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The Efficacy of Virtual Reality for Persistent Cancer Pain: A Call for Research

To the Editor,

Despite the availability of cancer pain guidelines, the management of pain in people with cancer remains inadequate.[1-3] As such, there is a need to develop innovative alternative therapeutic options, particularly those with no known adverse effects. One potential option that is gathering interest is the use of virtual reality (VR) devices. Developments in VR technology offer an alternative approach that has been used with good effect in the treatment of several medical and psychological conditions.[4,5] This technology shows promise in reducing pain and psychological symptoms in both the short and long term. However, given the significant lack of published research on the effects of VR on cancer pain, scoping or systematic reviews on this topic are not possible. We briefly discuss presently the VR technology and its clinical applications and highlight the need for research to explore its use in the management of cancer pain.

VR is a simulated creation of a 3D environment using computer technology.[6] Although early VR systems used computer screen technology, current VR systems include immersive head-mounted devices with 3D-enabled glasses with other sensory input devices such as headphones for noise-canceling, sound and music, head- and/or body-tracking sensors, and other input hardware such as joysticks and data gloves.[7] Together, this system forms a realistic multisensory experience. Over the previous decade, VR technology has been taken from the entertainment business sector to clinical medicine. Researchers and clinicians have

explored the use of VR technologies for physical rehabilitation, pain management, and psychiatric treatment, and for it use in surgical training and anatomical education.[7]

The mechanisms underlying the effect of VR on pain have been divided generally into two types or processes: distraction and neuroplasticity. These processes that are thought to contribute to the analgesic effect of VR have quite different mechanisms of action.[8] Distraction refers to the short-term diversion of attention away from pain toward an alternative stimulus. Here, VR may act directly and indirectly by "hijacking" attention, emotion, and memory away from pain using auditory and touch senses.[9] Neuroplasticity refers to long-term structural changes in neuronal populations. This may occur harmfully owing to a stroke, or positively after long-term practice of a skill such as playing a musical instrument. In the case of VR, repeated immersion into interactive real-time simulations of scenes or activities appears to be associated with positive neuroplastic alterations in sensory and motor brain regions.[10] Although cancer-related pain has strong contributions from a number of peripheral, spinal, and supraspinal nervous system mechanisms, pharmacological treatments using antidepressants and antiepileptics carry a significant adverse effect burden affecting quality of life as well as the potential for interactions with anticancer drugs.[11,12] VR may present an effective and relatively harmless alternative option for the management of pain in people with cancer.

Clinical Applications of VR

There has been rapid progress in the therapeutic use of VR for many clinical conditions, including acute and chronic pain management. Early studies have described its use in fibromyalgia,[13] spinal cord injury pain,[14] phantom limb pain,[15] and chronic migraine,[16] in addition to anxiety disorders,[17] neurorehabilitation,[18] and posttraumatic stress disorder.[19] In addition, VR technologies have also been used for pain and stress control during medical procedures, such as burn and wound debridement and chemotherapy.[20,21]

Currently, several VR studies show positive results for the reduction of pain and anxiety during cancer procedures, especially during chemotherapy.[20] Psychological factors, such as emotional distress and dysfunctional coping, are shown to increase the risk adverse consequences associated with chemotherapy-induced nausea and vomiting[22] and peripheral neuropathy,[23] and distraction interventions, such as relaxation and guided imagery, may reduce these symptoms. VR, which requires no practice and may be a compelling method to help patients detach from the anxiety produced by their clinical surroundings, has promise in these areas.

Currently, only two recent studies have investigated the short-term effects of VR on cancer pain. First, in a randomized trial, Mohammed and Ahmed examined the effectiveness of a single VR intervention as a distraction for reducing pain and anxiety in 80 female patients with breast cancer.[24] The intervention group (n-40) received an immersive VR HMDs, with headphones showing either a 15-minute deep sea diving or sitting on a beach, which timed to occur at the peak effect of a morphine dose,[25] whereas the comparison group received the morphine dose alone. Assessments (pain Visual Analogue Score and State Anxiety Inventory) were made just before giving morphine and 15 minutes after the peak morphine effect. There were significant postintervention differences between mean pain intensity scores of the two groups ($P < 0.001$), as well as between pretreatment and post-treatment mean pain intensity scores for both groups ($P < 0.001$). In addition, similar differences in reductions in state anxiety were found between the intervention and comparison groups, and between pre- and post-VR anxiety scores (both $P < 0.001$). Second, Kazuyuki and colleagues used a prospective multicenter single-arm study to investigate the use of simulated travel using VR for improving symptoms in 20 cancer patients with advanced illness.[25] Using Google Earth VR®, participants experienced one VR session of up to 30 minutes, depending on their wishes, and could travel to either "a memorable place" or "return home." Although the authors measured the effects of VR on many symptoms including drowsiness and shortness of breath, VR was most effective in reducing anxiety ($P < 0.001$).

