Study Protocol

Official Title: Improving Pain Management and Opioid Safety for Patients With Cirrhosis: Pilot Program

ClinicalTrials.gov ID (NCT number): NCT05128578

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Scientific Background

Approximately 79-86% of patients with cirrhosis have chronic pain, and nearly two-thirds of patients with cirrhosis and pain are prescribed opioid medications each year, often in a manner inconsistent with opioid safety guidelines. The PI's previous observational studies investigated the factors associated with pain and opioid use in patients with liver disease, and have highlighted how our current management of pain in this population affects clinical outcomes. The PI also found that, in patients with chronic liver disease (CLD), pain and opioid use are associated with increased hospitalizations and hepatology clinic visits, and that patients with cirrhosis often meet criteria for fibromyalgia even in the absence of hepatitis C. This led to investigations showing that pain and opioid use are associated with hospitalization in this population.

Preliminary work was completed to identify the needs of the patient population. Barriers to pain self-management for patients with cirrhosis included the complexity of pain management, absence of evidence-based intervention, and inadequate provider knowledge, time and training. The research team developed an intervention as the result of stakeholder input.

The PI also led a national survey of transplant centers to assess practices and policies around opioid use and opioid substitution therapy. In addition, she found that nearly half of Veterans with cirrhosis were prescribed opioids, and opioid prescriptions were associated with increased mortality (manuscript in progress).

This body of work has identified the scope of opioid use in individuals with CLD, the hospitalization associated with opioid use in this population, and policies to address opioid and opioid substitution therapy.

Despite the high prevalence of pain and its adverse consequences in patients with cirrhosis, there is limited guidance on how to manage pain in this patient population. Without understanding the barriers and facilitators affecting patients with cirrhosis and chronic pain, it remains unclear how to improve outcomes. The data provided by this study will help guide efforts to develop a safe, effective approach to managing pain in patients with cirrhosis.

Study Objectives

The purpose of this study is to conduct a pilot trial of a pain self-management intervention for patients with cirrhosis. The Liver Education About Pain (LEAP) intervention is a 12-week program that involves individual and group sessions with a health coach. The goal is to assess and optimize the intervention's feasibility and acceptability prior to conducting an efficacy trial, since no pain management interventions have been tested in this patient population.

Study Design & Methods

This interventional study with a pre-post design. Assessments will be completed either in-person (using a paper or electronic survey/app), online with a URL, or over the phone, based on patient

preference. Any in-person assessments will be completed in conjunction with a scheduled CLD visit, for the convenience of patients.

Research Procedures

Participants will go through a 6-week one-on-one behavioral intervention, followed by optional group sessions (n=6 weekly sessions). They will also complete assessment surveys/interviews conducted at multiple time points (baseline, end of 6 weeks, end of 12 weeks, and post intervention followup), each taking 30-60 minutes. All participants will receive their usual care from their hepatology team. This study will not impact their normal clinic care.

Intervention

Liver Education About Pain (LEAP) is a 12-week intervention involving weekly meetings with a health coach ("Pain Coach"), with 6 weeks of individual sessions and 6 weeks of optional group sessions. Timing for beginning the group sessions may vary to accommodate an adequate number of participants (ideally 3 or more) into the group, such that some individual session weeks may overlap with group session weeks. Each session will last approximately 1 hour. If participants miss a session, there will be the option to reschedule. As participants are consented and enrolled in the study, they will complete the baseline assessment and then be scheduled for their individual sessions with the Pain Coach.

Manual

The LEAP manual will be a guide to the intervention and used by the participants during the trial. Individual and group sessions will follow the LEAP manual. Topics to be addressed include an introduction to chronic pain and cirrhosis, physical activity, losing weight to improve pain, stress management, sleeping better, thinking differently about pain, talking with friends and family about pain, taking opioid pain medications, and coping with pain without drugs and alcohol. LEAP manuals will not be collected as part of the study; however, participants will tell the Pain Coach what they've been doing per the manual and in the "homework" sections.

Pain Coach

The Pain Coach will lead all sessions and take attendance as needed for the feasibility assessment post-intervention.

Individual Sessions

At the start of each individual session, the Pain Coach will go through the three-question PEG scale to keep a data set of each participants' pain week-to-week. Participants will pick topics they want to do and go through them with the Pain Coach, learn about new ways to improve on what they've already been doing, and keep track of what they've learned and how they're doing with their pain.

Group Sessions

The optional group sessions will provide a platform where patients will talk about how the individual sessions went and what tools were helpful. They will be able to learn from each other and get additional input from the Pain Coach.

Assessments
The research team will collect assessments from patients at the following timepoints:

- Survey at enrollment (baseline)
- Survey 6 weeks after the start of the intervention, i.e., after completion of individual sessions
- Survey & interview 12 weeks after the start of the intervention, i.e., after conclusion of group sessions
- Survey 3-months post-intervention (or 24 weeks after the start of the intervention, i.e., 12 weeks after conclusion of group sessions)

Assessments are expected to last 30-60 minutes each and will include a combination of medical record data and patient-reported outcomes. At baseline, patients will report demographic data, and at follow-up we will collect additional feasibility and acceptability data.

Audio Recording
Group and individual sessions will be audio recorded and de-identified to assess fidelity. Assessment surveys will be offered online, on paper, or by phone, as is most convenient for patients. Assessment interviews will take place virtually or by phone. Any phone calls/virtual meetings to collect data will be recorded and the transcripts of the calls will be subsequently de-identified.

Eligibility Criteria

Inclusion Criteria
All participants must be ≥18 years of age and fluent in English. Additional specific inclusion criteria include:

- Diagnosis of cirrhosis
- Receiving care at UPMC hepatology clinics
- Chronic pain

Exclusion criteria
Participants will be excluded if they are <18 years of age or are unable to provide informed consent for any reason. Additional exclusion criteria include:

- Prior liver transplantation
- Limited life expectancy (<6 months)

Analysis Plan and Statistical Considerations

The goal of this pilot study is to determine feasibility and acceptability outcomes in preparation for a larger trial. Emerging consensus, including NIH guidance, recommends against assessing preliminary efficacy in pilot studies, since small pilot sample sizes lead to imprecise estimates. The analysis will include summary statistics, including change in measures using appropriate analysis. Primary outcomes will include completion of at least 80% of individual sessions and satisfaction with intervention, measured using the TEQ (Likert-scale based assessment of 5

domains of satisfaction.) The former will be assessed using count data and the latter with means and standard deviations. Secondary analyses that include changes in scores over time will employ paired t-tests to measure within person change pre to post intervention.