Anti-phospholipid antibodies do not affect IVF success

The Practice Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

The assessment of anti-phospholipid antibodies (APA) is not indicated among couples undergoing IVF, and therapy is not justified on the basis of existing data. (Fertil Steril® 2008;90:S172–3. ©2008 by American Society for Reproductive Medicine.)

BACKGROUND

Anti-phospholipid antibodies (APA) including anticardiolipin antibody, lupus anticoagulant, and anti-phosphatidyl serine have been associated with recurrent pregnancy loss. Controversy exists regarding a possible association between these abnormalities and in vitro fertilization (IVF) failure (1–3). The proposed mechanism of such failure includes abnormal implantation, placentation, and early embryonic vascular compromise. Intravenous immunoglobulin (IVIG) and antithrombogenic therapy including aspirin and heparin have been proposed as treatments in the expectation of improving implantation or placentation (2, 3). Evidence for the association between APA and IVF failure can best be derived from studies in which one can compare IVF outcomes among APA-positive and -negative subjects who were free from any APA-related treatment. This document addresses the relationship between the presence of anti-phospholipid antibodies and successful IVF.

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METHODS

A current literature search using the identifier APA, IVF, and related terms located 16 studies. Of these, three included only treated subjects (2, 4, 5), three lacked cohorts of IVF couples (6–8), two commentaries included no original data (1, 9), and one included no IVF outcome data (10). From the remaining seven studies, we abstracted data on the patients with and without APA who underwent IVF therapy and did not receive APA-related therapy (3, 11–16). All but two included data on live birth or ongoing pregnancy as well as clinical pregnancy (3, 16). The definition of APA positivity was one or more abnormal results on anti-cardiolipin or anti-phosphatidyl serine (11, 13, 15), additional anti-phospholipids (3, 12, 14, 16), and various other autoantibodies (11, 13, 14). Three studies appeared to be prospective cohort studies (11, 12, 16), while the remainder appeared to be retrospective cohort studies.

The relevant studies were examined for estimates of the relative likelihood of pregnancy and live birth in APA-negative and positive IVF-treated infertile couples. The published

TABLE 1

Anti-phospholipid antibodies and IVF outcome.

Outcome	Authors	Odds ratio	(95% CI)
Pregnancy	Birdsall et al (11)	1.65	(0.50, 5.46)
	Denis et al (12)	0.91	(0.42, 1.97)
	El Roiey et al (13)	0.26	(0.04, 1.83)
	Gleicher et al (14)	1.34	(0.36, 4.95)
	Kowalik et al (15)	1.38	(0.52, 3.34)
	Kutteh et al (16)	.85	(0.21, 3.50)
	Sher et al (3)	.55	(0.13, 2.34)
Average for Pregnancy		.99	(0.64, 2.34)
Live Birth	Birdsall et al (11)	1.67	(0.50, 5.56)
	Denis et al (12)	.94	(0.44, 1.98)
	El-Roiey et al (13)	.18	(0.02, 2.14)
	Gleicher et al (14)	1.60	(0.39, 6.53)
	Kowalik et al (15)	1.10	(0.42, 2.90)
Average from Live Birth		1.07	(0.66, 1.75)

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data were combined by taking the average of the logarithms of the individual odds ratios, each weighted by the inverse of its variance. Confidence intervals and heterogeneity of the estimates were evaluated by standard means (17).

RESULTS

The APA and IVF outcome studies involved 2,053 patients, of whom 703 (34%) were APA positive. The aggregate clinical pregnancy rates and live birth rates were 57.0% and 46.0% in the APA positive patients and 49.2% and 42.9% in the APA negative patients, respectively. None of the studies revealed a significant effect of presence of APA on IVF success. Studies evaluating more antibody types were more likely to find a nonsignificant reduction in the likelihood of IVF conception. Overall, anti-phospholipid antibody abnormalities were not associated with IVF success as estimated by clinical pregnancy rate in seven studies (OR 0.99, 95% CI 0.64, 1.53) or by live birth in five studies (OR 1.07, 95% CI 0.66, 1.75) (Table 1).

CONCLUSION

Although an association between APA abnormalities and IVF failure has been suggested in some retrospective studies, no association is present in the prospective studies summarized here. However, these studies may not be representative of typical IVF candidates: 34% were APA positive and the live birth rate was 45%. Nevertheless, the assessment of APA is not indicated among couples undergoing IVF. Therapy is not justified on the basis of existing data.

Approved by the Practice Committee and Board of Directors of the American Society for Reproductive Medicine, August 1999.

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