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Impact of virtual reality with or without hypnosis before oocyte retrieval: A randomised study

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ABSTRACT

Objective of the study: Anxiety can affect pregnancy rate following an in-vitro-fertilisation procedure. Hypnosis reduces emotional distress associated with medical procedures. Virtual reality (VR) is an immersive 3D experience, created using a visual headset and headphones. The goal of this study was to evaluate the effect of VR session with and without hypnosis before sedation for oocyte retrieval (OR) on anxiety levels and on pregnancy rate.

Methods: After written informed consent, 342 women scheduled for OR under sedation were randomised in this double-blinded study (NCT03064061). A Visual Analogue Scale for anxiety (VAS) and a Spielberger State-Trait Anxiety Inventory (STAI) questionnaire before (baseline) and after VR session, and at hospital discharge were administered. VRD Group (n = 178) received a VR session (goal of distraction) and VRH group (n = 164) received the same VR session with hypnosis focused on slowing respiratory rhythm and suggestions of reusing the technique later as needed (AQUA Oncomfort/HypnoVR ™). The primary endpoint was ongoing pregnancy at 12 weeks. Mann Whitney, Wilcoxon signed rank test and Chi-square tests were used; p value < 0.05 considered significant.

Results: Although anxiety scores decreased from baseline in both VRD and VRH groups ($p < 0.001$ baseline vs post VR session and baseline vs hospital discharge), there was no difference between them. Nor was there a difference in pregnancy rate (18,6 % VRD group vs 22,5 % VRH group).

Conclusion: Although both VRD and VRH sessions before sedation for OR significantly reduced women's anxiety, the type of suggestions used during the hypnosis VR session did not influence the pregnancy rate.

1. Introduction

Anxiety in the context of infertility and infertility care is common and can induce stress in patients.[1] During assisted reproductive technology (ART), oocyte retrieval (OR) is often performed with anaesthesia, which can be an additional cause of stress and anxiety for the patients. The causes of preoperative anxiety may be waiting for surgery, fear of pain during and after intervention and concern about outcomes of the procedure e.g., number of oocytes collected. Matthiesen et al. have shown in their meta-analysis a small but significant association between stress and distress and reduced ART success.[2] Reducing anxiety could improve patients' ability to cope with stress and could promote pregnancy in this context.[3]

To reduce preoperative anxiety both pharmacological and non-pharmacological techniques can be used. Sedative and anxiolytic drugs like midazolam have adverse effects such as breathing problems, drowsiness and prolonged recovery. Therefore, non-pharmacological techniques are preferred.[4] Non-pharmacologic interventions to decrease preoperative anxiety showed a wide range of options. Communication strategies, cognitive-behavioral therapy, music therapy, preoperative preparation by video, aromatherapy, massage, meditation and guided imagery relaxation therapy, acupuncture are options which have showed promising results to decrease anxiety. However, there are some concerns about the availability, cost and required

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educated personnel to bring these methods into clinical practice.[4] Some techniques, such as psychological interventions, have already shown an effect on reducing anxiety and increasing the pregnancy rate.[5] In their recent meta-analysis, Kremer et al. have analysed the effectiveness of psychosocial interventions (music therapy, cognitive restructuring, emotional expression, assertiveness training as well as relaxation techniques and Yoga, expressive writing, breathing with mindfulness and progressive muscle relaxation, laughter therapy) for infertile women.[1] However, because of serious methodological inadequacies in all the studies, authors concluded that it is not possible to draw conclusions of psychological interventions influencing quality of life (anxiety, depression) and pregnancy rate in women with fertility disorders.

Hypnosis was also used to decrease anxiety and catastrophizing thoughts in the preoperative period[6,7] and its effect was found to be similar to midazolam in reducing preoperative anxiety in children.[8] Moreover, hypnosis has demonstrated promising results when used during embryo transfer (ET) in in vitro fertilization (IVF) cycles.[9] Hypnosis is defined as a "state of modified consciousness involving focused attention and reduced peripheral awareness characterised by an enhanced capacity for response to suggestions".[10]

Among more recent tools, virtual reality (VR) technology that allows a complete immersion in an artificial three-dimensional environment has been studied in non-clinical populations, to promote relaxation,[11] and reduce anxiety[12] notably through psychological, physiological and biochemical stress indicators.[13] This technology allows personalization of scenarios that can further facilitate user's sense of relaxation.[14]

Moreover, in medical populations VR has also been proposed as a tool of distraction and was shown to significantly reduce preoperative anxiety.[15] Virtual reality distraction (VRD) is a subjective immersive experience where the patient is isolated from the outside environment and is distracted. A VR system products immersive videos that replicate real environments. By leveraging visual, auditory and sensory cues, a convincing illusion of presence in a virtual setting is created.[16] This distraction technique allows a diversion of the patient's attention, which redirects the mind far from the current emotion such as anxiety. Music, which is an integral part of virtual reality sessions, activates the parasympathetic nervous system and reduces sympathetic nervous activity. By this way, it can decrease anxiety and help patients to become more relaxed and distracted from anxiety.[17,18] Emerging research lines have investigated the combination of virtual reality distraction and hypnosis. When using hypnosis and VR, some studies use hypnosis session followed by a session of virtual reality distraction and other use hypnosis session delivered through an immersive virtual reality environment (VRH). VRH has shown a significant reduction of preoperative anxiety.[19]

Anxiety is frequently found in the context of infertility and infertility care and it could negatively affect the patients' chances of pregnancy. Therefore, we can ask the opposite question of whether reducing anxiety, by using a VR session distraction-type (VRD) or a VR session associated with hypnosis (VRH) can improve pregnancy rates.

