Virtual reality for pain reduction during Intravenous injection among pediatrics: a systematic review and meta-analysis of controlled clinical trials

Running title
Virtual reality for pain reduction during Intravenous injection

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Abstract

Background: Intravenous (IV) injection often causes pain, fear, and anxiety in pediatrics. Virtual reality (VR) is a relatively new intervention that can be used to provide distraction during or to prepare patients for IV injections, however, so far no meta-analysis has been conducted to examine the evidence regarding the effectiveness of VR in reducing pain in pediatric IV injection.

Methods: The search in electronic databases of PubMed, Web of Science, Scopus, and the Cochrane Central Register of Controlled Trials was established on 7 August 2022. The methodological quality of the studies was measured by the Delphi checklist. Chi-squared (Chi2) test and measure its quantity by the I² statistic were applied for measuring the heterogeneity across studies. A summary measure of the mean difference in pain scores between virtual reality and control groups was obtained using a random-effects model. All statistical analyses were set at a significance level of 0.05 using Stata software, version 14.

Results: In total, nine studies were included. Findings reported interventions of virtual reality during intravenous placement among pediatrics. The meta-analysis of the difference in means of the pain score between the intervention and control groups showed significant reductions in the virtual reality group (MD 0.47; 95% CI: 0.3, 0.65; I² = 9.1%). There was no heterogeneity among the included studies.

Conclusion: Our results suggested that the use of VR is effective in reducing the pain of IV injection in pediatrics. There was no heterogeneity among studies that reported the effectiveness of using VR in reducing IV injection pain in pediatrics. The Delphi checklist was used to measure study quality.

Keywords: Virtual reality; Pain; Pediatric; Meta-analysis
key message

- This is first meta-analysis conducted to examine the evidence regarding the effectiveness of virtual reality in reducing pain in pediatric IV injection.
- Our results suggested that the use of VR is effective in reducing the pain of IV injection in pediatrics.
Introduction

While most medical treatments cause anxiety, distress, and associated pain, injections are still the most frightening and disturbing medical procedure for children. In a study on children aged 7 to 17 who underwent venipuncture, 52% of the children reported mild to severe pain (1).

To reduce pain during intravascular injection, drug and non-drug methods can be used. Despite the therapeutic effects of drugs, due to their side effects, nowadays the use of medicinal methods is less noticed by patients, and all kinds of non-medicinal methods are used as auxiliary and even alternative treatments due to the lack of side effects and risks (2). Several studies have been conducted in different countries in the field of using non-pharmacological methods to influence the quality and amount of pain during intravenous injection (3-6). The addition of technology in medicine is the use of virtual reality (VR).

VR has been defined as a “relatively new tool of human-computer interactions for a human becoming an active participant in a virtual world” (7). VR can be realized through several tools, including personal computer screens, mobile devices, and dedicated VR rooms. The most often used method for "immersion" into VR is a head-mounted visor, which can be connected to a personal computer or linked to a mobile phone (7).

So far, 1 meta-analysis and 3 systematic reviews have been conducted on the effect of using VR in children during medical procedures, but the age range of the three studies is different and therefore the number of studies has not been considered. The role of VR in changing the quality of pain in children during IV injection has not been investigated separately, so this systematic review and meta-analysis are designed to determine the effect of VR on the pain of IV injection in pediatrics based on observational studies.

Methods

Items for reporting systematic reviews and meta-analyses (PRISMA) were applied for performing the present meta-analysis (8).
Eligibility criteria

We included controlled trials randomized that reported the effect of VR on pain reduction during IV injection among pediatrics <18 years. VR was defined as a fully immersive computer-generated 3D environment displayed in an immersive stereoscopic view on a head-mounted display (HMD). We removed the studies of observational, meta-analysis, review, case report and series, and letter to the Editor from the present study.

Information sources and search

The search in electronic databases of PubMed, Web of Science, Scopus, and the Cochrane Central Register of Controlled Trials was established on 7 August 2022. The list of references included in randomized controlled trials was searched. There was no language limitation. The search terms were ‘Virtual reality or virtual reality exposure therapy’ and ‘Pain or ache’ and ‘Boy, child, childhood, girl, infant, kid, pediatrics, preschool, school, toddler, high school, juvenile, minor, prepubescent, prepuberty, pubescent, puberty, teen, teenager, under aged, youth, adolescent ‘and ‘intravenous injection, intravenous insertion, intravenous placement, venipuncture ‘and ‘clinical trial, controlled trial, randomized controlled trial’.

Study selection

The EndNote software was used for including the search findings and removing duplicate references. EJ and SB independently screened titles and abstracts. In addition, an evaluation of identified studies based on exclusion and inclusion criteria was performed by the same two authors. Any disagreement was discussed until a consensus was reached.

Data extraction

Two researchers (EJ and AS) independently extracted data on an electronic data sheet. Disagreements between the two authors were solved by consensus. We extracted information in the datasheet including the first author's name (year of publication), country, Assessment instruments
for pain, age of the child, the sample size in intervention and control groups, virtual equipment, and control program.

