Cover page:

Official Title of the study:

Effectiveness of recorded hypnosis, virtual reality or their combination in patients undergoing a bone marrow examination at the hematology unit

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Background:

A bone marrow (BM) examination is an invasive procedure performed at the hematology unit under sedation and local anesthesia. Before the procedure, most patients report anxiety, both related to the procedure itself and results' expectation. Moreover, BM examination itself may cause other symptoms including pain with an increase in the use of analgesics. Various non-pharmacological techniques, including hypnosis (H) and virtual reality (VR) exist today and are used as complementary tools in the treatment of anxiety and pain, including around procedures. Hypnosis is defined as "a state of altered consciousness that includes focused attention and reduced peripheral awareness, characterized by an improved ability to respond to suggestiveness." This technique is considered safe and allows the patient to be focused on his inner self, by including cognitive and behavioral components that allow the mind to influence the body's sensations and perceptions. Many studies show the positive effect of hypnosis on symptoms such as pain or anxiety. VR is another technique that gives the user the illusion that he is in a different realistic environment than he really is. Studies have shown that VR can isolate the patient from the external environment and distract attention from a painful stimulus. As for surgery or invasive procedures, a few studies have examined the effect of H, VR or their combination (VRH) with variable results.

Therefore, the purpose of the present study is to examine the effect of a hypnotic script (H), virtual reality (VR) or their combination (VRH) on common symptoms surrounding bone marrow examination.

Methods:

Study setting: We are planning a 4-arms open-label randomized-controlled trial that will take place at the Hematology Unit of Bnai Zion Medical Center in Haifa, Israel.

Ethics review: The study protocol was reviewed and approved by the Institutional Review Board in accordance with the Helsinki Declaration (0053-23-BNZ).

Study population: Eligible participants will be recruited from the hematological unit at Bnai-Zion Medical Center in Haifa, Israel. Inclusion criteria: (1) Aged 18 or older, (2) Candidate for a BM examination at the hematology unit, (3) Able to answer questionnaires in Hebrew, Arabic or Russian, and (4) Signed an informed consent form. Exclusion criteria include (1) Hearing impairment and (2) Visual impairment.

Randomization: Patients meeting the inclusion criteria who agree to participate in the study will be randomly assigned by blocked randomization in a 1:1:1:1 ratio to one of the following 4 groups: control group (C), hypnosis only group (H), virtual reality only group (VR) and combined hypnosis group with virtual reality (VRH).

Blinding: Due to the different types of interventions, the study cannot be blinded.

Interventions: All patients will underwent the BM procedure under local anesthesia with or without sedation according to local guidelines. Additionally, patients randomized to intervention groups (H, VR and VRH) will receive the different interventions after arriving to the clinic and when waiting for the procedure. These include:

Hypnosis (H): Patients will be given earphones to hear a hypnotic script that was recorded by Dr. Zahi Arnon, a psychologist specializing in hypnosis after observing about ten BM examinations at the hematology institute. The length of the recording is about 7 minutes.

Virtual reality (VR): Patients will be connected to a VR device that will transmit to the patient's choice a 3D screen and soothing noise for about 7 minutes.

Combined hypnosis and virtual reality (VRH): Patients will hear the same 7-minutes hypnotic script by earphones and simultaneously be connected to the VR device that will show the 3D screen without soothing noise.

Outcomes:

Primary outcome: The primary outcome will be the effect of the intervention on different symptoms experienced by patients undergoing BM procedure. This outcome will be evaluated by the Measure Yourself Concerns and Wellbeing (MYCAW) questionnaire that examines two main problems that are bothering the patient at the time, including a rating on a Likert scale from 0 to 6. Patients will fill out the questionnaire upon arrival to the clinic (before intervention), 10 minutes after intervention and before starting the procedure (or about 20 minutes after the first questionnaire filling for control group), and when waking up from the procedure. MYCAW questionnaire is appropriate due to its validity, translation into relevant languages, combination of both quantitative and qualitative data, and appropriateness to complementary medicine studies.

Secondary outcomes: The effect of the interventions on absorption, dissociation, immersion and time perception will be evaluated by a short validated questionnaire that will be given to the patients 10 minutes after intervention before the BM examination. The effect of the interventions on sedation and analgesics use during and after the BM examination will be evaluated by specifically recording the type and dose of sedatives and analgesics given to the patient during and after the procedure. Finally, the effect of the interventions on physiological indicators will be evaluated by measuring vital signs (blood pressure, pulse, respiratory rate) before and during the BM examination.

Safety and adverse events: The interventions are safe and no significant side effects are expected. Patients will be directly asked for the potential appearance of adverse events during or immediately after the intervention. All adverse events will be recorded, monitored and addressed accordingly. The intervention may be stopped if significant side effects are of concern.

Criteria for discontinuation: Participants may be discontinued from the study if they voluntary withdraw informed consent, for safety reasons or due to significant non-compliance with the study protocol as judged by the Principal Investigator. Reasons for discontinuation will be recorded and patients withdrawn from the study will be included in the intention-to-treat analysis.

Quality control: A Data Safety Monitoring Board constituted of five experts will control the safety, and quality of the intervention as well as data collection on a yearly basis. Dropout, withdrawal, treatment adherence and uncollected data will be recorded until completion of the study.

Sample size calculation: Since no previous study has evaluated similar data, we estimated that a minimum of 100 patients (25 patients in each group) was required to achieve a clinical effect of the interventions.

Statistical methods: Data analysis will be performed using IBM SPSS Statistics software.