Rescue ICSI revisited

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ICSI was first applied in cases of severe male factor infertility in which conventional IVF would be expected to fail or to give poor outcomes (Van Steirteghem et al., 1993). More recently, however, ICSI has been increasingly used in cases in which conventional IVF would not necessarily be inefficient. In such cases, ICSI is often preferred because of its reliability in terms of achieving high fertilization rates despite the occurrence and severity of different sperm abnormalities, some of which are not detectable by standard semen examinations. In fact, conventional IVF can give unwelcome surprises whose risk can only be limited, but not completely avoided, by performing specific sperm functional tests, such as the examination of spontaneous and stimulus-induced acrosome reaction, sperm– zona pellucida binding assay, sperm penetration test with zona-free oocytes or computerized analysis of sperm movement velocity and trajectory. Oocyte-borne failures of conventional IVF are also known, and the corresponding oocyte abnormalities are even more difficult to detect. Some failures of conventional IVF, such as those owing to the lack or dysfunction of sperm binding sites on the zona pellucida, would also be avoided if ICSI were used.

Rescue ICSI was first attempted in the late 1990s (Sjogren et al., 1995; Tsiirigotis et al., 1995; Morton et al., 1997; Yuzpe et al., 2000) as a back-up for cases that fell into one of the above categories without previous correct diagnosis and in which conventional IVF failure thus resulted from an indication error. However, these rescue attempts gave overall poor results, apparently because they were performed 1 day after in-vitro insemination, when significant changes related to ageing are likely to have occurred in the oocytes.

In this issue of Human Reproduction, Chen and Kattera (2003) report high fertilization and pregnancy rates (comparable to ICSI performed as the first choice) in cases in which rescue ICSI was done as early as 6 h after conventional in-vitro insemination. A conventional IVF attempt was considered as failed when the second polar body was not found at this time-point. Rescue ICSI was performed only in patients in whom all oocytes failed to be fertilized by conventional IVF.

These data are important because they provide, for the first time, an efficient back-up option for cases in which over-estimation of gamete fertilizing ability leads to erroneous indication of conventional IVF with subsequent fertilization failure. Paradoxically, the success of rescue ICSI can be expected to reduce the indication for ICSI as the first therapeutic choice. This can limit the additional risk, cost and laboratory load ICSI represents in comparison with conventional IVF.

Because an additional 6 h of in-vitro incubation of human oocytes before ICSI does not appear to compromise clinical outcomes, there is only one point of concern regarding the recourse to the 6-h-after rescue ICSI in cases of conventional IVF failure. It cannot be excluded with certainty that some of the oocytes that fail to extrude the second polar body by 6 h after in-vitro insemination are actually undergoing delayed fertilization and have already been penetrated by sperm. Additional ICSI, bringing a second spermatozoon to such oocytes, would thus lead to the generation of triploid, bispermy embryos. However, this condition would be distinguished easily by the observation of three pronuclei on the day after ICSI so that these embryos could be discarded. If, as described by Chen and Kattera in this issue, rescue ICSI is only performed if none of the oocytes inspected 6 h after in-vitro insemination presents the second polar body, the potential benefit from rescuing oocytes that have been correctly recognized as unfertilized—which obviously represent an overwhelming majority of the oocytes that lack the second polar body at this time point—would clearly justify the hypothetical risk of losing an oocyte undergoing delayed fertilization and thus subjected to rescue ICSI inadvertently. In fact, Chen and Kattera observed three pronuclei in only 6.6% of oocytes subjected to rescue ICSI. Most of these three-pronucleated zygotes had only one polar body, which means that the extra pronucleus did not result from bispemmy but rather originated through deficiency of the second meiotic anaphase owing to an oocyte activation anomaly. In the remaining three-pronucleated zygotes, the first polar body was fragmented and the presence or absence of the second polar body could thus not be assessed with certainty. Anyway, abnormalities of oocyte activation, leading to the retention of the second polar body and the formation of digynic triploids, is a common feature of ICSI, and the percentage of three-pronucleated zygotes in the reported series of rescue ICSI attempts does not exceed commonly reported figures.

As far as cost-effectiveness is concerned, couples consenting to the recourse to rescue ICSI in cases of total or near-total fertilization failure after a conventional IVF attempt would...
take advantage of not being charged the ICSI supplement unless strictly necessary. Moreover, costly advanced sperm functional tests, such as the acrosome reaction evaluation, computerized analysis of sperm movement or hemi-zona assay, could be avoided without exposing the couple to unreasonable risk of treatment attempt failure.

In conclusion, rescue ICSI, performed as early as 6 h after in-vitro insemination, is an interesting back-up treatment option to avoid complete failure of conventional IVF. Long-term evaluation of babies resulting from the application of rescue ICSI is needed to confirm empirically the safety of this method.

References


