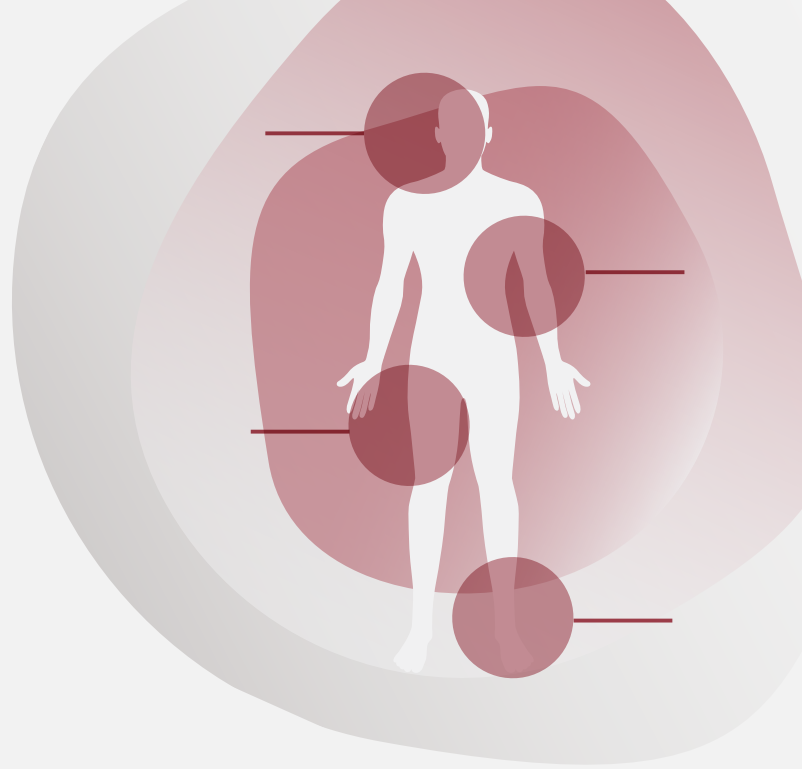


Chronic Pain Tips



Introduction

- Importantly, this document provides tips for the management of chronic pain (present for >3 months). Acute in-hospital pain management and pain management at the end-of-life in cirrhosis, although similar in some regard to chronic pain, do have distinct differences, including a shift in the risk-benefit profile in the latter setting. These topics are dealt with separately.
- Chronic pain is often the most important impediment to quality of life for patients with cirrhosis.
- Tension can arise between the patient's desire to avoid suffering and disability and the provider's fear of causing harm with pain treatment, particularly opioid analgesics, and even more so if the cirrhosis is the result of substance misuse.
- A clear understanding of the pathogenesis of chronic pain and adherence to simple treatment principles can help to allay some of these fears.
- Pain management goals can also be changed based on patient course of disease/prognosis (see link to goals of care discussions).

The Biopsychosocial model for pain

- As students, we learn that pain arises from nociceptive input following injury or disease. Many of us go on to assume that a linear correlation ought to exist between the amount of tissue damage present and the amount of pain a person has.
- A person with severe pain and minimal signs of disease is regarded with confusion or suspicion. Persons with low back pain and near-normal MRI scans or those with fibromyalgia are other common examples of this scenario. The tendency is to dismiss the pain complaint as false. This merely sets up the physician-patient dyad for conflict. The symptoms are, after all, completely real to the patient.
- Some patients with cirrhosis may have had challenges with drug or alcohol use disorder. Even if those behaviors are a thing of the past, their reports of pain are often viewed through that lens and may get misinterpreted as drug-seeking behavior.
- The way to make sense of these conflicts is to discard the only-tissue-damage-explains-pain theory and invoke a different explanatory model for pain.
- The one in current use by experts is the Biopsychosocial Model of Engel. This holds that pain is created not only by biological factors (things that can be seen on x-ray or physical

examination) but also by psychological factors (thoughts and feelings) and social factors (the attitudes of others to the index patient's). Thus, a person who reports severe and disabling pain in the face of scant physical findings might be particularly burdened by, for example, anxiety, depression, and/or adverse environmental factors such as poverty or bullying. In palliative care, this is known as "total pain". Other terms are 'chronic' 'functional' or 'non-organic' pain. No matter what it is called, failure to legitimize a pain complaint that is not obviously backed up by physical findings will lead to frustration and conflict.