2. Materials and methods

We used the CONSORT reporting guidelines[20] in this randomised trial (Appendix).

2.1. Population and study design

This double-blinded randomized controlled trial was approved on July 20, 2016 by the "Comité d'Ethique Hospitalo-Facultaire des Cliniques universitaires Saint-Luc" (2016/20JUL/346, Brussels, Belgium – Chairman: Prof. J-M Maloteaux) and registered on ClinicalTrials.gov (NCT03064061) before starting the inclusion of patients. The study was conducted at Cliniques universitaires Saint-Luc in Brussels, Belgium and written informed consent was obtained from all patients, according to the Declaration of Helsinki. Enrollment started on February 17, 2017 and was completed on June 30, 2019. All women between the ages of 18–42 years scheduled for OR under sedation (for IVF or intracytoplasmic sperm injection) and a fresh embryo transfer were eligible. Cycles with a preimplantation genetic diagnosis procedure were excluded. Other exclusion criteria were inability to hear in headphones or insufficient visual acuity, patients taking psychotropic medication.

A simple randomization was used. Patients were randomized in a 1:1 allocation to either receive virtual reality distraction (VRD) or virtual reality hypnosis (VRH), using computerized randomization (https://www.randomizer.org). The study nurses who carried out the various anxiety tests were blinded to group assignment. One nurse gave the questionnaires to be completed and performed the anxiety VAS scores and another nurse placed the virtual reality headset with the appropriate program. The anaesthetists who carried out the sedation were blinded to the patient group allocation as well as the gynaecologists performing the OR.

All enrolled patients underwent an ovarian stimulation with a GnRH antagonist protocol. Transvaginal ultrasound-guided oocyte retrieval was carried out 36–38 h after ovulation triggering, under sedation, with a single-lumen 18-gauge needle. Embryo transfer was performed after 3 or 5 days of culture. The number of transferred embryos was determined by the patient's age and embryo's quality. Luteal phase was supported by vaginal progesterone (Utrogestan 200 mg, trice daily) or oral dydrogesterone (Duphaston 10 mg, trice daily).

The day of OR, after insertion of the peripheral intravenous line, all patients received a VR session of 20 minutes.

2.1.1. VRD group

The VR session was an immersive experience in an undersea environment and soft music was present as auditory stimulus (SHAM Oncomfort/HypnoVR ™.) (Fig. 1)

2.1.2. VRH group

The VR session was an immersive experience in an undersea environment with a soft music (like in the VRD group), but as auditory stimulus, a session of hypnosis was added (AQUA Oncomfort/HypnoVR™). The patient experienced guided audio narratives designed to induce relaxation with a calming voice, meditative instructions. The audio was synchronized with immersive visuals to enhance the sense of calm helping patient focus on breathing (the patient has to breathe at the same rate as the movement of the tail of a whale moving in front of her), slowing respiratory rhythm and suggestions of reuse the technique later to find a feeling of well-being and calmness as needed.

2.1.3. The Hardware and software Equipment

VR device consists of a video headset, associated with a smartphone and headphones. Oncomfort's VR system utilized GSM (Global System for Mobile Communications) connectivity (essentially mobile network communication) to allow users to access VR content directly through

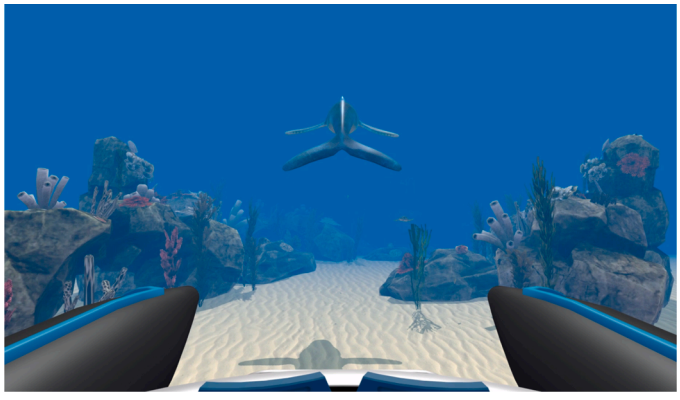

Fig. 1. Undersea environment seen by the patient with the permission of Oncomfort/HypnoVR ™.

their mobile device.

The headset has sensors that can track the movements of the user's head to give the illusion of movement in virtual space. A feeling of real immersion is given through visual and auditory stimuli.[21]

During OR, all patients received a standard sedation using remifentanil (0.1 μg/kg/min) and ketamine (0.15 mg/kg), as well as a paracervical block (lidocaine 1 %, 10 ml) and additional propofol boluses if needed.

