White paper

Clinical outcomes from studies on antioxidants

Introduction

Patients undergoing IVF are treated based on their indication, which may be an underlying female or male factor, hormonal- or gamete oriented.

The hormone treatment is often individualised while laboratory processes are increasingly standardised. Personalisation of the laboratory part is possible and a common factor that can vary is the culture duration, often depending on the number of available embryos, IVF or ICSI, genetic testing and more.

With the advent of culture systems fortified with media containing antioxidants that can increase the viability of embryos[2], there are reasons to consider what media to use for certain patient groups. Can such culture system have a positive impact on the more sensitive eggs and embryos coming from women of advanced maternal age (AMA)?

Investigating the impact of AMA

AMA is a significant factor affecting the success rate of in vitro fertilisation (IVF). Women over the age of 35 have a higher risk of infertility, miscarriage, and chromosomal abnormalities in their embryos. Researchers emphasize that this patient group has more sensitive oocytes and embryos due to a low mitochondrial activity[1].

Reactive oxygen species (ROS) have shown to impair embryo quality and viability[2]. ROS are required for normal cell function but may be present in excess during the IVF procedure. One action to limit excessive ROS production is to culture in 5% O_2[3], but many processes in the laboratory are still performed in ambient atmosphere[4]. A way to limit negative effects of ROS is to provide a protection by means of antioxidants.

Studies reporting ongoing pregnancy rate. Independent of age and culture method

Study	Experimental Events	Experimental Total	Control Events	Control Total	Risk Ratio	RR	95% CI
Ueno 2021 non-TL	96	265	139	485		1.26	[1.02; 1.56]
Ueno 2021 TL	75	243	126	394		0.97	[0.76; 1.22]
Gardner 2020 all	38	71	28	81		1.55	[1.07; 2.24]
Hardarson 2018 (all)	49	89	41	99		1.32	[0.98; 1.78]
Common effect model		**668**		**1059**		**1.19**	**[1.04; 1.36]**
Random effect model						**1.22**	**[1.01; 1.47]**
Heterogeneity: I^2 = 47%, τ^2 = 0.0168					0.5 1 2		

Studies reporting ongoing pregnancy rate in women of Advanced Maternal Age. Conventional incubation

Study	Experimental Events	Experimental Total	Control Events	Control Total	Risk Ratio	RR	95% CI
Ueno 2021 AMA n-TL	35	141	37	248		1.66	[1.10; 2.52]
Gardner 2020 AMA	19	38	8	31		1.94	[0.99; 3.81]
Common effect model		**179**		**279**		**1.73**	**[1.22; 2.46]**
Random effect model						**1.73**	**[1.22; 2.47]**
Heterogeneity: I^2 = 0%, τ^2 = 0					0.5 1 2		

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The effect of triple antioxidants in media

Throughout the last years, several clinical studies have been performed on media supplemented with the triple antioxidants, acetyl-L-carnetine, alpha lipoic acid and N-acetyl-L-cysteine. These studies are showing a significant positive effect on ongoing pregnancy rate in women overall and women of advanced maternal age in particular[5,6,7].

These three antioxidants are now available in the Gx-series, a media series based on the three G-series media products; G-MOPS PLUS, G-IVF PLUS and G-TL, and now including acetyl-L-carnetine, alpha lipoic acid and N-acetyl-L-cysteine. Media with triple antioxidant protection have shown to be safe and perform similarly or better than different controls. Showing significant effect on good quality day 3 embryos[6] and good quality blastocyst rate[8].

Discussion

The promising effects of antioxidants in culture media on pregnancy rate especially in women with AMA shows a potential for personalised medicine including laboratory culture systems. Nevertheless one should not underestimate the practical aspects of using the same culture system for all patients.

References

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