PA Pearls From the ER

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PAIN IN THE BUTT

Pain Management in the ER – Part 108

OPIOIDS AS A DOUBLE EDGED SWORD: OPIOID INDUCED HYPERALGESIA (OIH)

What is opioid induced hyperalgesia?

This is an entity which has been known for over 100 years although it is now coming under greater scrutiny because of the increased use of opioids in patients with chronic non-malignant pain. This condition is thought to be caused by the opioid sensitization of the central nervous system and peripheral nervous system to pain. That is correct – **the opioids paradoxically worsen the pain**. On careful neurological examination these patients are often found to be more sensitive to cold stimuli and to also have allodynia (non-painful stimulation of the skin results in pain) outside of the area of pain. The exact mechanism is unknown although it is speculated that it is the result of stimulation of NDMA receptors in the central and peripheral nervous system.

What is an NDMA receptor?

I have no idea as I develop severe dyspepsia (on a scale of 1 to 10, my dyspepsia would be an 8) every time I read about these receptors.

How frequent is opioid induced hyperalgesia?

No one seems to know although fortunately it appears to be uncommon.

How quickly does it develop?

Much to my amazement, there is evidence that high dose intra-operative opioids administered intrathecally (I assume this was done as part of "pre-emptive analgesia" management) can result in **increased** post operative pain in opioid naïve patients.

What are the other mechanisms that could explain increasing pain in a patient on opioids for chronic non-malignant pain?

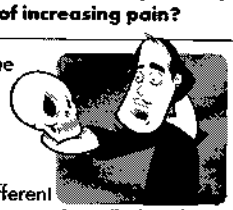
1. An exacerbation of the underlying condition such as a flare-up of osteoarthritis.
2. The development of opioid abuse.
3. The development of physiological tolerance to opioids.
4. The development of a new source of pain.
   I am particularly sensitive about this possibility as I can recall repeatedly seeing a male patient in his 70s because the "arthritis" in his back was getting more severe. After several months I finally decided it was time to obtain x-rays of his lumbosacral spine which revealed metastatic lesions of the lumbar vertebrae as well as the pelvis. A rectal examination revealed a hard nodule on his prostate. He was dead within one year. On the other hand I have also cared for patients with flare-ups of their chronic pain where I have over investigated their complaints. It is truly difficult to find a reasonable approach to patients whose conditions are known to wax and wane with time.
5. Loss of the placebo effect.
   It is well known that the placebo effect results in pain relief in approximately 30% of patients although rates much higher than this have also been reported.

So how do you determine the etiology of the increasing pain?

You do what you always have done. You take a good history to ensure that there is nothing different about the pain other than an increase in intensity. For example, has the pain changed in character, in location, it now aggravated by different factors (e.g. a long history of a "migraine headaches" which are now exacerbated by coughing, sneezing and other valsalva manoeuvres especially in the morning)? You then examine the patient looking for new findings such as evidence of increased intracranial pressure (e.g. papilledema) or focal neurological signs in your headache patient. If you have any concerns you will arrange for further investigation and/or consultation with an appropriate specialist if indicated. **Listen to your gut!**

If you are comfortable there is nothing suspicious going on, do you increase your patient's opioid because of increasing pain?

As Shakespeare would say, *"Ay, there's the rub"*.



Frequently, the first step is to switch to a different opioid using an equianalgesic conversion chart as this will often decrease the pain intensity in a patient with OIH. Remember, as a general rule you initiate the new opioid at 50% of the equianalgesic dose of the discontinued opioid.

You can also consider switching to **methadone**. At least six studies have shown that methadone is particularly effective in OIH, perhaps because it is a weak NMDA receptor antagonist (here comes my dyspepsia again). Methadone is a particularly "tricky" analgesic that only should be prescribed by physicians with expertise with this medication. A special license is required in Saskatchewan to prescribe methadone for pain management.

Interestingly, OIH has also been reported in former opioid addicts who are on methadone maintenance.

PAIN IN THE BUTT (con't)

Other approaches to OIH include:

- if you are courageous, reduce the opioid dose by 10% a day in the hope of decreasing the pain

  A recent review article by Chu made the following comment:

  "Considerable clinical confidence is required to reduce opioid doses in patients experiencing large amounts of pain."

- institute other analgesics such as the NSAIDs (particularly the coxibs) which have been shown to be effective in some patients with this disorder

- refer the patient to a pain specialist for assessment for procedures such as nerve blocks, intrathecal infusions and other interventions (this strikes me as a very pragmatic approach).