2.2. Evaluation of anxiety

Evaluation of anxiety was performed by a Visual Analogue Scale for anxiety and a baseline Spielberger State-Trait Anxiety Inventory (STAI) questionnaire, two validated instruments to measure anxiety. The VAS anxiety consists of asking the patient to quantify their degree of anxiety at that moment by putting a mark on a VAS scale of 0–100 mm with 0 corresponding to no anxiety and 100 to the maximum anxiety level a person can imagine.[22,23] The STAI questionnaire consists of 20 statements used to determine a patient's current anxiety level. Each statement is rated on a four-point scale for the patient's agreement with the statement (not at all, somewhat, moderately so, and very much so). The total score for STAI ranges from a minimum of 20 to a maximum of 80.[24]

2.3. Times of evaluation of anxiety

The first evaluation of anxiety was performed after the insertion of intravenous line (VAS A baseline/STAI baseline). The second evaluation of anxiety was performed just after the VR session (VAS A post VR session/STAI post VR session) and finally, the third evaluation of anxiety was realised after the patient has been informed of the number of oocytes recovered during the surgery and just before leaving the hospital (VAS A hospital discharge/STAI hospital discharge).

2.4. Side effect

Side effects like nausea or vomiting were recorded after the VR session.

2.5. Outcomes

The primary outcome was ongoing pregnancy rate at 12 weeks assessed by ultrasound. The secondary outcomes were the anxiety measured by the VAS A and by the STAI questionnaire, propofol consumption, implantation rate, pregnancy rate measured by blood β-hCG level 14 days after pick-up, clinical pregnancy at 6 weeks confirmed by vaginal ultrasound as well as the live birth rate.

2.6. Statistical analysis

Power calculation for our primary outcome could not be calculated as to the best of our knowledge, no studies are available concerning the effect of VR to decrease anxiety in IVF procedures. We hypothesized that we would have a significant decrease in anxiety score, a variable which could improve pregnancy rate. An increase in pregnancy rates of 5 % was considered to be clinically relevant. Internal data showed a success rate of 25 % of ongoing pregnancy at 12 weeks. With an alpha at 0.05 and a power (1-beta) at 0.8, a minimum of 241 subjects was necessary in each group to show a difference of 5 % in the primary endpoint. To calculate the power of our study, we were interested in assessing how our observed data align with theoretical expectations, therefore we have opted for comparing an observed proportion to a theoretical proportion. Moreover, we have used a one-sided test because our research hypothesis was directional, meaning we were interested in determining if the observed proportion was significantly greater than or less than the theoretical proportion, but not both. Virtual reality is well known to be efficient to reduce anxiety and therefore in both groups (VRD and VRH) we expected that our observed proportion will be higher than the theoretical proportion based on our hypothesis.

A planned interim analysis was performed after 50 patients in each group (100 in total) to be sure that VR sessions were useful to decrease anxiety in this context. After the inclusion of the first 100 patients, a significant decrease in anxiety scores was well demonstrated and a difference of ongoing pregnancy at 12 weeks of 8,3 % between the groups was shown. Accordingly, the size of the study was re-calculated including a 6 % difference between the two groups and a minimum number of 164 subjects was required in each group. We included 359 patients to take into account potential dropouts.

A Kolmogorov-Smirnov test was used to check the normality of the data. Continuous data are presented as median and Percentile 25-Percentile 75 or means $\pm$ standard deviation. Categorical data are presented as numbers and percentages.

A Mann Whitney *U* test or a student's *t*-test were used to compare continuous data. A Chi-square test was used to compare categorical variables. A binary regression analysis was used to seek an association between baseline VAS A and positive blood β-hCG and between baseline STAI and positive blood β-hCG. A Wilcoxon signed rank test was performed to compare within group changes in VAS A and in STAI. A p value < 0.05 was considered as statistically significant. All analyses were performed using IBM SPSS Statistics version 27.

3. Results

Among 359 patients screened, eight patients were not eligible for participation (n = 5) or declined to participate (n = 3; consent not given). A total of 351 patients were randomized among which 182 patients were assigned to the VRD group and 169 patients to the VRH group. Nine patients were excluded from the final analysis after giving their written consent. In the VRD group, two patients did not longer want to participate and in two situations the VR device was not functional on the day of the OR. In the VRH group, one patient did not want to put on the VR headset, two patients did not want longer to participate and twice the RV device was not functional. Finally,178 and 164 patients were analysed in VRD and VRH groups respectively (Fig. 2).

There was no statistically significant difference between the demographic data of both groups except for the weight (kg): patients were heavier in the VRH group: 65.6$\pm$ 14.4 vs 69.4 $\pm$ 16.1 in the VRD group (p = 0.013). (Table 1).

Clinical data presented in Table 2 showed no statistically significant difference between the VRD and the VRH groups concerning propofol consumption in mg (30 vs 30), embryo transfer rate per cycle (87.6 % vs 84.1 %), number of embryos transferred (means $\pm$ SD) (1.71 $\pm$ 0.67 vs 1.65 $\pm$ 0.67), transfers performed on day 3 (94.2 % vs 91.3 %), transfers with at least one good quality embryo (89.1 % vs 84.1 %) and implantation rate (18.2 % vs 20.6 %).

