

Efficacy of distraction on reduction of procedural pain associated with venipuncture in the pediatric post-cardiac transplant population

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1. Introduction

Rationale: Children with chronic illnesses experience frequent painful experiences over extended periods of time, and may be at risk to develop long-term physiological, psychological and behavioral sequelae. Painful stimuli may have long-term impacts on neuronal development, impacting thresholds of pain, sensitivity and anxiety. Research to support this has primarily focused on infants where studies have looked at the impacts of circumcision, frequent heel lancing and other medical interventions in premature infants on later responses to pain (1-3). The pathophysiology behind alterations in central neural sensitization has been proposed to involve the impacts of noxious afferent input to the dorsal horn neuron's NMDA receptor ion-channel complexes, levels of excitatory amino acids (e.g. glutamate) and C-fiber neuropeptides (e.g. substance P), ultimately stimulating protein kinases and new gene expression. However, these pathways and the translation of these theories to ultimate behavioral and psychological sequelae, relevant to our clinical practice, have not been well described (3, 4).

There is strong evidence to show that distraction is effective in reducing pain during painful procedures and is a low cost method that is both easily used and has virtually no adverse risks (5). The theory behind behavioral strategies for pain reduction suggests that distraction alters nociceptive responses and can produce positive affects, such as laughter, which are incompatible with distress (6, 7).

However, the evidence describing the effectiveness of pain reduction methods for treating the most common painful procedure in children, venipuncture, has primarily focused on children who are previously well. Children with chronic disease who undergo venipuncture are an understudied population. Integrative strategies, such as distraction, are particularly of interest in children with chronic disease, as they have the potential for effectively treating procedural pain and distress without exposing these children to additional medications or pharmacologic therapies. Children with cardiac pathology, particularly those who have received cardiac transplantation, are a population of children with chronic disease who undergo frequent venipuncture, as often as multiple times per week. There is currently no evidence for an effective method for pain reduction during venipuncture for pediatric cardiology patients having blood drawn in phlebotomy or in the pediatric cardiology clinic as an outpatient, **There is a need for well-designed, randomized control studies to evaluate the effectiveness of the use of distraction during venipuncture in children with chronic disease.**

Review of the Literature: There is strong evidence to show that distraction is effective in reducing pain during painful procedures. A Cochrane review meta-analysis in 2013 included 39 RCTs studying different psychological interventions during needle-related procedures (IV line insertion, venipuncture, vaccination), 19 of which used only distraction with a total of 1759 participants. The distraction techniques varied widely including listening to music, watching cartoons, toys, books, games, etc. There was a statistically significant effect for distraction studies on self-reported pain scales, with a SMD of -0.61 (95% CI -0.91 to -0.32). However, there was large variability in pain scales used for assessment. The authors also report high bias scores relating to bias in selection, detection and performance bias. (5).

We found no studies studying distraction or any other pain reduction technique in patients with chronic disease and none comparing children with chronic disease vs

children who are previously healthy.

One cross-sectional study at an Italian children's hospital did look at differences in self-reported pain and observational distress scores between children suffering from chronic disease (n=82) and those who had no previous health problems or previous experience of venipuncture (n=148). In this study those children with chronic diseases who had been exposed to invasive procedures and venipuncture previously reported more pain and showed more signs of behavioral distress than controls (median pain score of 8 vs 2 on the Wong or numeric scales, $p=0.00001$ and median OSBD score of 27 vs 5, $p=0.00001$). The authors postulate that these results may be secondary to a higher level of anticipatory anxiety in this population. The results of this study contradicts the common notion that children with chronic disease have a higher pain threshold than those who are previously well (8).

As we were unable to find any prior randomized controlled trials studying patients with chronic disease, for the purpose of sample size calculations we searched for papers that studied pain during venipuncture and used FPS-R as their primary outcomes measure. We found 10 studies fitting these criteria. Amongst these, interventions varied widely and included Vapocoolant spray, EMLA, and a variety of different distraction techniques (9-15). We excluded three studies in our analysis either because the study did not look at an intervention, mean changes in FPS-R scores were reported as the outcome, or because the study pooled data from different pain scales (14, 16, 17).

2. Hypothesis

Specific Aim #1: To determine the efficacy of distraction in reducing self-reported pain associated with venipuncture in pediatric post-cardiac transplant patients. We hypothesize that patients receiving distraction will experience less self-reported pain compared to those who do not receive distraction.

