3,001 pg/mL]. Generally, the hCG trigger was given when the two lead follicles attained a mean diameter > 17 mm. Oocyte retrieval was performed using transvaginal ultrasound guidance approximately 35-37 hours after hCG administration under conscious sedation. Oocyte maturity was determined by the presence of a polar body after stripping of the cumulus complex.

Study Variables

Demographic characteristics of donors included age, BMI (kg/m^2), ABO blood type and Rhesus factor type. Baseline parameters recorded prior to initiating ovarian stimulation included follicle stimulation hormone (FSH, mIU/mL), luteinizing hormone (LH, mIU/mL) and E_2 (pg/mL) levels. COS parameters recorded were as follows: total days of ovarian stimulation, total days of GnRH antagonist administration, total dosage of gonadotropins administered (IU), peak E_2 level (pg/mL), peak endometrial stripe (mm), total number of oocytes retrieved, and total number of mature oocytes. Patients were sub-grouped based on ABO blood types.

Statistical analysis

Categorical variables were expressed as number of cases (n) and percentage of occurrence (%). Normally distributed variables were expressed as mean \pm standard deviation (SD). Analysis of variance (ANOVA) and chi-square tests were used to compare means and percentages of recorded ovarian stimulation response parameters between ABO blood types. The number of mature oocytes retrieved was considered the primary outcome. All statistical analyses were performed using STATA version 13 (College Station, TX: StataCorp LP). $P < 0.05$ was considered statistically significant.

Results

Five hundred four patients met inclusion criteria. The distribution of ABO blood types in the cohort was as follows: 32.7% (A), 4.37% (AB), 14.9% (B), and 48.0% (O). Of the 504 patients, 441 (87.5%) patients were Rhesus factor positive and 63 (12.5%) patients were Rhesus factor negative. The mean (\pm SD) age, BMI and AMH level of the study cohort was 27.5 (\pm 3.70) years, 22.5 (\pm 4.61) kg/m², and 2.08 (\pm 0.69) ng/mL, respectively. Table 1 summarizes the baseline demographics and IVF characteristics of the overall study cohort.

Age (years)	27.5 (\pm 3.70)
BMI (kg/m ²)	22.5 (\pm 4.61)
Basal FSH (mIU/mL)	2.37 (\pm 0.44)
Basal LH (mIU/mL)	1.76 (\pm 0.22)
Basal E ₂ (pg/mL)	30.1 (\pm 10.6)
AMH (ng/mL)	2.08 (\pm 0.69)
Blood Type	
A	165 (32.7%)
AB	22 (4.37%)
B	75 (14.9%)
O	242 (48.0%)
Rhesus Factor	
Positive	441 (87.5%)
Negative	63 (12.5%)

Table 1: Overall baseline characteristics of study cohort (n = 504). Data are presented as mean \pm standard deviation (SD) and n (%). BMI: Body Mass Index; FSH: Follicle Stimulating Hormone; LH: Luteinizing Hormone; E₂: Estradiol; AMH: Anti-mullerian hormone.

Table 2 summarizes the demographic and baseline characteristics of the study cohort based on blood type. There was no difference in the mean age, BMI, or distribution of Rhesus factor types between blood type sub-groups. Furthermore, there was no difference in the baseline serum FSH, LH, E₂ or AMH levels. Table 3 compares the ovarian stimulation response and oocyte yield in donors based on blood type. There was no difference in the total days of ovarian stimulation, total days of GnRH antagonist administration, total dosage of gonadotropins administered, peak E₂ level, peak endometrial stripe, or total number of oocytes retrieved. The overall mean (\pm SD) number of mature oocytes retrieved was 17.9 (\pm 4.12), which was comparable across all blood types.

Discussion

Our findings suggest no association between ABO blood type and oocyte yield in oocyte donors undergoing ovarian stimulation at our center. Therefore, the value of ABO blood type in predicting ovarian stimulation response in oocyte donors is currently limited.

The antigens of the ABO blood group system are complex carbohydrate molecules expressed on the surface of red blood cells [9]. However, these antigens are also expressed on the surface of other human cells, including the sensory, vascular endothelium and platelets [9,10]. There is accumulating evidence that certain ABO blood types may be associated with coronary artery disease, venous thromboembolic disease, gastric and pancreatic cancer [9,10]. Previous studies have also explored the association between ABO blood type and gynecologic conditions such as endometriosis [11] as well as gynecologic cancers [12]. In 2008, Binder, *et al.* first suggested an association between ABO blood type and response to ovarian stimulation, reporting a possible association between blood type A and OHSS [13]. Since then, new studies exploring the predictive value of ABO blood type and serum markers of ovarian reserve have emerged.

