Pediatric Coping during Venipuncture with Virtual Reality: A Randomized Controlled Trial

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1. Abstract

Pediatric emergency rooms and hospitals are anxiety provoking and often painful places for pediatric patients and families. Children of all ages present to the Johns Hopkins emergency room and are admitted to the hospital for a wide range of medical conditions, many of which require medical interventions. Many of these interventions are the source of anxiety and pain, including burn debridement or dressing changes, laceration repair, or intravenous (IV) line placement. The standard of care to reduce pain and improve coping during pediatric procedures ranges from no intervention to support from child life specialists.

As an adjunct to the existing methods of promoting comfort during painful procedures, non-invasive virtual reality (VR) therapy is showing promise as a means of distraction and coping with various medical procedures. The user is transported into a relaxing/distracting VR environment that diverts user's attention away from pain and anxiety. VR has demonstrated efficacy in the reduction of pain and anxiety experienced by individuals undergoing anxiety and pain inducing procedures. While there is early data from small or narrow populations that show some improvement in pain and anxiety with VR use during pediatric procedures, some studies show no improvement.[1,2] No studies to date have used objective outcome measures of coping, which may be more clinically meaningful. Since caregiver's response influences children's coping, understanding caregiver behaviors may clarify theevidence for VR during pediatric procedures.

The investigators propose to fill this gap in the literature with a randomized, controlled, un-blinded study of coping and distress between virtual reality engagement and child life support in pediatric patients undergoing painful medical procedures.

2. Objectives (include all primary and secondary objectives)

Primary:

The primary objective is to determine whether use of VR improves pediatric patient and caregiver coping and distress during medical procedures.

Secondary objectives are as follows:

To determine whether use of VR improves pediatric patient and caregiver pain and anxiety ratings during medical procedures.

To determine whether use of VR affects resource utilization for procedures in children (e.g. duration of procedure, adjunct medications, personnel to immobilize or restrain the child)

To determine whether certain medical/psychiatric diagnoses (e.g. ADHD, anxiety) are associated with reduced pain during VR use.

3. A. Background

Pediatric emergency rooms and hospitals are anxiety provoking and often painful places for pediatric patients and families[3]. Children, ages 1 day to 22 years, present to the emergency room and are admitted to the hospital for a wide range of medical conditions. Many conditions require painful interventions for care, including burn debridement, burn dressing change, lactation repair, intravenous (IV) line placement, abscess incision and drainage, fracture reduction, and implanted central venous port placement accessing. As an adjunct to the existing methods of anxiolysis and analgesia, non-invasive VR therapy is showing promise as a means of distraction and coping with various medical procedures.[4-9] The user is transported into a relaxing/distracting VR environment that diverts their attention away from pain and anxiety. VR has demonstrated efficacy in the reduction of pain and anxiety experienced by individuals undergoing anxiety and pain inducing procedures[2,3]. Current research in VR is lacking in pediatric populations undergoing common painful procedures, such as IV placement, laceration repair, abscess drainage, fracture reduction, burn debridement, or burn dressing changes. Data is lacking on objective measures of coping and distress.

B. Current Routine Care for Painful Procedures:

At the Johns Hopkins Children's Center, when a painful medical procedure is deemed medically necessary there are various methods of anxiolysis and analgesia. Medication based analgesia and anxiolysis are the primary stalwarts with benzodiazepines, opiates, and ketamine. Topical and injectable agents such as Lidocaine-Epinephrine-Tetracaine (LET) topical gel, Eutectic Mixture of Local Anesthetics (EMLA) topical cream, injectable lidocaine and/or lidocaine with epinephrine are also employed for local anesthesia. The selection of these agents is done by the patient's physician and/or nurse. These medications are often combined with coping strategies such as positive visualization, distraction with an iPad or toys, Child Life support, and parental assistance. All of these have varying degrees of success and associated risks.