Specific Aim #2: To determine the efficacy of distraction in reducing procedural distress associated with venipuncture in pediatric post-cardiac transplant patients. We hypothesize that patients receiving distraction will experience less procedural distress compared to those who do not receive distraction.

Specific Aim #3: To determine if distraction can improve the success of venipuncture in pediatric post-cardiac transplant patients. We hypothesize that patients receiving distraction will have shorter times to successful venipuncture and require fewer attempts to achieve successful venipuncture.

3. Methods

Patients and Setting: We will conduct a randomized control trial comparing two groups: Distraction versus standard of care (i.e. no distraction). We will include patients between the ages of 4 and 17 years (inclusive) with a history of cardiac transplant who are undergoing venipuncture. We will exclude patients who are having blood drawn from a central line.

Intervention: We will block randomize children to receive distraction or the standard of care. Distraction will be administered using an iPad, and allowing the child to self-select a developmentally appropriate distraction (e.g. game, movie, music). Patients randomized to the standard of care will not receive any form of distraction aside from usual conversation (we will be collecting pilot data to confirm that this is standard of care in x% of patients in our population of interest).

Outcomes:

Specific Aim #1: Self-reported pain associated with venipuncture will be measured using the Faces Pain Scale – Revised (FPS-R). The FPS-R is a self-report measure of pain that has strong validity and reliability in children ages 4 to 17 years old (18, 19). To assess the FPS-R, we will use a standardized depiction of the FPS-R and a script in the patient’s primary language. We will obtain a baseline self-report measure of pain prior to the intervention and venipuncture. After the intervention and venipuncture is completed, we will immediately obtain a second self-report measure of pain from the child describing the pain intensity associated with the venipuncture.

Specific Aim #2: Procedural distress associated with venipuncture will be measured using the Observational Scale of Behavioral Distress – revised (OSBD-r). The OSBD-R is an observational scale that has demonstrated strong validity in children ages 2 to 20 years old for measuring the amount of distress a child is experiencing during a painful procedure. To assess the OSBD-r, we will videotape the patient before (baseline), during (procedure), and after (post-procedure) the venipuncture. Two trained assessors will independently score the videotape to obtain the OSBD-r score for each patient.

Specific Aim #3: Successful venipuncture will be measured using two outcomes: time to successful venipuncture [need to define start and end point] and number of attempts to achieve successful venipuncture.

Statistical Analysis and Sample Size: We will analyze continuous variables (FPS-R, OSBD-r, time to successful venipuncture) using the independent samples t-test. We will analyze ordinal outcomes (number of attempts to achieve successful venipuncture) using the Mann-Whitney U or Wilcoxon rank sum test. To determine our sample size, we took the root mean square of the outcome SDs of 7 prior studies of pain reduction techniques in children undergoing venipuncture and using FPS-R as their primary outcomes measure (9-15). The result of these calculations was a SD of 3.22. It has been shown that a reduction of 2 on the FPS-R score is the minimum clinically significant difference in pain in children (20). We would therefore need 42 patients in group 1 and 42 patients in-group 2 for a Power of 0.80 and Alpha of 0.05.

4. Subject Selection: There are currently about 150-200 pediatric patients who have received heart transplantation and being followed at CHONY by our Pediatric Heart Failure and Transplantation group. Approximately 2/3 of these patients are over the age of 4. We chose this population as a focus as they undergo a high frequency of venipuncture. An average patient will have twice weekly blood-work immediately post-transplant, which is then subsequently spaced to weekly, bi-monthly and eventually monthly. This group also reliably has from the time of diagnosis had multiple prior hospital admissions and procedures (i.e. catheterizations, biopsy). We will enroll patients between the ages of 4-17yo with a history of prior heart transplantation who are having blood drawn in phlebotomy. We will exclude patients who are having blood drawn from a central line.

5. Miscellaneous: We have identified a number of outstanding issues while creating this protocol. We first plan to obtain pilot data, by observing and collecting data on baseline procedures and workflow in the phlebotomy lab on the weekday during which we plan to perform our study. Information we hope to obtain include what percent of patients are

distracted by their parents during venipuncture and what means are used, how many different phlebotomists are present, and average time to successful venipuncture. This will help us confirm our assumption that there is currently no standard of care for pain reduction during venipuncture at this time.

Areas of heterogeneity amongst our study population that could confound our results include time from transplant, age of patients and variations in skill amongst different phlebotomists. We hope to enroll enough patients in each of these groups to include a regression analysis in our statistical analysis.

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