

THE ADJUSTMENT OF OXIDATION REDUCTION POTENTIAL (ORP) LEVELS IN CULTURE MEDIA TO THE OVERALL LEVELS OF FOLLICULAR FLUID PRODUCES SIGNIFICANTLY HIGHER EMBRYO PLOIDY RATES IN PATIENTS: A PROSPECTIVE RANDOMIZED STUDY OF SIBLING OOCYTES.

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INTRODUCTION

Due to a rise in popularity of assisted reproduction technologies (ART), the number of births from Advanced Maternal Age (AMA) pregnancies has markedly increased over the last decade. Nevertheless, successful pregnancy rates are significantly lower than in younger patients. Lower ovarian reserve leads to obtain less embryos for transfer. It is also well documented that embryos from AMA patients have higher aneuploidy rates. Consequently, increased miscarriage rates are observed.

AMA patients have a significantly higher prevalence of poor quality blastocysts with higher aneuploidy rates. Adjusting the levels of oxidation-reduction potential (ORP) in embryo culture medium to physiological levels found in follicular fluid of young donors has been shown to significantly reduce these aneuploidy rates in cycles of AMA patients, thus, favoring good quality euploid blastocysts.

Since a higher rate of euploid embryos would increase successful implantation rates, the main objective of this study was to explore if the adjustment of the ORP level in embryo culture medium to levels similar to those found in follicular fluid of donor oocytes improves usable blastocyst formation and embryo ploidy rates in infertile patients.

MATERIALS AND METHODS

This study used a total of 901 zygotes deriving from 1348 inseminated oocytes (65.2%) obtained from 79 subfertile patients undergoing ART (ICSI) with a mean of age of 36.9 years. Sibling oocytes were split into 2 groups:

- Group 1 consisted of 675 oocytes that were inseminated and cultured until blastocyst stage in medium that was ORP-adjusted by adding a combination of antioxidants (EmbryoORP[®]) every 12 hours to match the overall ORP levels of follicular fluid from oocyte donors (86.0±14.8 mV).
- Group 2: 673 oocytes were inseminated and cultured in commercial culture medium without ORP adjustment until blastocyst stage. Blastocysts underwent Preimplantation Genetic Testing for Aneuploidies (PGT-A).

A total of 202 embryos were biopsied. Group 1: 102 blastocysts were biopsied out of 675 oocytes. Group 2: 100 blastocysts were biopsied out of 673 oocytes. All biopsied day-5/6 blastocysts were analyzed by Next Generation Sequencing Technique (NGS). Statistical analysis was performed using t-test after Kolmogorov-Smirnov test for normal distribution. A P-value of P<0.05 was considered significant.