In the VRD group, a pregnancy rate (PR) per transfer of 30.8 % was observed, compared to a PR per transfer of 33.3 % in the VRH group. Consequently, clinical pregnancy rate at 6 weeks, and ongoing pregnancy rate at 12 weeks (primary endpoint) were 42/156 (26.9 %) and 29/156 (18.6 %) in the VRD group and they were 39/138 (28.2 %) and 31/138 (22.5 %) in the VRH group, respectively. There was no significant difference regarding positive β-hCG at 14 days after OR, clinical pregnancy at 6 weeks and ongoing pregnancy rate at 12 weeks between the two study groups. Twin pregnancy rate was also similar between groups (8.3 % in the VRD group and 13 % in the VRH group). Three patients suffered a late miscarriage: one in the VRD group and two in the VRH group. One patient had a medical termination of pregnancy because of foetus genetic disease in the VRH group. Live birth rate (LBR) per transfer (17.9 % in the VRD group vs 20.3 % in the VRH group) did not show statistically significant difference between the two groups.

VAS Anxiety scores were respectively in VRD and VRH groups (median; Percentile25 - Percentile75): baseline: 36 (24−53) and 45 (26−58); post VR session: 19.5 (9−36) and 20 (8.5−36) at hospital

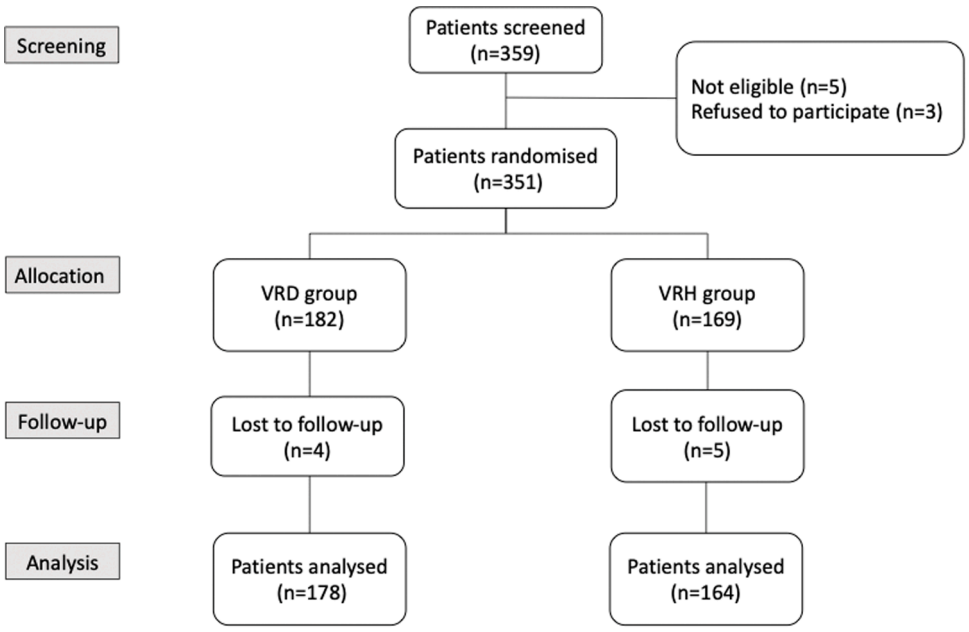

Fig. 2. Flowchart.

Table 1
Patient's characteristics.

Variable	VRD n = 178	VRH n = 164	p
Age (yr)	34.5 ± 4.7	35 ± 4.8	0.169
Height (cm)	165 ± 6.3	165 ± 6.7	0.364
Weight (kg)	65.6 ± 14.4	69.4 ± 16.1	0.013
Primary infertility (%)	86/178 (48.3)	75/164 (45.7)	0.633
Attempts rank 1 (%)	38.8	36.0	0.070
Attempts rank 2 (%)	23.6	19.5	
Attempts rank 3 (%)	21.9	14.6	
Attempts rank 4 (%)	9	12.2	
Attempts rank 5 (%)	2.8	10.4	
Attempts rank 6 (%)	3.4	4.9	
Attempts rank > 6 (%)	0.6	2.4	

Data are presented as mean ± SD; values are presented as numbers (%).

Table 2
Propofol consumption during OR and clinical outcomes.