- Note that the act of accepting the pain at face value does not in any way oblige the practitioner to then blindly engage in prescribing.

Pain Assessment

- Assessment of any given pain problem in a patient with cirrhosis can be readily folded into the overall initial and follow-up assessment. The goal is to classify the pain by type. This is necessary because some types of pain require specific therapeutic solutions, and treatments that work for one type won't necessarily work for another. The **OPQRSTUV model for symptom history taking** (Link to "Follow a general process for symptom assessment" by Fraser Health). This assesses onset, provoking/palliating factors, quality, radiation, severity, treatment, understanding/impact and values.
- The PEG is an ultra-brief pain measure derived from the Brief Pain Inventory that although not specifically evaluated in cirrhosis, has demonstrated reliability and sensitivity to change (Krebs et al. 2009, PMID 19418100)

1. What number best describes your pain on average in the past week:										
0	1	2	3	4	5	6	7	8	9	10
No pain						Pain as bad as you can imagine				
2. What number best describes how, during the past week, pain has interfered with your enjoyment of life?										
0	1	2	3	4	5	6	7	8	9	10
Does not interfere						Completely interferes				
3. What number best describes how, during the past week, pain has interfered with your general activity?										
0	1	2	3	4	5	6	7	8	9	10
Does not interfere						Completely interferes				

- The conversion of a patient 's narrative into a working diagnosis is a fundamental clinical skill. From the pain management point of view, the most important things are the pain's **location, intensity and character**. Physical examination is mandatory; tight, tender muscles and sensory abnormalities are important examples of findings that are often missed by history alone. Following that process, the clinician will be faced with one or more pain problems that will fit into one of the following categories.

Nociceptive pain

- **Somatic pain.** This arises from soft tissue, bones and joints. The pain is **easily localized** and may be associated with localizing signs such as swelling and bruising or deformity. In general, movement makes somatic pain worse and rest makes it better. Somatic pain is the

most analgesic responsive type of pain. An important subtype of somatic pain is myofascial pain (sometimes referred to as 'deconditioning'). This describes the all-too-common finding of pain arising from muscles which have become stiff through disuse. The identification of myofascial pain is important because it is only minimally responsive to analgesic drugs. It requires the patient to exercise, which may mean beginning from very low levels indeed.

- **Visceral pain.** This refers to pain that arises from the vital organs in the thorax, abdomen and pelvis. Visceral pain is often perceived at a location distant from the organ that is causing the trouble, such as in the common example of shoulder to pain being caused by diaphragmatic irritation. Visceral pain is often disproportionately severe compared to the amount of pathology in play and is also more likely than other pain types to be associated with autonomic phenomena such as tachycardia and sweating. Visceral pain is often unaffected by changes in position and can have a colicky pattern. In cirrhosis, this may be related to hepatic capsular distension, splenomegaly or tense ascites.

- **Neuropathic pain.**

These pains arise from structural or functional derangement of the tissues of the nervous system itself. Most clinicians are familiar with the typical descriptors that patients use to describe the pain that results. Adjectives like **burning or electrical** are often likely to be indicative of neuropathic pain. The most convincing diagnoses of neuropathic pain are accompanied by a positive physical finding, such as weakness, numbness or hypersensitivity to touch. There is a tendency to try and shoehorn other pain complaints into this category because of the misperception that the drugs that are used to treat it are inherently safer than opioids. A valuable exercise is for the clinician who makes a provisional diagnosis of neuropathic pain to run through the mental exercise of explicitly deciding which nerve or nerves are thought to be culpable and what pathology is thought to be responsible. If you can't convince yourself of either fact, the pain is unlikely to be neuropathic in origin.

