Are spermatid injections of any clinical value?

Testicular sperm extraction and intracytoplasmic sperm injection

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There is still a great deal of confusion with regard to the use of testicular spermatozoa in association with intracytoplasmic sperm injection (ICSI). There are also different definitions and different techniques in use, both of which also increase the confusion. In this discussion paper, we shall try to define the different techniques precisely in relation to existing pathologies. Silber and Johnson (1998) raised the issue of the clinical value of spermatid injections. In principle, the use of testicular spermatozoa is indicated in azoospermia. Azoospermia may occur in different clinical conditions, i.e. obstructive and non-obstructive azoospermia. Although the history and the clinical picture may indicate whether azoospermia is obstructive or non-obstructive, a definitive diagnosis can be made only by histological confirmation. Obstructive azoospermia implies mechanical dysfunction, while spermatogenesis is normal. Non-obstructive azoospermia implies testicular dysfunction in which spermatogenesis is pathological.

Obstructive azoospermia

The diagnosis of obstructive azoospermia may be based on the history of the patient, including post-vasectomy and post-infection histories, and on clinical examination, as in bilateral congenital absence of the vas deferens. In cases of doubt, a testicular biopsy can be taken in order to confirm the presence of normal spermatogenesis. It has been clearly demonstrated that in cases of obstruction, spermatozoa are present in the biopsy specimens at the wet preparation. Such spermatozoa may be free or attached to the Sertoli cells, motile or non-motile. In 1993, when our first series of attempts at using such testicular spermatozoa in association with ICSI was carried out, we decided to name this procedure testicular sperm extraction (TESE). This first series was published by Devroey et al. (1994). It has to be emphasized that in cases of obstructive azoospermia spermatozoa are always found and used for ICSI.

It goes without saying that in this condition there is no reason for the use of round spermatids nor any need for any kind of ‘so-called’ maturation. Since spermatogenesis is normal in obstructive azoospermia, two important options are open. The first option is to freeze testicular tissue (Romero et al., 1996). The freezing of testicular tissue allows a biopsy to be performed which is not connected with the spouse’s cycle. Furthermore, it avoids repetitive testicular biopsies. The second option is to perform fine needle aspiration (FNA) (Bourne et al., 1995; Craft et al., 1997).

Non-obstructive azoospermia

Non-obstructive azoospermia implies pathological spermatogenesis. The final diagnosis has to be made on the basis of histology.

In general, two different pathological conditions may be detected, i.e. Sertoli cell-only syndrome and maturation arrest. It is clear that conflicting terminologies are circulating. Sertoli cell-only syndrome relates to a clinical condition of (mostly) reduced testicular size and azoospermia (Del Castillo et al., 1947). However, on histological examination two distinct conditions may be distinguished, i.e. total absence of germ cells or the presence of normal spermatogenesis in some tubuli. Sertoli cell-only syndrome can therefore imply a partial or total syndrome.

I am convinced that less confusion would exist if the terms partial or total germ-cell aplasia were used. The fact that germ-cell aplasia (Sertoli cell-only syndrome) may be only partial, implies the possibility of normal spermatogenesis and leads to the use of TESE and ICSI in non-obstructive azoospermia (see Devroey et al., 1995). The difference between the use of TESE and ICSI in germ-cell aplasia and obstructive azoospermia relates to the recovery rate of spermatozoa. In germ-cell aplasia in only 50% of the cases can spermatozoa be extracted and this only after many biopsies. It must be stressed in this respect that since the distribution of tubuli with spermatogenesis is not homogeneous, a previous biopsy will not be able to predict the presence of spermatozoa at the moment of the ICSI procedure. A previous biopsy will indicate the diagnosis of germ-cell aplasia, but will not be able to define its partial or total character. It is possible for no spermatogenic activity to be found on the initial biopsy while for the ICSI treatment foci with normal spermatogenesis may be found after multiple biopsies, but the reverse is also possible. It has been suggested that a quantitative analysis of the number of spermatids per seminiferous tubulus is predictive for the presence of spermatozoa at the moment of egg retrieval (Silber et al., 1997). Although this suggestion is meaningful it has not been possible to limit testicular sampling. Nowadays on many occasions multiple testicular sampling is still mandatory (Tournaye et al., 1996). Neither sensitivity, nor specificity are significantly reliable (Tournaye et al., 1997). In cases of germ-cell aplasia, two different strategies can be developed. The first strategy is to perform a testicular biopsy or multiple biopsies at the moment of the ICSI procedure. In this strategy no spermatozoa will be found in 50% of the cases and the
spouse’s oocyte will therefore not be injected. It has been suggested that FNA is less successful in men with non-obstructive azoospermia. For this reason the use of an open biopsy is the preferred method of sperm retrieval (Friedler et al., 1997). One option here is to propose the use of donor spermatozoa after extensive pretreatment counselling. A second strategy is to perform a prior biopsy and to freeze the testicular tissue for later use if any spermatozoa are found (Oates et al., 1997). In germ-cell aplasia there is no need for the use of round spermatids.

Maturation arrest relates to a clinical condition with mostly normal testicular size and azoospermia. The final diagnosis has to be made on the basis of histology. As for germ-cell aplasia, maturation arrest can be either complete or incomplete. If it is incomplete, spermatozoa can be used in a micro-injection procedure (Silber et al., 1996). As in cases of germ-cell aplasia, a prior biopsy does not have predictive value (Tournaye et al., 1997). Spermatozoa are found in the wet preparation and can be injected for ICSI in only 50% of the cases. Sensitivity and specificity are not reliable. The same strategies for treatment can be developed as for germ-cell aplasia, i.e. prior freezing of testicular tissue or the optional use of frozen donor spermatozoa.

It has been demonstrated that ultrasonographic abnormalities occur in the tests after open biopsies. These abnormalities suggest the presence of inflammation or haematoma. For those reasons it is advisable to wait approximately six months before performing a new biopsy (Schlegel and Su, 1997). The critical question is if round spermatids can be used in cases of maturation arrest. There is a general consensus that the arrested development is found at meiosis and that no conditions are described where only round spermatids are found. If round spermatids are present, elongated ones are also detected. In other terms, the blockage is not at the level of spermiogenesis (G.Verheyen, personal communication).

The above statements raise several questions. Theoretically, one could argue that if not enough elongated spermatids/ spermatozoa are present, round spermatids may be injected. Further questions centre on whether in the future round spermatids might be cultured in-vitro to elongated ones and whether spermatocytes might be cultured to spermatids.

Conclusions

At present, the use of round spermatids is most debatable. At present, only 50% of couples with non-obstructive azoospermia can benefit from the use of TESE in combination with ICSI.