**Methodological quality**

The methodological quality of the studies was measured by the Delphi checklist (9). Items of the checklist is including standard randomization, the allocation of intervention concealed, the patient blinded, the care provider blinded, the outcome assessor-blinded, the two groups similar at baseline, the eligibility criteria well-defined, the variability of the outcome presented and intention-to-treat analysis performed. In this study, items of the patient blinded, the care provider blinded and the outcome assessor-blinded were deleted due to the nature of the virtual reality method. Therefore, based on the checklist, we considered a maximum score of six for each study.

**Heterogeneity and publication biases**

Chi-squared (Chi$^2$) test (10) and measured its quantity by the I$^2$ statistic were applied for measuring the heterogeneity across studies (11).

**Summary measures**

A summary measure of the mean difference in pain scores between virtual reality and control groups was obtained using a random-effects model (12). All statistical analyses were set at a significance level of 0.05 using Stata software, version 14 (StataCorp, College Station, TX, USA).

**Results**

**Description of studies**

Table 1 summarizes the Characteristics of the studies in the meta-analysis. The excluded references with reasons were reported in S1. In total, nine studies (3-6, 13-17) were organized that examined interventions of VR during IV injection among pediatrics based on the selection process (Figure 1). Of the 9 included articles, 3 were conducted in Korea, 2 in Taiwan, 2 in Canada, one in Poland, and one in Turkey. To assess pain, 3 studies used the Visual Analogue Scale, in 3 studies they used the
Wong-Baker FACES scale, one study used the Numerical Rating Scales, one study used the Faces Pain Scale-Revised and one study used the FLACC scale. The present meta-analysis had 646 subjects (324 in the control group and 322 in the intervention group). These studies were conducted between 2006 and 2022 (Table 1). All the included studies have been published in English.

**Effects of exposure**

Figure 2 reported interventions of VR during IV injection among pediatrics. The meta-analysis of the difference in means of the pain score between the intervention and control groups showed significant reductions in the VR group (Mean difference (MD) 0.47; 95% CI: 0.3, 0.65; $I^2 = 9.1\%$). There was no heterogeneity among the included studies.

**Publication bias**

The Begg's test was not reported publication bias among trials. The p-value for Begg’s regression was 0.881.

**Quality of the studies**

The quality of studies based on the Delphi checklist was presented in Table 1.

**Discussion**

To the best of our knowledge, this is the first meta-analysis that reports the effectiveness of using VR in pediatric IV injection based on observational studies. Our findings reported that VR use is a feasible distraction method for pediatrics during IV injection. There was no heterogeneity among studies that reported the effect of using VR during IV injection.

In VR, users interact with a computer-simulated 3D environment. VR technology provides multi-sensory information that helps a person to be fully immersed in the simulated world. Users wear head-mounted displays, which are helmets that provide a visual stereo image, thereby creating a sense of space and depth. A motion detector in the head-mounted display helmet measures the position of the head and adjusts the visual image accordingly. As a result, users feel like they can
look around and move around in the simulated environment. The headphones provide sounds that further help one immerse in the virtual world (18, 19), thus causing the mind to deviate from the pain (20).

Triberti et al., in their review study aimed at investigating the psychological factors affecting pain reduction based on VR, after reviewing 11 studies, showed that distraction has the greatest effect on pain reduction. Also, the feeling of being in another environment is an effective tool for creating a distraction(21).

Although several systematic review studies and meta-analyses have been conducted on the effect of using VR on various pains in different age groups, according to the review of the literature, the present study is the first meta-analysis that examines the effect of using VR in reducing pain during IV injection in pediatrics.

In the systematic review and meta-analysis study by Eijlers et al. regarding the effect of VR on pain and anxiety in children during medical procedures such as venous blood sampling, dental procedures, burns, and chemotherapy after reviewing 17 articles like our study, it showed that VR reduces children’s pain and anxiety during the mentioned procedures are effective, however, in this study, the contribution of studies on the effect of VR on burns was more than other procedures(22).

Similar to our study, a systematic review and meta-analysis by Chan et al. aimed at the effect of VR on acute pain after reviewing 16 articles showed that VR is effective in reducing acute pain. However, unlike our study, this study had high clinical and statistical heterogeneity, so it can be concluded that VR is more effective in pediatrics than in adults (23).

The subgroup analyses were needed to clarify the association between VR in reducing pain in pediatrics during IV injection in terms of the type of VR, its duration, and the gender of the child. However, the pain reduction by VR experience may differ depending on the age and disease group of the study subjects. Therefore, this was the limitation of the present studies.
Conclusions:

Pain management during medical care is considered a basic human right and affects patient satisfaction. In addition, effective management of acute pain contributes to improved outcomes and patient satisfaction. Considering the positive effect of VR in reducing pain in pediatrics during IV injection, it is suggested to use this tool to reduce pain; Also there was no heterogeneity among studies that reported the effectiveness of using VR in reducing IV injection pain in pediatrics.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

Funding

This meta-analysis was supported by Hamadan University of Medical Sciences with Ethical Code IR.UMSHA.REC.1401.533.