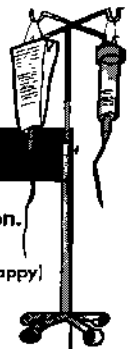
How long does it take for OIH to disappear after discontinuing the opioid or switching to a different opioid?

This is a slow process and diminished pain may not be noticed by the patient for weeks or months (or even longer).

Click here to download 7 PowerPoint slides on Opioid Induced Hyperalgesia.

Source: Hay et al. "Hyperalgesia in Opioid-Managed Chronic Pain and Opioid-Dependent Patients". Journal of Pain, In Press 2009.

Chu et al "Opioid Induced Hyperalgesia in Humans". The Clinical Journal of Pain, July/August 2008.



MYTH OF THE MONTH

All patients with an acute myocardial infarction (AMI) should receive IV beta- blockers unless there is a contraindication.

REALITY: For years the gospel was to beta-block the AMI patient to decrease the heart rate and blood pressure which resulted in a decreased cardiac work load which is "a good thing" This made sense and was borne out by numerous studies in the **prethrombolytic era** Therefore, it became standard practice to administer the beta-blocker metoprolol in an IV dose of 5 mg every 5 minutes to a total dose of 15 mg to the acute AMI patient The standard contraindications were observed including:

- active asthma or reactive airway disease
- PR interval >0.24 seconds or a 2nd or 3rd degree AV heart block
- systolic bp <90 mm Hg
- signs of peripheral hypoperfusion.

Several years ago it became common to administer metoprolol **orally** if the patient was not tachycardic or hypertensive as this route was considered safer than (and just as effective as) the IV route.

What was the COMMITT/CCS-2 trial?

This was a trial involving 42,852 patients who received either IV metoprolol or placebo within 24 hours of a suspected AMI. The findings were surprising.

For every 1000 patients treated with IV metoprolol there were:

- 5 fewer infarcts
- 5 fewer cases of ventricular fibrillation
- 11 **more** cases of cardiogenic shock.

As well as being associated with an increased incidence of cardiogenic shock, metoprolol was also associated with more cases of hypotension and bradycardia. Therefore, the safety of beta-blockers has become a concern in the era of thrombolysis.

How is this reflected in the 2007 recommendations on AMI patients with ST elevation (STEMI) from the American Heart Association/American College of Cardiology?

Oral beta-blocker therapy should be initiated in the first 24 hours for patients who do not have any of the following:

1) Signs of heart failure.
2) Evidence of a low output state.
3) Factors associated with an increased risk for cardiogenic shock **(unless left ventricular function has been assessed)** such as.

   - age >70 years
   - systolic blood pressure <120 mm Hg
   - sinus tachycardia >110 bpm **(this one makes me very, very unhappy)**
   - heart rate <60 **bpm**
   - increased time since onset of symptoms of STEMI.

   The risk of developing cardiogenic shock increases with the number of the above factors involved.

4) Relative contraindications to beta-blockade include PR interval >0.24 seconds, 2nd or 3rd degree AV heart **block**, active asthma or reactive airway disease (**relative** = phone a cardiologist).

How do you assess left ventricular function in a patient with a risk factor for cardiogenic shock?

I am not certain how one is expected to evaluate left ventricular function in the ER as this is not described in the AHA/ACC guidelines; however, I suspect it involves an echocardiogram. This means that many small rural ERs without echo capabilities will be stuck between a rock and a hard place as the patients who you want to beta-block the most (e.g. the tachycardic patient) are also the ones who are at highest risk for cardiogenic shock. It is in times like this that the reason God created cardiologists becomes clear – phone one!

What is the oral dose of metoprolol?

The American Heart Association/American College of Cardiology recommends starting oral metoprolol at 50 mg q6H and if tolerated well can be converted to 200 mg daily (or the maximum dose tolerated) the following day. Many physicians will start at a lower dose (e.g. 25 mg) and titrate slowly over several days until the patient cannot tolerate the side effects or a maximum dose of 200 mg/day is reached. Atenolol can also be used instead of metoprolol. The dosage is the same for both drugs.

What if there is a contraindication to beta-blockers in the first 24 hours?

The 2007 guidelines recommend:

> *"Patients with early contraindications within the first 24 hours of STEMI should be re-evaluated for candidacy for beta-blocker therapy as secondary prevention".*

The guidelines also state:

> *"Patients with moderate or severe LV failure should receive beta-blocker therapy as secondary prevention with a gradual titration scheme".*