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ARTICLE

External quality control for embryology laboratories

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Abstract Participation in external quality control (EQC) programmes is recommended by various scientific societies. Results from an EQC programme for embryology laboratories are presented. This 5-year programme consisted of the annual delivery of (i) materials to test toxicity and (ii) a DVD/CD-ROM with images of zygotes and embryos on days 2 and 3, on the basis of which the participants were asked to judge the embryo quality and to take a clinical decision. A high degree of agreement was considered achieved when over 75% of the laboratories produced similar classifications. With respect to the materials analysed, the specificity was 68% and the sensitivity was 83%. Concerning embryo classification, the proportion of embryos on which a high degree of agreement was achieved increased during this period from 35% to 55%. No improvement was observed in the degree of agreement on the clinical decision to be taken. Day-3 embryos produced a higher degree of agreement (58%) than did day-2 embryos (32%) ($P < 0.05$). Participation in EQC increased the degree of inter-laboratory agreement on embryo classification, but not the corresponding agreement on clinical decision taking. It is necessary to introduce measures aimed at standardizing decision taking procedures in embryology laboratories.

KEYWORDS: embryology, embryo quality, quality control

Introduction

Participation in external quality control (EQC) programmes is recommended by various scientific societies (the Practice Committee of the American Society for Reproductive Medicine [ASRM] and the Practice Committee of the Society for Assisted Reproductive Technology Magli et al., 2008; [SART], 2006) in view of its utility in improving laboratory performance. These programmes should be aimed both at tangible elements (staff, instrumentation, equipment and

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supplies) and at intangible elements (protocols and techniques) (Elder and Kastrop, 2003).

With respect to tangible elements, the laboratory products used in assisted reproduction and which come into direct or indirect contact with zygotes and/or embryos should have no negative influence on their viability (Parinaud et al., 1987; Quinn, 2004). Therefore, all such products need to be tested beforehand to determine their degree of toxicity before clinical use (De Jonge et al., 2003; Elder and Kastrop, 2003; Go, 2000; the Practice Committee of the ASRM and the Practice Committee of the Lane et al., 2008; Magli et al., 2008; SART, 2006). In every laboratory, there should be a reliable bioassay for testing the toxicity of media and materials (Go, 2000). The most appropriate bioassay for this purpose is one that provides a sensitive system for approximating the real conditions under which zygotes and embryos are cultured *in vitro* (De Jonge et al., 2003).

There exist a wide variety of bioassays, but none provide an ideal system for testing for embryo toxins (Elder and Kastrop, 2003). Among the most commonly employed are the culture of 1- or 2-cell mouse embryos (Clarke et al., 1995; Gardner et al., 2005; Van den Bergh et al., 1996), the survival of human or hamster spermatozoa (Bavister and Andrews, 1988; Claassens et al., 2000; Elder and Kastrop, 2003; Go, 2000; Rinehart et al., 1988), the use of a small number of surplus oocytes from patients receiving assisted reproduction treatment (Elder and Kastrop, 2003), the culture of somatic cell lines (Elder and Kastrop, 2003; Go, 2000), the culture of multipronucleate embryos (Elder and Kastrop, 2003) and the use of mouse embryo stem cells (Genschow et al., 2000; Kim et al., 2005). As yet, there is no agreement as to which test is the most suitable for this type of assay, and so it has been suggested that it is preferable to simultaneously perform several different test procedures rather than just one (Gardner et al., 2005). In order to ensure that the method used is indeed an appropriate one, the laboratory in question should participate in an EQC programme (De Jonge et al., 2003).

With respect to intangible elements such as protocols and techniques, the evaluation of embryo quality is a crucial laboratory task, as it affects the decision as to how many and which embryos should be transferred, which in turn is directly related to the effectiveness of an IVF cycle and to the probability of a multiple pregnancy. Many factors may influence the assessment of embryo quality, including the different systems by which embryos and zygotes are classified, and intra- and inter-observer differences (Arce et al., 2006; Baxter et al., 2006; Keck et al., 2004). It is important that all the members of a team should follow the same criteria in order to be able to work in unison and take coherent decisions; this implies that there should be a degree of standardization of systems for embryo evaluation and for the ongoing training of embryology staff (Arce et al. 2006; Go, 2000; Keck et al., 2004). Concerning inter-laboratory differences in embryo evaluations, differences have been inversely related to the degree of activity, with fewer differences reported among laboratories with high levels of activity (Baxter et al., 2006) and among experienced embryologists (Arce et al., 2006). Therefore, it is necessary to establish mechanisms to standardize embryo evaluation among laboratories. These factors, together with the absence of an EQC programme for human reproduction laboratories in Spain that includes bioassays and embryo evaluation, led us to design, develop and assess a programme with these characteristics.

Materials and methods

All the data utilized in the analysis were obtained from the Spanish EQC programme for human reproduction laboratories, organized by Centro de Estudio e Investigación de la Fertilidad (CEIFER, 2008) and under the auspices of the Spanish Association for the Study of Reproductive Biology (ASEBIR). Over 40 laboratories throughout Spain took part in the programme from 2003 to 2007. The programme examined the evaluation of embryo quality and of the toxicity of materials, using bioassays. An annual examination was made of various materials, from 2003 to 2007 (Table 1). Some of these materials were treated with Armil (Bristol-Myers Squibb, USA) diluted with sterile PBS at a concentration of 1:100 for 5 min and subsequently dried at 37°C for 120 min and sterilized in an autoclave. Armil is a liquid disinfectant derived from quaternary ammonium (benzalkonium chloride). This concentra-

Table 1 Participation in external quality control programme (bioassay testing and embryo evaluation) from 2003 to 2007.

	2003	*2004*	*2005*	*2006*	*2007*
Bioassay					
No. of laboratories participating	14	21	15	13	14
Newly joined laboratories (%)	100	57	13	15	29
Material delivered	Tip[a]	Yellow straw[a]	Petri dish[b]	Tip[a]	Tip
	Transfer catheter	Blue straw[a]	Petri dish	Tip[a]	Tip
	Pasteur pipette	Red straw	Petri dish	Tip	Tip
Embryo evaluation					
No. of laboratories participating	30	22	18	19	16
Newly joined laboratories (%)	100	41	6	5	13

All tips were 200 μl. Petri dishes were Falcon 1006.
[a] Treated with Armil 1:100.
[b] Batch unsuitable for embryo culture.