Parameter	Blood Type A (n = 165)	Blood Type AB (n = 22)	Blood Type B (n = 75)	Blood Type O (n = 242)	P
Age (years)	28.1 (± 4.29)	27.2 (± 3.97)	27.7 (± 3.89)	27.9 (± 3.36)	0.70
BMI (kg/m ²)	21.6 (± 4.56)	22.3 (± 3.92)	21.8 (± 3.81)	21.3 (± 5.05)	0.69
Rhesus Factor					
Positive	147 (89.1%)	19 (86.4%)	64 (85.3%)	211 (87.2%)	0.87
Negative	18 (10.9%)	3 (13.6%)	11 (14.7%)	31 (12.8%)	
Basal FSH (mIU/mL)	2.56 (± 0.57)	2.41 (± 0.58)	2.52 (± 0.59)	2.45 (± 0.34)	0.11
Basal LH (mIU/mL)	2.11 (± 0.69)	2.06 (± 0.61)	2.17 (± 0.38)	2.05 (± 0.66)	0.50
Basal E ₂ (pg/mL)	29.8 (± 11.5)	31.1 (± 8.88)	32.7 (± 10.7)	29.6 (± 9.41)	0.13
AMH (ng/mL)	2.09 (± 0.57)	2.12 (± 0.68)	2.19 (± 0.51)	2.05 (± 0.64)	0.37

Table 2: Baseline characteristics of oocyte donors distributed by blood type (n = 504).

Data are presented as mean ± standard error of the mean and n (%).

BMI: Body Mass Index; FSH: Follicle Stimulating Hormone; LH: Luteinizing Hormone;

E₂: Estradiol; AMH: Anti-mullerian hormone.

Parameter	Blood Type A (n = 165)	Blood Type AB (n = 22)	Blood Type B (n = 75)	Blood Type O (n = 242)	P
Total stimulation days	9.92 (± 2.45)	9.81 (± 2.30)	10.0 (± 2.12)	9.87 (± 2.85)	0.98
Total antagonist days	4.79 (± 1.54)	4.91 (± 1.61)	4.71 (± 1.46)	4.58 (± 1.52)	0.49
Total FSH administered (IU)	1492.1 (± 674.8)	1387.7 (± 617.4)	1409.9 (± 621.6)	1508.2 (± 655.3)	0.62
Total hMG administered (IU)	991.5 (± 395.8)	918.4 (± 400.1)	945.8 (± 370.7)	934.7 (± 389.7)	0.51
E ₂ on day of trigger (pg/mL)	2196.1 (± 890.7)	2009.5 (± 799.8)	2069.1 (± 762.9)	2141.9 (± 815.7)	0.61
Peak endometrial stripe (mm)	11.4 (± 4.33)	10.8 (± 4.69)	11.3 (± 3.52)	11.0 (± 4.49)	0.78
Number of oocytes retrieved	21.2 (± 5.53)	21.5 (± 5.49)	20.2 (± 5.65)	20.5 (± 4.05)	0.32
Number of mature oocytes	17.9 (± 4.41)	18.4 (± 4.92)	18.0 (± 4.69)	17.6 (± 4.97)	0.80

Table 3: Ovarian stimulation outcomes of oocyte donors distributed by blood type (n = 504).

Data are presented as mean ± standard error of the mean and n (%).

FSH: Follicle Stimulating Hormone; hMG: Human Menopausal Gonadotropin.

Nejat., *et al.* [1] first explored the role of ABO blood type as a predictor of ovarian reserve. They reported that patients with blood type O were more likely to have diminished ovarian reserve (defined as FSH > 10 mIU/mL) than those with blood types A or AB (OR 2.14, 95% CI 1.22-3.80). The authors posited that the A antigen was protective for ovarian reserve by citing a significantly higher representation of blood type A and AB in the group with normal ovarian reserve. To explain this association, the authors theorized that an enzyme called A transferase, associated with the A antigen, played a critical role in oocyte accrual. In a subsequent study, Lin., *et al.* [2] reached a different conclusion - their study population had significantly more patients with blood type O with FSH < 10 mIU/mL than with FSH > 10 mIU/mL (OR 1.41, 95% CI 1.30-1.54). They also found higher percentages of patients with blood type B and type AB with FSH > 10 mIU/mL (OR 8.2, 95% CI 0.76-0.84 for blood type B; OR 8.4, 95% CI 0.75-0.94 for blood type AB). According to the authors, the racial and ethnic differences in blood type distributions could have explained the differences in their findings when compared to Nejat., *et al.* [1] study cohort. All other investigations have failed to show a significant association between ABO blood type and ovarian reserve, as indicated by serum FSH or AMH levels [3-6].