C. Virtual Reality:

Virtual reality (VR) is defined as almost or near reality where technology manipulates the perception of several of the innate senses, most frequently vision and hearing, using computer generated three dimensional environments that can be interacted with and explored by the user. In order to create this environment, a person wears a lightweight headset with a mounted screen and varying degrees of sensors and computers in a safe physical environment. The field of virtual reality is rapidly expanding with new head mounted devices and advances, many of which are applicable in medicine. Head mounted displays (e.g.Gear VR, Oculus Go) use built-in gyroscopes, accelerometers, and proximity sensors, linked with Field of View (FOV) and Interpupilary Distance (IPD) sensors, all driven by the processing power of the cell phone to track the head movement of the user and to simulate this environment.[7]

The commercial simulated environments are highly variable but can range from viewing the top of Mount Everest to playing games like Fruit Ninja or dodgeball. VR offers an adjunct method of distraction from pain and anxiety involved with medical procedures. For the purposes of using VR in a pediatric patient undergoing a medical procedure, VR games would be narrowed to those that involve passive gameplay, or active gameplay requiring minimal movement.

4. Study Procedures

a. Study design:

This is a stratified, randomized, controlled, un-blinded study comparing differences in coping and distress between child life-supported virtual reality engagement to support by child life specialists alone (e.g. routine care) in children undergoing a painful medical procedure in the pediatric emergency department.

Randomization will use block randomization in blocks of 10, stratified by each procedure type.

Research staff will identify those who need to undergo a procedure, and screen for inclusion/exclusion criteria. Research staff will obtain informed verbal consent from patients' legal guardian. The patients < 18 years of age will give verbal assent. Patients will be offered a $5 gift card as incentive to participate.

Enrolled patients will be randomized to traditional, routine care (as described in section 3B above) or routine care plus up to 30 minutes virtual reality experience using the equipment (Oculus Go, Facebook Technologies, LLC).

Research staff will screen for inclusion/exclusion criteria, obtain verbal informed consent, set up the equipment, monitor the subject during the experience, troubleshoot technical issues, and collect pre/during/post procedure data. A child life specialist will be present at the bedside for each procedure to observe the child's tolerance of VR. Routine clinical staff will perform procedures based on existing Johns Hopkins Children's Center policies and will not play a role in enrolling patients or collecting data for this study.

Once enrolled, research staff will collect additional information (e.g. pain scales), before and after the procedure. All patients in the control and study groups will receive routine care for analgesia and anxiolysis as determined by the patient's nurse or physician.

For those in the study group, Child-Life Specialists will conduct additional screening of patients' developmental stage, coping mechanisms, temperament, and previous gaming experience to select age appropriate virtual reality experiences. Before use, VR equipment will be hygienically sanitized and fitted with a disposable paper or foam barrier and a disposable head cap. After the completion of this study, patients will be offer the same standard of care for post-procedure care and follow up.

An external control group will be recruited. These patients will meet the same inclusion/exclusion criteria as above. These patients will not receive any standardized form of support and will be recruited during hours that VR and child life are not available. This group will not be included in the randomization due to the ethics of denying a child of child life support when they need it.

b. Study duration and number of study visits required of research participants:

The study will last from October 2018 to October 2020. Subjects will be required to participate in only one visit.

c. Blinding:

Due to the nature of this study participants and providers cannot be blinded to either having the VR equipment in place or not.

d. Justification of why participants will not receive routine care or will have current therapy stopped.

All patients will have routine care and no change in their therapeutic plan.

e. Justification for inclusion of a placebo or non-treatment group.

A non-treatment group is required to serve as an active control group to measure for statistical differences in outcomes measures. The external control (reference) group will not receive child life support because child life is not available at certain hours of the day. Given that standard of care will be provided in all arms of the study, there will be no harm to the control or non-treatment group.

Furthermore, since use of VR is not the standard of care, and not universally proven to reduce pain and anxiety during procedures. Therefore, the control group who does not receive VR will not experience inferior care. The non-treatment or active control group may have desire or disappointment in being randomized without VR. We will offer play time with VR to the control group, after their procedure at the child's request.

f. Definition of treatment failure or participant removal criteria.

Participants will be removed from the study (e.g. we will remove the VR headset) if the subject is unable to tolerate VR simulation due to fear, over-stimulation, cybersickness, personal preference, or any other reason brought forth by the study participant, parent, or consenting guardian.

An alternative reason participants will stop using VR is if the medical team changes the management plan, such that the patient meets exclusion criteria. For example, if the medical team determines the patient requires midazolam or ketamine sedation, then VR will be discontinued.

g. Description of what happens to participants receiving therapy when study ends or if a participant's participation in the study ends prematurely.

Patients will continue to get routine medical care, as per the most recent definition of standard of care for given condition.

