Impact of the microbiome on fertility and fertility treatment outcomes

Strategic delivery:	☒ Safe, ethical, effective treatment	☐ Consistent outcomes and support	☐ Improving standards through intelligence
Details:			
Meeting	SCAAC		
Agenda item	6		
Paper number	HFEA (04/02/2019)06		
Meeting date	4 February 2019		
Author	Rasheda Begum, Scientific Policy Officer		
Output:			
For information or decision?	For information		
Recommendation	Members are asked to • Consider the research that focuses on the microbiome and provide their thoughts on what influence the microbiome may have in fertility treatment • Review whether any outputs from HFEA are required addressing the microbiome in fertility treatment • Advise the Executive if they are aware of any other recent developments		
Resource implications	N/A		
Implementation date	N/A		
Communication(s)	N/A		
Organisational risk	☒ Low	☐ Medium	☐ High

1. Introduction

1.1. In the most recent horizon scanning process, the possible effect of the microbiome on fertility and fertility treatment outcomes was identified as a high priority area. High priority is given to techniques or issues that may require ongoing monitoring or provision of patient information.

1.2. The microbiome refers to the microorganisms which inhabit a particular environment, for example, the body or part of the body. Our understanding of the microbiome has developed rapidly in recent years, along with our understanding of its role in human health and disease.

1.3. Researchers have long been interested in the possible interactions between the male and female reproductive tract and its microbiome. If the composition of the microbiome is shown to be related to fertility, or indeed, fertility treatment outcomes, there may be potential for development of interventions aimed at altering the microbiome to improve outcomes for patients.

1.4. This paper looks at recent studies investigating the possible relationship between the human microbiome and fertility.

2. Recent studies

Investigating fertility

2.1. The testicular bacterial microbiome (BM) was compared between five normozoospermic men and five men with idiopathic non-obstructive azoospermia (iNOA) in a study by Alfano et al., 2018, to see whether the BM could be associated with male-factor infertility. The iNOA group had increased amounts of bacterial DNA. The authors concluded that the findings on testicular BM could support future translational therapies of male-factor infertility.

2.2. Babu et al., 2017 compared vaginal flora of 84 healthy women and 116 women with infertility problems. The study found that women with infertility problems had higher prevalence of asymptomatic vaginosis and increased amounts of bacterial vaginosis associated bacteria.

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2.3. A systematic review by Haahr et al., 2018 looked at 12 studies which collectively consisted of 2980 infertile in vitro fertilisation (IVF) patients to assess whether the prevalence of bacterial vaginosis (BV) or abnormal vaginal microbiota (AVM) had any association with IVF outcomes including live birth rate, early spontaneous abortion rate and clinical pregnancy rate. BV did not significantly impact live birth rate or clinical pregnancy rate; however, a significant association was found with early spontaneous abortion. The authors addressed that the quality of the evidence is low and further research is required.

2.4. In a study by Haarh et al., 2017, a patient who had two failed IVF cycles was diagnosed with abnormal vaginal microbiota (AVM) and was treated with oral Clindamycin. Although the authors described the treatment of AVM as successful, after two subsequent frozen embryo transfer cycles the patient did not achieve pregnancy. The authors suggested further randomised clinical trials should be carried out to investigate the impact of AVM treatment.

2.5. A systematic review by Bracewell-Milnes et al., 2018 looked at 26 studies, 19 of which studied the vaginal microbiome and seven which studied the uterine microbiome to assess the microbiome, specifically with regard to improving the outcome of assisted reproductive technology (ART). AVM was not associated with ART outcome in studies using culture-based techniques but showed a negative effect on ART in studies that used sequence-based technologies. Abnormal uterine microbiome did impact ART outcome in all of the studies which used culture-based methods and the most extensive of the two sequencing studies.

2.6. In a study by Moreno et al., 2016, it was found that endometrial fluid in patients undergoing IVF with a receptive endometrium consisted of either a Lactobacillus-dominated microbiota or a non-Lactobacillus-dominated bacteria. Decreased rates of implantation, ongoing pregnancy and live birth were associated with non-Lactobacillus-dominated microbiota.

2.7. An upcoming study (Koedooder et al., 2018) will be looking at whether the urogenital microbiome can be a predictor for ART outcomes. The study aims to analyses the urinary and vaginal microbiome of 300 women and will record whether pregnancy is achieved after fresh embryo transfer and with the subsequent year after inclusion.

3. Conclusions

3.1. There is growing interest in exploring whether the microbiome can be a key indicator for investigating fertility and developing interventions based on the elements of the microbiome.

3.2. There is a need for further research into the impact of the microbiome on fertility before assumptions can be made about the value of assessing the microbiome in fertility treatment.

4. Recommendations

4.1. Members are asked to

- consider the research that focuses on reproductive tract microbiome and provide their thoughts on what influence the microbiome may have on fertility and fertility treatment outcomes
- considering that the HFEA does not currently provide patient information on the microbiome, review whether any outputs from HFEA are required addressing the impact of the reproductive tract microbiome on fertility and fertility treatment outcomes
- advise the Executive if they are aware of any other relevant recent developments.

5. References

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