Comment

Current treatments for cancer pain have major limitations, and inadequate pain relief occurs despite multiple guidelines.[26] Consequently, alternative and/or adjunct therapeutic options are needed by many patients. Given the encouraging findings of prior research, immersive VR is a promising new approach that may be effective and safe adjunctive therapy for cancer pain. In addition, immersive VR has become progressively more accessible due to increases in affordability, which makes the potential for long-term use in the home possible for more patients.

However, when translating information from previous VR studies to the treatment of people with cancer-related pain, it is crucial to consider the complex and multifactorial mechanisms that may underlie

cancer-related pain. Research is badly needed to guide the adoption of VR for this purpose. There are significant opportunities for randomized studies that evaluate both the short-term and long-term benefits of VR in patients with cancer pain. Studies are needed to explore:

- Long- and short-term use of immersive VR as a stand-alone or an adjunct in reducing pain and anxiety in hospitalized patients undergoing cancer treatment and inpatients who are receiving palliative care alone.
- Long-term use of immersive VR as a stand-alone or an adjunct in reducing pain and anxiety in home-based cancer patients with persistent baseline cancer pain and more severe breakthrough pain.
- Long-term use of immersive VR for the management of persistent severe pain in cancer survivors.

In addition to studies that confirm the effectiveness of VR, research is needed to examine clinical outcomes in relation to the quality and level of immersion, and the type and number of different senses provided by immersive VR applications. All these factors must be considered when developing future cancer pain VR studies.

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End of Life in the Neurological Intensive Care Unit: Is Extubating to Comfort Care Comfortable?

To the Editor:

Patients extubated to comfort care in the neurological intensive care unit (Neuro-ICU) comprise a unique population because their end-of-life signs of distress can be related to both neurological pathology and multisystem dysfunction. Previous studies have examined time to cardiac death after extubation to comfort care and its predictors,[1,2] but there are few studies describing patients' distress developed after extubation and the time required to achieve observable distress control.[3-7] The goal of this study is to determine if Neuro-ICU patients demonstrate persistent signs of distress after transitioning to comfort care and how long these take to treat.

Methods

This was a retrospective medical record review of all patients who died in the Neuro-ICU at one tertiary academic hospital from October, 2016, to October, 2017. The study was exempt from institutional review board oversight because it involved only patients who had died before the investigation. Inclusion criteria were neurological injury as cause of death and mechanical ventilation with extubation to comfort care. Exclusion criteria included age less than 18 years, pregnancy, penetrating brain injury, brain death, and receiving cardiopulmonary resuscitation within 24 hours of cardiac death. Also excluded were deaths with incomplete documentation of life support withdrawal, medication administration, and responses to distress. Neuro-ICU patients whose physical location of death was in another unit were also excluded because of logistical difficulties.

The study's primary outcomes were to determine if neurologically devastated patients developed distress after extubation to comfort care and whether this persisted. Secondary outcomes included both time to distress control and time to cardiac death. Because the patients evaluated during this study were unconscious, signs of distress were collected from nursing notes, the documented reason for as needed (PRN) medication administration, and from the Pain Assessment Tool for Non-Cognizant Adults (Non-Cog), developed by University of California, Los Angeles, and used primarily in the intensive care units to evaluate for pain in nonverbal or unconscious adults.[8]

Because these patients were neurologically devastated and unable to report symptoms, the term "signs of distress" was used rather than "symptoms." Developing signs of distress immediately after extubation was defined as within 30 minutes after extubation. A persistent sign of distress was defined as requiring greater than 50% of the time between extubation and cardiac death to achieve control. We defined distress control as not receiving any PRN medications nor requiring any opioid dose adjustments to infusions or boluses for at least 1 hour. Time to distress control was reported in hours and derived from objective scales such as the Non-Cog, subjective nursing documentation, and the medication administration record.

Statistical Analysis

Continuous data such as time required to achieve distress control and time from extubation to cardiac death were reported as means, medians, and standard deviations (SD).

Results

Of the 79 deaths in the Neuro-ICU whose charts were reviewed, 41 were excluded (16 did not meet inclusion criteria, 22 met exclusion criteria, two had poor documentation, and one was restricted). The mean age of the 38 patients whose records were selected for review was 63.1 years (median 65.0, SD 16.9, range 20–96.9), with 22 patients (58%) identified as female. The three most common diagnoses before Neuro-ICU admission included hypertension (44.7%), malignancy (31.6%), and atrial fibrillation (21.1%). The most prevalent diagnoses for admission to the Neuro-ICU were nontraumatic subarachnoid or intracerebral hemorrhage (28.9%), traumatic subarachnoid or subdural hemorrhage (21.1%), cerebral infarction (21.1%), and