Despite their prominence in earlier studies of ovarian reserve vis-à-vis blood type, serum FSH and AMH levels only serve as indirect biomarkers for ovarian reserve. In women undergoing COS, quantitative ovarian response to gonadotropins, specifically oocyte yield, ultimately reflects ovarian reserve. In a recent study of 1889 IVF cycles, Spitzer, *et al.* [14] investigated the association between ABO blood type and ovarian reserve by measurements of cumulus oocyte complexes (COCs) and metaphase II (MII) oocytes collected after COS. In this study, the authors found similar number of COCs and MII oocytes across all blood types and ages. Our findings remain consistent with the results of the aforementioned study, showing no relationship between ABO blood type and number of oocytes. This lack of association was also found in a different study cohort (patients with diminished ovarian reserve) from our center [15].

A significant strength of this study is its unique patient population, i.e., oocyte donors, who represent a large majority of normal responders. The large sample size and inclusion of several quantitative ovarian response parameters to assess response to gonadotropins and subsequent oocyte yield are additional strengths. We also acknowledge a few limitations. First, our analysis only included response to GnRH-antagonist based protocols. As our center does not employ GnRH-agonist based flare protocols for oocyte donors, we remain uncertain whether our findings hold true in the context of non-GnRH-antagonist based protocols. Second, our study did not account for confounders such as ovarian surgery or smoking status. Last, given the retrospective study design, we remain uncertain whether our findings would hold true in a prospective study of a larger cohort.

Conclusion

Our findings add to the emerging body of literature investigating the association between ABO blood type and oocyte yield following ovarian stimulation. While our current study suggests no association between blood type and oocyte yield in oocyte donors, it possible that prospective data may suggest novel mechanisms that underlie previously reported associations between blood type and ovarian reserve in other study cohorts.

Acknowledgments

None.

Conflicts of Interest

The authors declare no conflicts of interest.

Bibliography

1. Nejat EJ, *et al.* "Implications of blood type for ovarian reserve". *Human Reproduction* 26.9 (2011): 2513-2517.
2. Lin S, *et al.* "Effect of ABO blood type on ovarian reserve in Chinese women". *Fertility and Sterility* 102.6 (2014): 1729-1732.
3. de Mouzon J, *et al.* "Blood type and ovarian reserve". *Human Reproduction* 27.5 (2012): 1544-1545.
4. Timberlake KS, *et al.* "Association of blood type and patient characteristics with ovarian reserve". *Fertility and Sterility* 100.6 (2013): 1735-1739.
5. Sengul O, *et al.* "Only female age, and not blood type, is associated with ovarian reserve". *International Journal of Fertility & Sterility* 8.2 (2014): 143-146.
6. Pereira N, *et al.* "Association of ABO blood type with ovarian reserve". *Journal of Nature and Science* 1.2 (2015): e40.
7. Center for Disease Control and Prevention. Assisted Reproductive Technology (ART).
8. Pereira N, *et al.* "Impact of elevated peak serum estradiol levels during controlled ovarian hyperstimulation on the birth weight of term singletons from fresh IVF-ET cycles". *Journal of Assisted Reproduction and Genetics* 32.4 (2015): 527-532.
9. Liumbruno GM and Franchini M. "Beyond immunohaematology: the role of the ABO blood group in human diseases". *Blood Transfusion* 11.4 (2013): 491-499.
10. Franchini M and Liumbruno GM. "ABO blood group: old dogma, new perspectives". *Clinical Chemistry and Laboratory Medicine* 51.8 (2013): 1545-1553.
11. Matalliotakis I, *et al.* "ABO and Rh blood groups distribution in patients with endometriosis". *Archives of Gynecology and Obstetrics* 280.6 (2009): 917-919.

Citation: Nigel Pereira, *et al.* "Association of ABO Blood Type and Ovarian Stimulation Response in Oocyte Donors". *EC Gynaecology* 2.1 (2015): 126-131.

12. Yuzhalin AE and Kutikhin AG. "ABO and Rh blood groups in relation to ovarian, endometrial and cervical cancer risk among the population of South-East Siberia". *Asian Pacific Journal of Cancer Prevention* 13.10 (2012): 5091-5096.
13. Binder H., *et al.* "Blood group A: an overseen risk factor for early-onset ovarian hyperstimulation syndrome?" *Reproductive Bio-medicine Online* 17.2 (2008): 185-189.
14. Spitzer D., *et al.* "Implications of Blood Type for Ovarian Reserve and Infertility - Impact on Oocyte Yield in IVF Patients". *Geburtshilfe and Frauenheilkde* 74.10 (2014): 928-932.
15. Pereira N., *et al.* "Is ABO blood type associated with ovarian stimulation response in patients with diminished ovarian reserve?" *Journal of Assisted Reproduction and Genetics* 32.6 (2015): 985-990.

Volume 2 Issue 1 August 2015

© All rights are reserved by Nigel Pereira., *et al.*