	VRD (n = 178)	**VRH (n = 164)**	p
Propofol consumption (mg)	30 (10–50)	30 (10–50)	0.924
Embryo transfer / cycle (%)	156 (87.6)	138 (84.1)	0.353
No. of embryos transferred	1.71 ± 0.67	1.65 ± 0.67	0.241
Transfer on day 3 (%)	147/156 (94.2)	126/138 (91.3)	0.331
At least 1 good quality embryo transferred (%)	139/156 (89.1)	116/138 (84.1)	0.203
Implantation rate (%)	49/228 (18.2)	47/228 (20.6)	0.254
Positive β-hCG / transfer (%)	48/156 (30.8)	46/138 (33.3)	0.638
Clinical pregnancy at 6 w / transfer (%)	42/156 (26.9)	39/138 (28.2)	0.768
Ongoing pregnancy at 12 w / transfer (%)	29/156 (18.6)	31/138 (22.5)	0.411
Multiple ongoing pregnancy (%)	4/48 (8.3)	6/46 (13.0)	0.8
Live birth rate / transfer (%)	28/156 (17.9)	28/138 (20.3)	0.610

Propofol consumption is presented as median (Percentile 25- Percentile 75)
No. of embryos transferred is presented as means ± SD
Values are presented as numbers (%).

discharge: 5 (0–20) and 5.5 (0–20). STAI scores were respectively in VRD and VRH groups (median; Percentile25 - Percentile 75): baseline: 37 (31–48) and 39 (31–49); post VR session: 28 (23–37) and 30 (22.5–35.5); at hospital discharge: 26 (22.5–35) and 26 (21–35.5). There was no difference in VAS anxiety scores nor in the STAI scores between the study groups at different time points but the anxiety scores significantly decreased within both groups ($p < 0.001$ baseline vs post VR session and baseline vs hospital discharge) (Fig. 3).

There was no association between baseline anxiety scores and occurrence of positive β -hCG [Odds ratio (95 % confidence interval)]: [0.996 (0.984–1.007)]; $p = 0.464$ or the STAI score [Odds ratio (95 % confidence interval)]: [0.997 (0.973–1.021)]; $p = 0.804$.

No side effects (nausea, vomiting) were reported in the groups.

4. Discussion

In this randomised controlled trial, VRD and VRH were compared to reduce preoperative anxiety before sedation for oocytes retrieval. Our findings demonstrated that both virtual reality sessions significantly decreased anxiety scores in the same way. However, we did not notice any significant difference in clinical pregnancy rates, implantation rates, or ongoing pregnancy rates at 12 weeks between the two groups,

A meta-analysis published in 2019, showed that hypnosis was highly effective to reduce anxiety.[25] There are few studies published with the use of VRH notably in orthopaedic surgery. Touil et al. showed that VRH was effective to manage preoperative anxiety in orthopaedic surgery with a decrease of 60 % of VAS Anxiety[19] and Rougereau et al. showed that VRH before surgery modestly reduced postoperative and predischarge anxiety.[26]

Preoperative anxiety causes physiological and psychological changes by releasing cathecolamine. Finding method for reducing anxiety is interesting because prevalence of preoperative anxiety is high (48 %)[27] and anxiety is correlated with prolonged postanesthesia recovery, increased need for anesthetics agents, increase postoperative pain and higher analgesic consumption.[28] If the need to treat preoperative anxiety is no longer to be demonstrated, the routine use of anxiolytic sedatives is well controversial notably because of their side effects.[29] Moreover, younger and female patients as well as those with a high need for information have been found more prone to preoperative anxiety.[28] Women generally have more concerns about pain, surgical

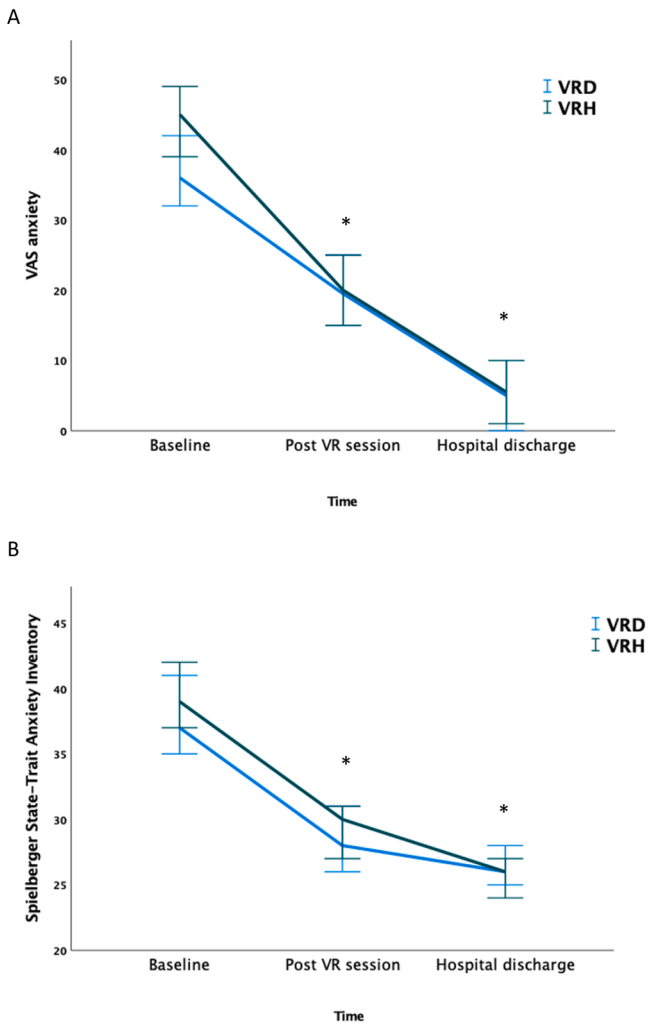

Fig. 3. Evolution of Anxiety scores at different times. median and bars: 95 % Confidence Interval. * : $p < 0.001$ baseline vs post VR session and Basline vs Hospital discharge. VAS Anxiety= Visual Analogue Scale for anxiety, scale 0–100 mm. Spielberger State-Trait Anxiety Inventory: range from 20 to 80.

complications and anesthesia while men are probably often less expressive or less sensitive to certain sources of stress. Our study has showed a reduction in preoperative anxiety after a VRD or a VRH session in a population of women of reproductive age. However, in other studies VRH and VRD have been used in older populations, regardless of gender,[19,30] supporting the idea of using the technique for a broad preoperative population.