References

Table 1: Characteristics of the studies in the meta-analysis

<table>
<thead>
<tr>
<th>1st aut, year</th>
<th>Country</th>
<th>Sample size intervention/Control</th>
<th>VR Equipment</th>
<th>Control program</th>
<th>Scale for measuring pain</th>
<th>Age (range based on year)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piskorz, 2017</td>
<td>Poland</td>
<td>Intervention:19 Control:19</td>
<td>Oculus Rift DK2</td>
<td>Standard care</td>
<td>Visual Analog Scale</td>
<td>7-17</td>
<td>1</td>
</tr>
<tr>
<td>Hsu, 2022</td>
<td>Taiwan</td>
<td>Intervention:69 Control:65</td>
<td>The VR headset HTC Vive</td>
<td>Educational photo book about intravenous placement before intravenous placement</td>
<td>Wong-baker faces</td>
<td>6-12</td>
<td>5</td>
</tr>
<tr>
<td>Gold, 2006</td>
<td>Korea</td>
<td>Intervention:30 Control:33</td>
<td>Street Luge</td>
<td>Standard care</td>
<td>Wong-baker faces</td>
<td>7-12</td>
<td>5</td>
</tr>
<tr>
<td>Dumoulin, 2019</td>
<td>Canada</td>
<td>Intervention:20 Control:15</td>
<td>An immersive game developed by the UQO Cyberpsychology Lab using Virtools 4</td>
<td>Standard care</td>
<td>Visual Analog Scale</td>
<td>8-17</td>
<td>5</td>
</tr>
<tr>
<td>Gold, 2021</td>
<td>Korea</td>
<td>Intervention:53 Control:54</td>
<td>Two mobile-based VR head-mounted displays</td>
<td>Standard care</td>
<td>Faces pain scale-revised</td>
<td>12.8-16.9</td>
<td>2</td>
</tr>
<tr>
<td>Lee, 2021</td>
<td>Korea</td>
<td>Intervention:5 Control:9</td>
<td>VR animation through the dome screen within 1 minute after intravenous replacement</td>
<td>Without virtual reality distraction</td>
<td>FLACC*</td>
<td>2-6</td>
<td>3</td>
</tr>
<tr>
<td>Litwin, 2021</td>
<td>Canada</td>
<td>Intervention:24 Control:24</td>
<td>stereoscopic display mounted on a lightweight wireless HMD</td>
<td>Children were given a tablet playing a video of fish and sea turtles swimming in the ocean</td>
<td>Numbering rating scale</td>
<td>8-17</td>
<td>5</td>
</tr>
<tr>
<td>Chen, 2020</td>
<td>Taiwan</td>
<td>Intervention:68 Control:68</td>
<td>roller coasters, space exploration, a wildlife park, and travel destinations</td>
<td>Routine intravenous injection procedure</td>
<td>Wong-baker faces</td>
<td>7-12</td>
<td>5</td>
</tr>
<tr>
<td>Erdogan, 2021</td>
<td>Turkey</td>
<td>Intervention:34 Control:37</td>
<td>A smartphone, VR glasses and a headset</td>
<td>No intervention</td>
<td>Visual Analog Scale</td>
<td>7-12</td>
<td>2</td>
</tr>
</tbody>
</table>

* FLACC: Face, Legs, Activity, Cry, and Consolability scale
Figures titles

**Figure 1**: Flow of diagram of the systematic process

**Figure 2**: Meta-analysis of the randomized controlled trials reporting the interventions of virtual reality during intravenous placement among pediatrics
Identification
No of records identified through database searching (n = 1635)  No of additional records identified through other sources (n = 268)

Screening
No of duplicates removed (n = 111)

No of records screened (n = 1792)  No of records excluded (n = 1778)

Eligibility
No of full-text articles assessed for eligibility (n = 14)  No of full-text articles excluded, with reasons (n = 5)

Included
No of studies included in qualitative synthesis (n = 9)

No of studies included in quantitative synthesis (meta-analysis) (n = 9)
Study ID | SMD (95% CI) | Weight
---|---|---
Piskorz, 2017 | 0.64 (0.17, 1.50) | 6.59
Hsu, 2022 | 0.40 (0.06, 0.75) | 21.58
Dumolin, 2019 | -0.15 (-0.87, 0.56) | 5.71
Gold, 2006 | 0.00 (-0.88, 0.88) | 3.88
Gold, 2021 | 0.54 (0.16, 0.93) | 17.64
Lee, 2021 | 0.41 (-0.69, 1.52) | 2.47
Litvin, 2021 | 0.57 (-0.01, 1.15) | 8.57
Chen, 2020 | 0.37 (0.03, 0.71) | 21.92
Ertogen, 2021 | 0.89 (0.40, 1.36) | 11.64
Overall (I² = 9.1%, p = 0.360) | 0.47 (0.30, 0.65) | 100.00

NOTE: Weights are from random effects analysis