Figure 1: Flow diagram depicting experimental design

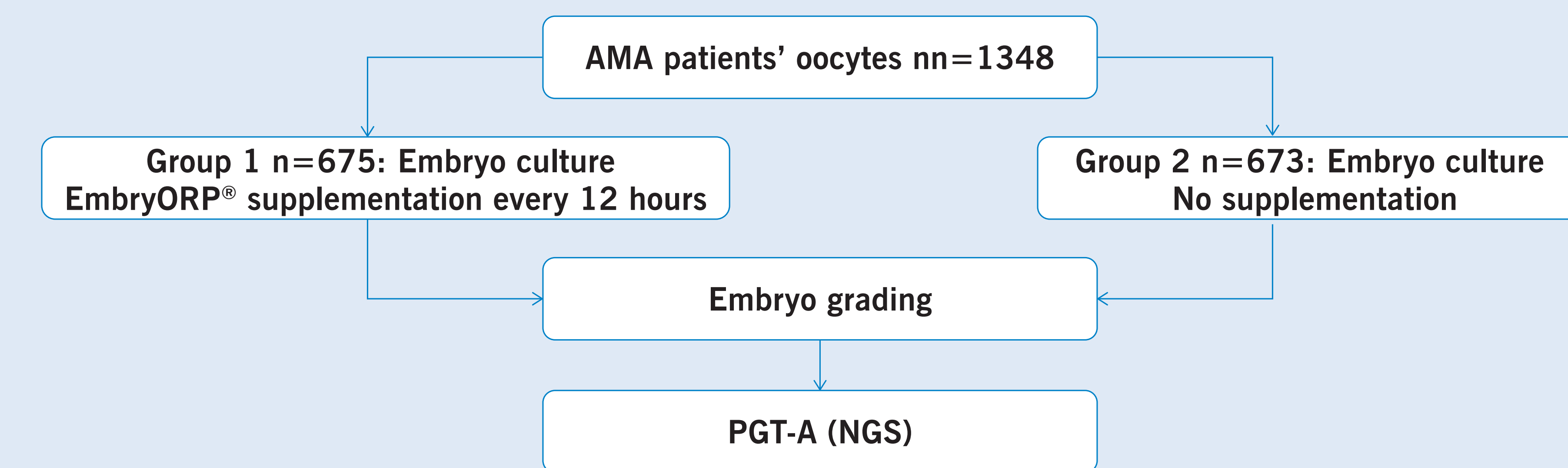


Figure 2 ORP adjustment and embryo culture with antioxidants

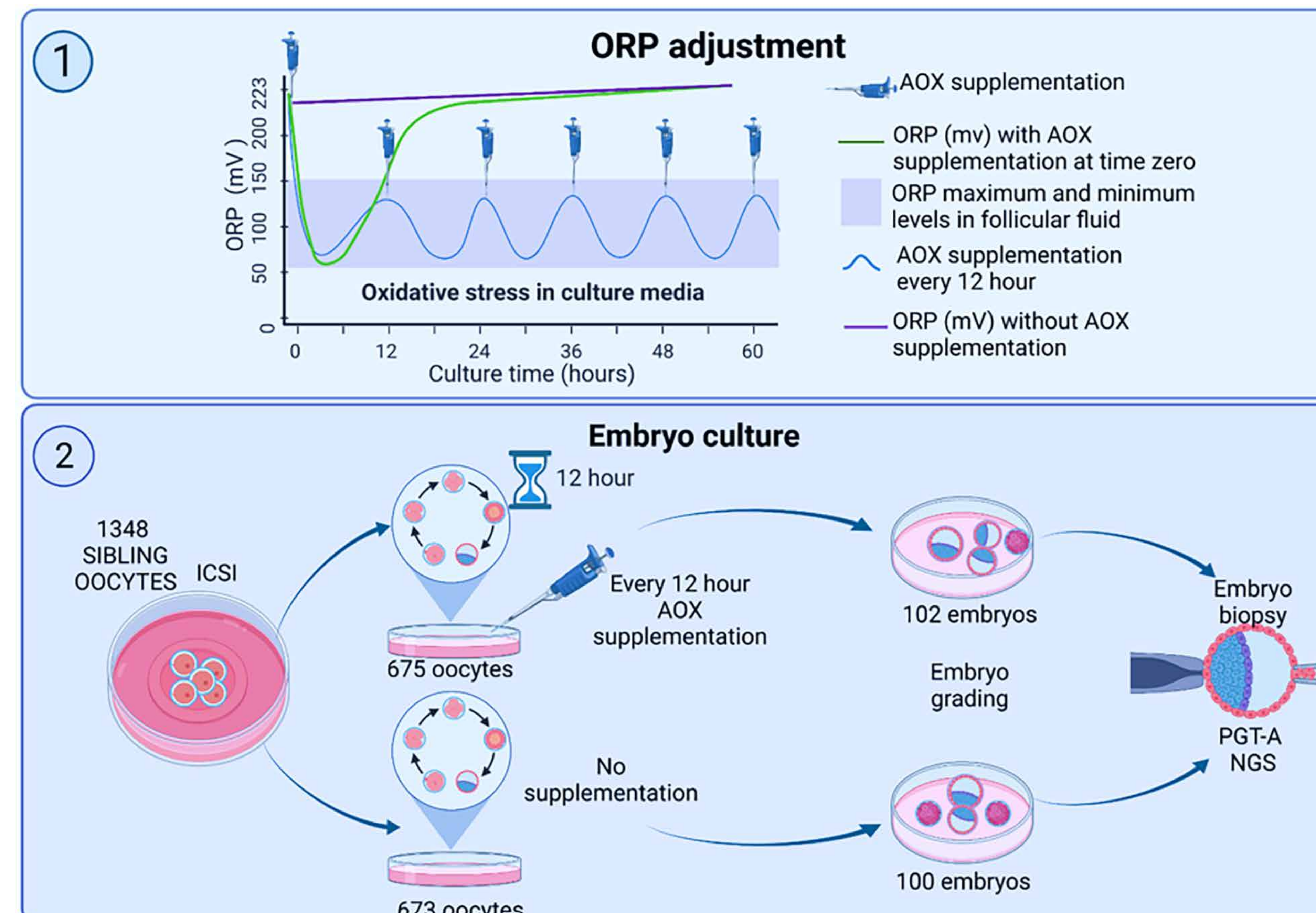


Table 1

No differences were found in biopsied embryos rate

	Group 1		Group 2		Pvalue
	Adjusted ORP media every 12h (86 mV± 14.8)		Non adjusted ORP media		
Mean of Patient age	36.9 Years				
Oocyte number	675		673		
Biopsied Blastocyst rate	102/675	15%	100/673	14.80%	

Table 2

The rates of cumulative usable and total expanded blastocysts at Day-5 plus Day-6 of development was statistically higher in Group 1 compared to the Group

	Group 1		Group 2		Pvalue
	Adjusted ORP media every 12h (86 mV± 14.8)		Non adjusted ORP media		
Oocyte number	675		673		
Euploid Blastocysts	51/102	50%*	32/100	32%	0.0389

RESULTS

- No differences (P>0.05) between the two groups were found in blastulation rates as well as the rate of biopsied embryos from collected oocytes. Group 1: 102 biopsied blastocysts out of 675 oocytes (15.1%) vs. Group 2: 100 blastocysts out of 673 (14.8%), respectively (Table 1).
- The blastocyst ploidy rate was significantly (P= 0.0389) higher in Group 1: 51 euploid embryos out of 102 biopsied (50%) vs. Group 2: 32 out of 100 biopsied (32%), with a 95% of CI for the mean in Group 1: 25.14 to 42.99 ±4.4735 and Group 2: 38.35 to 56.71 ±4.6116 (Table 2).

CONCLUSION

The adjustment of the ORP level every 12 hour of the embryo culture to physiological levels in patients undergoing PGT-A may increase the embryonic ploidy rate compared to that in embryos cultured in regular embryo culture medium with suprphysiological levels of ORP. These preliminary results may also suggest that an improvement in ploidy rates is not always following an increased number of blastocysts usable for PGT-A analysis.