- **Total Pain/Chronic Pain.**

This is the diagnostic category into which pains which cannot be readily explained in pathoanatomical terms can be given due legitimacy. Important clues to this diagnosis are readily obtainable: Patients may describe pain beginning for no identifiable reason, or prolonged suffering after an apparently self-limiting injury: the archetype is back pain for months or years following a trivial lifting injury. Pain which intensifies month over month and year over year is almost always of this type unless there is a concomitant escalating explanatory disease process. Pain which begins in one body part and spreads to others is typical, as is inexorable loss of ability to perform daily activities. The quantum of suffering caused by pain in this category often eclipses that which comes from the others. **Patients must deal with a triple threat;** i) the pain, ii) the worry that a serious underlying diagnosis is being missed, and iii) the worry that their doctor doesn't believe what they are telling them. The likelihood of that scenario is directly proportional to the amount of mental and social disorder that the patient must face along with their liver disease. Failure to attend to this type of pain is probably the most common reason for the patient's quality of life to remain constrained and the scenario in which the misuse (intentional or otherwise, prescribed or otherwise) of analgesic medications is likely to cause trouble. **It is important to determine how the pain is affecting the patient's life and function.**

Other

Cirrhosis patients can, of course, suffer from other pain syndromes which don't readily fall into these categories. Examples include chronic daily headache, rare specific neurological pain syndromes, chronic pelvic pain and others. These should be treated by separate methods.

Drug Therapy

In general, **the most that can be expected from outpatient drug treatment for chronic pain is a 30-50% reduction in intensity.** This should be stated to the patient from the outset. To the surprise of many clinicians, patients find this degree of relief worthwhile, and are willing to endure some risks and side effects in order to achieve it. **Armed with this knowledge, the physician patient dyad can set realistic goals for therapeutic trials.**

Patients who persistently seek complete elimination of their pain with medications, particularly those who do so in the face of significant side effects and especially those who seem unwilling to consider non-drug approaches should arouse particular caution. These patients should not be cast aside, but it should be made clear to them, in a persistent and kindly manner, that they're asking the impossible.

Although the liver plays a crucial role in the metabolism of most drugs, **there is no readily available method of estimating how much the liver disease underlying the cirrhosis will change drug performance** (unlike, for example, our ability to use creatinine clearance as a way of determining dose reduction in chronic kidney disease). The basic principle, therefore, is to **start with a small dose of drug, evaluate effect and side effects frequently and adjust as necessary. If one class of drug fails provide meaningful relief, the most efficient strategy is to abandon it and move onto the next category.** Combinations of drugs from different classes are much more likely to result in hard-to-interpret toxic side effect profiles. If a trial of the most potent analgesics fails, it is better to accept the fact that the pain is not analgesic responsive. (This does not mean the same thing as giving up and abandoning the patient).

Drug Therapy

Acetaminophen -

Contrary to popular belief, it is permissible to use acetaminophen in liver disease. Doses of up to 2 g a day have been shown to be safe in cirrhosis, and the short-term permissibility of up to 4g is advocated by others. It is the ideal drug for the short-term aches and pains that afflict cirrhosis patients as much as they do everybody else and has advantages of non-cumulation and minimal side effects. It can be used in isolation or together with an opiate.

NSAIDS -

are not recommended in patients with cirrhosis. Topical preparations are generally associated with very low systemic absorption and are probably safe if used over small areas.

Opioids -

The use of opioids can be a polarizing topic for practitioners managing patients with cirrhosis. The appropriate quest for pain control needs to be balanced by the potential to increase the risk of falls, hepatic encephalopathy and addiction in the setting of substance use disorder.

- Although clinicians often regard the initiation of opiate analgesics with some trepidation, when indicated, there are robust and easy to follow guidelines which remind the clinician how to do this safely. The three essential skills that a clinician needs in this regard are:
- A willingness to do right by the patient.
- The ability to screen for opiate use disorder and call for expert help promptly when it is suspected.

- To manage the prescription carefully and keep meticulous records.

Opioids are not a panacea, and while they sometimes work where other agents have failed, their administration should be regarded as a therapeutic trial, with **improved quality of life and function (not merely reduced pain intensity) as the goal**. If that does not happen, the trial has failed and the opioid should be discontinued. Explain this to the patient prior to starting the opioid.

