INAHTA Brief

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Title Processing and cryopreservation of ovarian tissue prior to or after gonadotoxic treatment to preserve fertility in females for the future

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Reference Milverton, J, Mittal, R, Carter, D, Kessels, S, Newton, S, Schubert, C, Parsons J, Merlin, T. (2017). Processing and cryopreservation of ovarian tissue prior to or after gonadotoxic treatment to preserve fertility in females for the future. MSAC Application 1435 Part B, Assessment Report. Commonwealth of Australia, Canberra, ACT.

Aim

To assess the clinical evidence, and perform an economic analysis of processing and cryopreservation of ovarian tissue for preserving fertility, in response to an application for public funding made to the Australian Department of Health.

Conclusions and results

Safety

Cryopreservation of ovarian tissue (OTC) appears to be a safe procedure relative to oocyte cryopreservation, however, the evidence was of low quality.

Comparative (but low level) evidence in *adults (aged 18 to 40 years)* found that compared to oocyte cryopreservation, OTC had fewer reported complications (0.37% versus 3.9%). The reporting of complications may be unreliable, as they may have in fact been technical issues.

The frequency of complications for ovarian tissue transfer (OTT) was assessed in one study of *adolescent and adult* patients. Out of 455 OTT procedures there were 4 adverse events reported (0.88%). One case required conversion from laparoscopy to open laparotomy procedure.

There was no evidence identified that compared the safety of OTC with no fertility preservation or other listed comparators for *pre-pubertal patients*. OTC should still be considered experimental in this younger population due to the small number of procedures that have been performed.

Transfer of malignant cells is considered a serious risk for OTT, particularly for leukaemia and lymphoma patients, and other haematological or systemic malignancies. No cases were reported of transferred malignancy leading to recurrence of disease.

Effectiveness

There was little comparative evidence identified to enable conclusions on the relative effectiveness of OTC. Evidence from case series indicated that OTC followed by OTT can provide an option for achieving pregnancy and live birth in *post-pubertal women*, but comparative success rates could not be determined.

Due to the small numbers of OTC procedures that have been performed in *pre-pubertal aged girls*, no conclusions can be drawn about its comparative effectiveness.

Economic analysis

Due to the lack of clinical data, a cost-effectiveness analysis could not be performed. Cost analysis estimated procedure-related costs to be $5,176 per patient in the Australian setting. For *post-pubertal women*, total average costs, (including downstream storage, conception and pregnancy, discounted as appropriate) range from $7,326 (no tissue utilised and no conception attempted) to $37,149 (tissue is transplanted, assisted reproductive techniques are used and live birth occurs). For *pre-pubertal women* these costs ranged from $13,575 to $26,975.

Recommendations

The application was not supported for public funding. OTC may be an important option for women and girls for whom this is the only option for fertility. However there are safety concerns, in particular with the risk of malignancy transference. In addition, the clinical effectiveness was uncertain due to the paucity of evidence.

Methods

A systematic review was undertaken. Peer-reviewed and grey literature sources were searched on the 6th of June 2017. Study selection criteria defined in the protocol were applied to select relevant articles by one researcher. A 10 per cent sample selected by a second researcher was compared for consistency. Disagreements were resolved through consultation with a third researcher.

A quality appraisal was performed for each included study using a checklist appropriate to the study design. The quality of evidence for individual outcomes was performed using the GRADE rating tool (Guyatt et al. 2011). Meta-analysis of the evidence was not possible due to the paucity of evidence, so a narrative synthesis of results was provided.

Further research/reviews required

Suggestions for future applications for the support of ovarian cryopreservation were to include

- a protocol showing how malignancy in the cryopreserved tissue can be excluded
- evidence of clinical benefits and quality of life
- further data on utilisation including proportion of females who subsequently use the preserved tissue
- the incremental cost per live birth (all associated costs)

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