Masoumi et al., have reported in their systematic review on psychiatric interventions used for anxiety disorders in infertile couple, that the majority of psychosocial interventions can be effective in reducing anxiety in infertile women.[31] However, a more recent meta-analysis published by Kremer et al., concluded that it is not possible to draw conclusions about psychological interventions influencing quality of life (anxiety, depression) and pregnancy rate in women suffering from fertility disorders.[1] There is no formal evidence in the literature that reducing anxiety has a positive impact on pregnancy rates. The causal link between the two, therefore, still remains hypothetical.

During VRH session, patients received suggestion of reusing the technique later to find well-being and calm, however, we did not ask them if their used it during embryo transfer (ET) and we do not know if this could influence pregnancy outcomes.

Csemiczky et al. have reported state anxiety levels in patients who did not achieve pregnancy being slightly higher than in those who became pregnant ($p < 0.06$).[32] Similarly, a multicenter study showed a significant independent negative relation of state anxiety with pregnancy.[33] In their study, patients had a state anxiety score of 36 (20−74) (median (P25-P75)). In our study, we reported a baseline state anxiety of 37(31−48) in the VRD group and 39 (31−49) in the VRH group, comparable to the score mentioned by Smeenk.[33] In contrast with these two studies, we did not observe an association between baseline anxiety score and lack of pregnancy. This could be explained by the positive impact of VR on anxiety reduction observed in both groups. This is in contrast with the previous trials where no treatment was performed to reduce anxiety and as such the pregnancy rate. Indeed, in our study we have observed that both VR sessions prior to OR significantly decreased anxiety scores (between baseline and post VR session and baseline and hospital discharge) without significant difference between the two study groups. The reduction between baseline and post VR session could be attributed to the use of VR sessions. Reduction between baseline and hospital discharge may be expected due to the completion of a stressful procedure. In the same way, Terzioglu et al. have determined that the mean state anxiety score before OR (41.96 +/- 5.43) was clearly higher than the mean state anxiety score after embryo transfer (34.79 +/- 8.90) ($p < 0.05$).[5]

In our study, VR sessions were performed before OR, since this stage is known to generate acute anxiety. However, the ET is also a crucial step, which can be a source of anxiety and can generate uterine contractions.[34] We can therefore ask whether the VR session performed before ET could have had a different impact on pregnancy rates. To our knowledge, this has not yet been studied in fresh cycles. In frozen ET cycles, preliminary results of a study suspended due to Covid-19 assessing VRD use before ET showed no reduction in patient's anxiety levels and no significant difference in clinical pregnancy rate between the study and the control groups.[35]

VRH, VRD and usual care were compared in the context of patients hospitalized for trauma and results indicated there were no significant differences between the groups on any outcomes measures (pain, anxiety, opioid use, hospital length of stay).[36] In our study, both VRH and VRD allowed a reduction of VAS Anxiety (difference was not statistically significant between the groups), but comparison to a group without any VR session or to a group with hypnosis performed by a hypnotherapist was not done, because it would not have been possible to do this in a double-blinded study. These comparisons could be made in future studies.

As the efficiency of both VR and VRH were demonstrated in the preoperative period, future studies should test its use during oocyte retrieval (and not only before the procedure). Indeed, although the discussion only focuses on the anxiolytic effect of VR, its interest as an analgesic has been largely demonstrated and therefore its use during oocyte retrieval should be examine.

5. Limitations

Our study has several limitations. First of all, we compare two VR techniques to decrease anxiety score but, a control group without VR was not planned. Therefore, we cannot compare if the effect on anxiety should influence pregnancy rate in comparison with a group without VR intervention. Secondly, we did not evaluate the absorption degree (tendency to become fully involved in the experience), the degree of immersion and presence in the VR environment nor the time perception (estimation of the time elapsed in minutes since they started the session). These parameters could have helped us to compare the effects of the different VR sessions to better understand their mechanism of action as described by *Rousseaux et al.*.[37] Likewise, we did not ask to the patients in the VRH group if they had reused the technique during the embryo transfer. And finally, we want to remember that we did a per protocol rather than an intention to treat analysis.

6. Conclusions

To our knowledge, it is the first time that VRD and VRH are compared to reduce anxiety before sedation for oocytes retrieval. Both virtual reality sessions significantly decreased anxiety scores; however, there was no difference in anxiety reduction between the two study groups. It seems that the suggestions received during the VRH session had no influence on IVF success, because no significant difference on pregnancy rate was shown in our study.