Successful opiate analgesia in the cirrhosis patient can be achieved with many of the currently available preparations but a strong case can be made for the sole use of hydromorphone and suboxone (buprenorphine).

- Hydromorphone is only metabolized by one intrahepatic pathway and its metabolites are minimally-toxic. It can be given orally or injected and is inexpensive. For the most part, there is no reason to prefer any other opiate agent over it.
- Suboxone (buprenorphine/naltrexone) has eclipsed methadone to become the agent of choice in opiate agonist therapy for opiate use disorder. However, it is a potent analgesic in its own right and has a number of intrinsic features which make it safer than other long-acting opiate preparations. The initiation of suboxone (buprenorphine/naltrexone) requires some special steps which must be followed but are easy to learn. In cases where there is suspected or overt drug misuse, suboxone (buprenorphine/naltrexone) is the first-line opioid for the prescriber who is not trained in Addiction Medicine. It is contraindicated with Child Pugh C liver disease. Use caution in patients with Child Pugh B liver disease - not recommended for induction in these patients (can precipitate withdrawal). For maintenance, naloxone clearance is reduced in cirrhosis and buprenorphine may be less effective.

The use of a single agent (as opposed to one for background use and another for 'breakthrough pain') makes life easier for the prescriber and safer for the patient. Short acting pills are best. Low dose, by the clock regimes are a good place to start. Even if the first prescription makes no difference to quality of life and function goals, it will stand as a powerful emblem of the prescriber's commitment and will help deepen the therapeutic alliance. That should be used as the basis for carefully monitored dose escalation. However, if that does not then result in pro rata improvement in quality of life and function, the drug should be discontinued. If a trial of hydromorphone does not work (i.e. ZERO benefit), there might be other factors causing pain that need to be explored. Consider a chronic pain consult.

In expert practice, problems are often seen from failure to discontinue ineffective opioid regimes. The typical scenario is that opioids initially provide good relief from pain, but no improvement in quality of life/function. The development of tolerance leads to dose increases, and the patient then gets stuck at an unsafe opioid dose, gaining little from it. At high doses, an entity called Opioid Induced Hyperalgesia makes pain worse, but, mistaken for tolerance, leads to yet further dose increases. De-escalation of the opioid is attempted too rapidly, or in overly large steps. This is particularly common when high-dose pills are used. That leads to withdrawal, of which the most common symptom is pain. The solution is to reduce the total daily dose extremely slowly taking the long-term view. A good rule of thumb is to break the prescription into the smallest pill sizes possible, ask the patient how many pills per week s/he thinks could be eliminated, then go half that fast. Entrenched high dose opioid prescriptions can easily take a year or more to be eliminated. The literature would suggest that the removal of ineffective opioid prescriptions is associated with measurable improvements in quality of life. When to consult a Pain management specialist

When to consult a Pain management specialist

The best use of a consultant in Pain Medicine is for an opinion about safety and the limits of therapy, and for access to multidisciplinary care. Most appropriate questions can be answered by telephone.

Some advice (such as an imperative to stop drinking or start exercising) might carry more weight if delivered by a specialist in a hospital setting. Where first-line drugs are contraindicated or have failed, it might make more sense to obtain an opinion about what to do next before choosing new preparations. A patient on opioids in whom liver transplantation is being contemplated might benefit from a second look to see if the opioid therapy can be reduced or eliminated. Those with pain and a psychiatric or physical comorbidity might benefit from expert advice when treatment options are all contraindicated to some extent. If available, a properly constituted multidisciplinary pain clinic can deliver psychologically based treatment in single-user or group settings and can provide guidance on reactivation in the case of a disabled sedentary patient with myofascial disease. However, it is incumbent upon primary care practitioners to know the strengths of the program they are referring their patient to. Not all facilities offer the same options, or even the same philosophy of care.

Some patients with cirrhosis have suffered or continue to suffer from substance use disorders. These are very difficult cases to manage in solo practice, and the involvement of a consultant in Addiction Medicine at an early stage is a good idea. At end-of-life, palliative care can provide important guidance here as well.