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Sperm analysis parameters as an indication for intracytoplasmic sperm injection (ICSI) instead of in vitro fertilization (IVF)[1]

Executive Summary

[1] Translation of the executive summary of the final report *Spermiogrammparameter für eine Indikation zur Intracytoplasmatischen Spermieninjektion (ICSI) statt In-vitro-Fertilisation* (Version 1.0; Status: 10 September 2014). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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This report was prepared in collaboration with external experts.

The responsibility for the contents of the report lies solely with IQWiG.

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IQWiG thanks the external experts for their collaboration in the project.

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[2] Due to legal data protection regulations, employees have the right not to be named.

Executive summary

On 27 August 2012 the Federal Joint Committee (G-BA) wrote to the Institute for Quality and Efficiency in Health Care (IQWiG) to commission the assessment of sperm analysis parameters as an indication for intracytoplasmic sperm injection (ICSI) instead of in vitro fertilization (IVF).

Research question

The goals of this research were

- the benefit assessment of ICSI treatment in comparison with IVF treatment depending on sperm analysis parameters (subgoal 1)
- the benefit assessment of ICSI treatment in comparison with further IVF treatment depending on fertilization failure in the previous IVF attempt (subgoal 2)

in couples with involuntary childlessness with regard to patient-relevant outcomes.

Research results on the strength of the association between observed effects and sperm analysis parameters were supposed to identify and characterize sperm analysis parameters for determining the indication for ICSI instead of IVF.

Research results on the strength of the association between observed effects and fertilization failure in a previous IVF attempt – corresponding to the respective definition used in the studies – were supposed to assess which extent of fertilization failure in a previous IVF attempt justifies the determination of an indication for ICSI instead of further IVF.

Methods

Randomized controlled trials (RCTs) were included that compared ICSI and IVF with regard to patient-relevant outcomes and that also contained information on sperm analysis parameters or fertilization failure.

For this purpose, a systematic literature search was performed in the following databases: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (Clinical Trials). In addition, a search for relevant systematic reviews took place in the databases MEDLINE and EMBASE in parallel with the search for relevant primary studies. Searches were also conducted in the databases Cochrane Database of Systematic Reviews (Cochrane Reviews), Database of Abstracts of Reviews of Effects (Other Reviews), and the Health Technology Assessment Database (Technology Assessments). The last search was conducted on 17 June 2014.

Furthermore, systematic reviews were scrutinized for further relevant studies and publicly accessible trial registries, and information that had been provided in the hearing procedure for the preliminary report plan and for the preliminary report were also screened. Finally, the authors of relevant study publications were contacted in order to clarify important questions.

The selection of relevant studies was performed by 2 reviewers independently of each other for the result from the bibliographic literature search and from the search in publicly accessible trial registries, and for potentially relevant studies from systematic reviews. The selection of relevant studies from the remaining search sources was performed by one reviewer and checked by a second reviewer.

Data extraction was conducted in standardized tables. To evaluate the certainty of results, the risk of bias at study and outcome level was assessed and rated as low or high respectively. The results of the individual studies were described, organized by outcomes. If the studies were comparable regarding the research question and relevant characteristics, the individual results were pooled quantitatively by means of meta-analyses.

A validation of the surrogate outcome (in vitro fertilization success) for the patient-relevant outcome “live birth” was aimed for.

Results

No adequate data were available for surrogate validation: Only one RCT was identified that investigated effects both on the surrogate outcome “in vitro fertilization success” and on the patient-relevant outcome of interest “live birth” in the framework of the given area of indication and within comparable interventions. Hence the outcome “in vitro fertilization success” could not be validated and was therefore not considered.

4 studies were included in the benefit assessment of ICSI treatment in comparison with IVF treatment depending on sperm analysis parameters (subgoal 1). The studies investigated the differences between ICSI and IVF with regard to different outcomes.

The studies are unsuitable to identify thresholds of sperm analysis parameters that justify ICSI instead of IVF because they only included couples with normal sperm analysis. Under these limitations, the following results were found.

Only one study was available for the outcome “live birth”. According to this study, there is no statistically significant difference between the 2 interventions in couples with idiopathic infertility.

3 studies presented results on the outcome “miscarriage”. The meta-analysis conducted did not show a statistically significant effect in favour of ICSI or IVF.

Adverse effects in form of ovarian hyperstimulation syndrome (OHSS) were only reported in one study. No statistically significant difference was found for this outcome either.

No study was available for the benefit assessment of ICSI treatment in comparison with IVF treatment depending on fertilization failure in the previous IVF attempt (subgoal 2).

Conclusions

Only 4 RCTs on the comparison of ICSI versus IVF also reported sperm analysis parameters, but these 4 RCTs only referred to men with normal sperm analysis. Hence the available evidence is inadequate to record a possible interaction between treatment effects of ICSI and sperm analysis parameters. On this basis, conclusions can only be drawn for couples with normal sperm analysis parameters (normozoospermia) in the man.

The evidence base is unsuitable to prove the benefit of ICSI treatment in comparison with IVF treatment depending on sperm analysis parameters for any of the outcomes considered (subgoal 1).

Since no study could be identified that reported data on the benefit assessment of ICSI treatment in comparison with further IVF treatment depending on fertilization failure in the previous IVF attempt, subgoal 2 cannot be assessed.

Keywords: sperm injection – intracytoplasmic, fertilization in vitro, infertility, benefit assessment, systematic review

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