Ethical compliance statement

This study was conducted in accordance with the Declaration of Helsinki and approved by the "Comité d'Ethique Hospitalo-Facultaire des Cliniques universitaires Saint-Luc" (2016/20JUL/346, Brussels, Belgium – Chairman: Prof. J-M Maloteaux) and registered on ClinicalTrials.gov (NCT03064061) before starting the inclusion of patients. Written informed consent was obtained from all patients, Informed consent was obtained from all participants prior to their involvement in the study.

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CRediT authorship contribution statement

Christine Watremez: Investigation, Conceptualization. **Maria-Grazia Giudice:** Investigation. **Christine Wyns:** Investigation. **Pascale Laurent:** Writing – original draft, Investigation. **Céline Pirard:** Writing – original draft, Investigation, Conceptualization. **Fabienne Roelants:** Writing – original draft, Investigation, Conceptualization. **Mona Momeni:** Formal analysis.

Declaration of Competing Interest

There is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Prior presentation

Preliminary results of this work have been presented at the 2018 Euroanaesthesia meeting and at the 2018 annual congress of the Société française d'anesthésie-réanimation. Final results were presented at the 2024 Euroanaesthesia meeting.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ctim.2024.103125.

References

1. Kremer F, Ditzen B, Wischmann T. Effectiveness of psychosocial interventions for infertile women: a systematic review and meta-analysis with a focus on method-critical evaluation. *PLoS One*. 2023;18(2), e0282065. https://doi.org/10.1371/journal.pone.0282065.
2. Matthiesen SMS, Frederiksen Y, Ingerslev HJ, Zachariae R. Stress, distress and outcome of assisted reproductive technology (ART): a meta-analysis. *Hum Reprod*. 2011;26(10):2763–2776.
3. Frederiksen Y, Farver-Vestergraad I, Gronhoj Skovgard N, Ingerslev H, Zachariae R. Efficacy of psychosocial interventions for psychological and pregnancy outcomes in infertile women and men: a systematic review and meta-analysis. *BMJ Open Jan*. 2015;5(1), e006592, **28**.
4. Wang R, Huang X, Wang Y, Akbari M. Non-pharmacological approaches in preoperative anxiety, a comprehensive review. *Front Public Health*. 2022;10, 854673, **11**.
5. Terzioglu F, Turk R, Yucel C, Dilbaz S, Cinar O, Karahalil B. Investigation into effectiveness of counselling on assisted reproductive techniques in Turkey. *J Psychosom Obstet Gynecol*. 2001;22:133–141.
6. Saadat H, Drummond-Lawis J, Maranets I, et al. Hypnosis reduces preoperative anxiety in adult patients. *Anesth Analg*. 2006;102:1394–1396.
7. Potié A, Roelants F, Pospiech A, Momeni M, Watremez C. Hypnosis in the perioperative management of breast cancer surgery: clinical benefits and potential implications. *Anesth Res Pr*. 2016, 2942416. https://doi.org/10.1155/2016/2942416.
8. Calipel S, Lucas-Polomeni M, Wodey E, Ecoffey C. Premedication in children: hypnosis versus midazolam. *Paediatr Anaesth*. 2005;15:275–281.
9. Levitas E, Parmet A, Lunenfeld E, et al. Impact of hypnosis during embryo transfer on the outcome of in vitro fertilization-embryo transfer: a case-control study. *Fertil Steril85:1404-1408*. 2006.
10. Elkins GR, Barabasz AF, Council JR, Spiegel D. Advancing research and practice: the revised APA Division 30 definition of hypnosis. *Am J Clin Hypn 57*. 2015:378–385.
11. Riches S, Azevedo L, Bird L, Pisani S, Valmaggia L. Virtual reality relaxation for the general population: a systematic review. *Soc Psychiatry Psychiatr Epidemiol*. 2021;56(10):1707–1727. https://doi.org/10.1007/s00127-021-02110-z.
12. Pardini S, Gabrielli S, Olivetto S, et al. Personalized virtual reality compared with guided imagery for enhancing the impact of progressive muscle relaxation training: pilot randomized controlled trial. *JMIR Ment Health*. 2024;30(11), e48649. https://doi.org/10.2196/48649.
13. Mazgelytė E, Rekienė V, Dereškevičiūtė E, et al. Effects of virtual reality-based relaxation techniques on psychological, physiological, and biochemical stress indicators. *Healthcare*. 2021;9(12):1729. https://doi.org/10.3390/healthcare9121729.
14. Pardini S, Gabrielli S, Dianti M, et al. The role of personalization in the user experience, preferences and engagement with virtual reality environments for relaxation, 13 *Int J Environ Res Public Health*. 2022;19(12):7237. https://doi.org/10.3390/ijerph19127237.
15. Koo C-H, Park J-W, Ruy J-H, Han S-H. The effect of virtual reality on preoperative anxiety: a meta-analysis of randomised controlled trials. *J Clin Med;*. 2020;9(10):3151.
16. Wang Y, Sun J, Yu K, et al. Virtual reality exposure reduce acute postoperative pain in female patients undergoing laparoscopic gynecology surgery: a Randomized Control Trial (RCT) study. *J Clin Anesth*. 2024;97, 111525. https://doi.org/10.1016/j.jclinane.2024.111525.
17. Aitken J, Wilseon S, Coury D, Moursi A. The effect of music distraction on pain, anxiety and behavior in pediatric dental patients. *Pedia Dent*. 2002;24:114–118.
18. Jia T, Ogawa Y, Miura M, Ito O, Kozuki M. Music attenuated a decrease in parasympathetic nervous system activity after exercise. *Plos ONE*. 2016. https://doi.org/10.1371/journal.pone.0148648.
19. Touil N, Pavlopoulou A, Momeni M, et al. Evaluation of virtual reality combining music and hypnosis session to reduce anxiety before hand surgery under axillary plexus block: a prospective study. *Int J Clin Pract*. 2021;75(12), e15008.
20. Schulz K.F., Altman D.G., Mother D., for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials.
21. Li A, Mointano Z, Chen V, Gold J. Virtual reality and pain management: current trends and future directions. *Pain Manag*. 2011;1(2):147–157.
22. Kindler CH, Harms C, Amster F, Ihde-Scholl T, Scheidegger D. The visual analog scale allows effective measurement of preoperative anxiety and detection of patients anesthetic concerns. *Anesth Analg*. 2000;90:706–712.
23. Facco E, Stellini E, Bacci C, et al. Validation of visual analogue scale for anxiety (VAS-A) in preanesthesia evaluation. *Minerva Anesth*. 2013;79(12):1389–1395.
24. Spielberger CD, Lushene RE, Jacobs GA. *Manual for the State-Trait Anxiety Inventory (STAI: Form Y)*. Palo Alto: consulting Psychologists Press; 1983.
25. Valentine K, Milling L, Clark L, Moriarty C. The efficacy of hypnosis as a treatment for anxiety: a meta-analysis. *Int J Clin Hypn*. 2019;67(3):336–363.
26. Rougereau G, Sandiford MH, Lévêque R, Ménigaux C, Bauer T, Hardy A. Management of anxiety for ambulatory hallux valgus surgery with a virtual hypnosis mask: randomized controlled trial. *Foot Ankle Int*. 2023;44(6):539–544.
27. Abate S, Chekol Y, Basu B. Global prevalence and determinants of preoperative anxiety among surgical patients: a systematic review and meta-analysis (|) *IJS Open*. 2020;25:6–16. https://doi.org/10.1016/j.ijso.2020.05.010.
28. Friedrich S, Reis S, Meybohm P, Kranke P. Preoperative anxiety. *Curr Opin Anaesthesiol*. 2022;35(6):674–678. https://doi.org/10.1097/ACO.0000000000001186.
29. Bucx MJ, Krijtenburg P, Kox M. Preoperative use of anxiolytic-sedative agents; are we on the right track? *J Clin Anesth*. 2016;33:135–140. https://doi.org/10.1016/j.jclinane.2016.03.025.
30. Rousseaux F, Dardenne N, Massion P, et al. Virtual reality and hypnosis for anxiety and pain management in intensive care units: a prospective randomised trial among cardiac surgery patients. *Eur J Anaesthesiol*. 2022;39:58–66.
31. Masoumi SZ, Parsa P, Kalhori F, Mohagheghi H, Mohammadi Y. What psychiatric interventions are used for anxiety disorders in infertile couples? A systematic review