5. Inclusion/Exclusion Criteria

Inclusion:

1. Pediatric patients requiring painful or anxiety inducing procedures:
    a. Burn debridement
    b. Burn dressing change
    c. Lactation repair
    d. Intravenous (IV) line placement or phlebotomy (blood draw)
    e. Abscess incision and drainage
    f. Fracture reduction and/or cast placement
    g. Implanted central venous port placement accessing
    h. Skin biopsies
    i. Laser skin therapy
2. Subjects ages 7 to 26 years of age (age 26 is the upper limit treated at JHCC)

a. Ages were chosen based on that previously published in the literature on pediatric patients with VR. [4]

Exclusion:

1. Patients with a known history of a seizure disorder.
2. Patients with an active infection, burn, or trauma that interferes with the mask placement, and may include involvement of the periorbital skin, eyes, nasal bridge, external ear, and/or scalp or hair.
3. Patients with Blindness.
4. Developmental delay significant enough to interfere with the subject's ability to participate in the session, including autism spectrum disorders.
5. Patients with active psychosis or exhibit signs of active intoxication.
6. Known history of severe motion sickness
7. Medical urgency (at the medical providers' discretion)
8. Non-verbal children
9. Children or parents/legal guardians who are non-English speakers

6. Drugs/ Substances/ Devices

a. Study Device:

We will be using the Oculus Go headset. We chose this equipment based on the technical specifications and needs, ease of use of equipment, lack of need for external computing power, broad array of applications available, ability to sanitize and use Styrofoam facial barriers, and lightweight design.

b. Justification and safety information if FDA approved drugs will be administered for non-FDA approved indications or if doses or routes of administration or participant populations are changed.

N/A. This product is not classified as a FDA medical device.

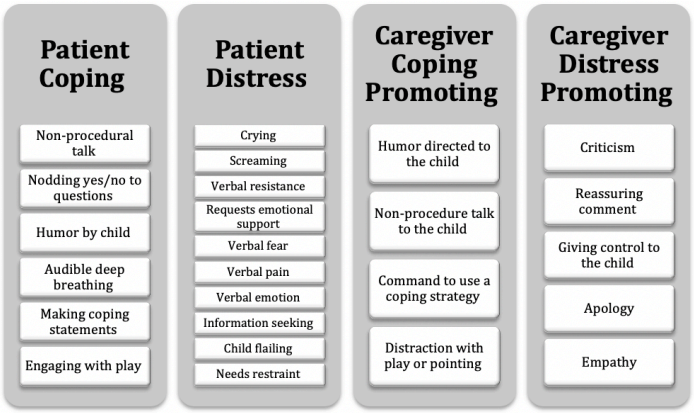
c. Justification and safety information if non-FDA approved drugs without an IND will be administered.

N/A

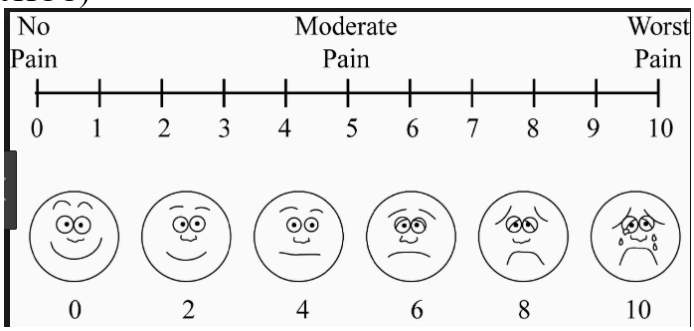
7. Study Statistics

a. **Primary outcome variables:**

Patient coping and distress and caregiver coping promoting/distress promoting behaviors using a validated scale (CAMPIS-SF)[10]



b. Secondary outcome variables:

- Pain Scale: The Visual Analog Scale (1-10) combined with Wong-Faces Scale (standard of care at JHCC)
  - 

- Anxiety Scale: Subjective Units of Distress
  - 

Resource utilization including:

- Duration of procedure (minutes)
- Need and dosage (in mg) of adjunct medications: midazolam, opiates, local lidocaine
- Personnel use for patient restraint (number of people, likert scale of level of force applied), wrapping
- During IV/phlebotomy procedures: number of total attempts until success (i.e. 1, 2, 3, etc)

Ease of completing procedure by proceduralist:

- Likert scale

Side effects:

- Presence of cybersickness using the Simulator Sickness Questionnaire [11]

Patient characteristics:

- Associated medical or psychiatric conditions

c. Statistical plan

1. Sample size of each group is estimated at 123 patients
    a. Assumptions are using t-test to calculate a 10% difference in mean coping, assuming alpha error 0.05, power 0.80, and ratio of each group 1:1
    b. Analysis of variance (ANOVA) will be used for differences in age, coping, distress, pain, anxiety, procedure duration, ease of procedure between groups.
    c. Fisher's exact test will be used for differences in sex, race, ethnicity, cybersickness incidence, restraint use, and venipuncture success.

d. Early stopping rules:

Patient will be removed from the virtual environment at the first sign of distress or by request of the parent or patient, report of cybersickness, equipment malfunction, or any staff concerns. This will be tracked and reported. The study will be stopped if there is clear evidence of harm (physical or emotional) harm to the study population.

8. Risks

a. Medical risks:

Few if any risks or discomforts are anticipated.

The headset will be adjusted for each individual subject to maximize comfort level.

Rarely, patients immersed in a virtual reality experience may experience headache, eye strain. Patients may also experience nausea, lightheadedness, or dizziness, often referred to as cybersickness.[12] Cybersickness is defined as motion sickness induced by the immersion of stationary users in moving scenes using computer generated VR, particularly with head-mounted displays.[12] These discomforts will be monitored for during the session and subjects will complete a survey, both before and after the session about whether they experienced these side effects. While the rates of cybersickness are not well defined in the literature, particular in pediatric populations, some smaller scale studies suggest rates around 20-30% of first time users will experience mild cybersickness.[11] We will be collecting data on the rates of cybersickness in the pediatric population in this study by using the validated Simulator Sickness Questionnaire developed by Kennedy et al, considered to be the goal standard.[11] The treatment for cybersickness is removal from the VR environment with usual complete resolution of symptoms between <1-2 hours.[11-14] Also, the software described above are not primarily motion based VR immersions, and the hardware listed above utilizes low lag Oculus software and FOV and IPD sensors; drastically lowering the risk of cybersickness. Finally, we are not going to be using fully immersive VR systems, such Oculus Rift or HTC Vive, which utilize subject positional tracking to manipulate environments based on subject physical movement, thus lowering the risk of cybersickness as well.

While traditional motion sickness has been associated with drowsiness, decreased salivation, depression, faintness, decreased appetite, confusion, and vomiting, several studies have shown that

these are not seen with cybersickness, and this was very recently confirmed by Gavgani et al.[11,12,14,15]

The risk of falling while using VR systems will be mitigated by keeping subjects still lying in bed, during the entirety of the experience. The experience will be immediately stopped if a subject gets up from the seated position.

b. Steps to minimize the risks:

The child life specialist, who will be present for every enrolled procedure in this study, will monitor the patient for signs of cybersickness. (S)he will verbally check in with the patient to ensure the child is tolerating VR sufficiently.

An infection control protocol has been developed to minimize any infectious risks that may arise from using a shared device among multiple subjects, which will include sanitizing all equipment and use of one-time use guards on all headsets.

c. Reporting of unanticipated problems or study deviations:

Upon discovery of unanticipated problems or study deviations we will promptly report to the IRB in writing any protocol violations/deviations, unanticipated problems involving risks to subjects or others, and adverse events (AEs), within the time specified by IRB policy.

d. Data safety and Monitoring

Presence of side effects (e.g. cybersickness) will be monitored and recorded for each patient. If an excess number of patients experience symptoms of cybersickness (> 10%), the study will be stopped and data will be reported to IRB.

9. Benefits

There are great benefits for both study subjects and for society including, decreased anxiety and pain during procedures, improved patient tolerance of procedures, better patient satisfaction, improved resource utilization amongst medical personnel, and the advancement of the field of medical virtual reality.

Few if any risks are associated with this study. Patients may derive direct benefit from the virtual reality experience serving as a distraction technique to help mitigate their experience of pain and anxiety. They may derive indirect benefit from knowing this research may be helping others who undergo similar procedures.

10. Payment and Remuneration

Subjects will receive a $5 gift card, by way of financial renumeration for their involvement in this study. Subjects who enroll but cannot complete the study (e.g. remove the VR headset due to preference or side effects) will still receive the $5 gift card for participating.

11. Costs

There is no cost to the subject for their participation in this study. The study is funded through a grant from The Thomas Wilson Foundation.

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