study. *Iran J Psychiatry*. 2019 Apr;14(2):160–170. PMID: 31440298; PMCID: PMC6702283.
32. Csemiczky G, Landgren B, Collins A. The influence of stress and state of anxiety on the outcome of IVF-treatment: psychological and endocrinological assessment of swedish woman entering IVF-treatment. *Acta Obstetrica Gynecologica Scandinavia*. 2000;79(2):113–118.
33. Smeenk J, Verhaak C, Eugster A, van Minnen A, Zielhuis G, Braat D. The effect of anxiety and depression on the outcome of in-vitro fertilization. *Hum Reprod*. 2001; 16(7):1420–1423.
34. Fanchin R, Righini C, de Ziegler D, Olivennes F, Ledee N, Frydman R. Effects of vaginal progesterone administration on uterine contractility at the time of embryo transfer. *Fertil Steril*. 2001;75:136–1140.
35. Dviri M, Marom Haham L, Mashiach Friedler J, et al. The use of virtual reality technology in infertile women undergoing in vitro fertilization-embryo transfer: a randomized controlled trial. *Fertil Steril*. 2020;114:e223–e224.
36. Wiechman S, Jensen M, Sharar S, Barber J, Soltani M, Patterson D. The impact of virtual reality hypnosis on pain and anxiety caused by trauma: lessons learned from clinical trial. *Int J Clin Exp Hypn*. 2022;70(2):156–173.
37. Rousseaux F, Faymonville M-E, Nyssen A-S, et al. Can hypnosis and virtual reality reduce anxiety, pain and fatigue among patients who undergo cardiac surgery. *a Random Control Trial BMC*. 2020;21:330.