Opioid Dependence

Physical dependence is described as abrupt discontinuation of oral or parenterally administered opioids leading to opioid withdrawal or abstinence syndrome; opioid tolerance is a predictable pharmacologic adaptation (continued opioid exposure results in a rightward shift in the dose–response curve, and patients require increasing amounts of drug to maintain the same pharmacologic effects); psychological dependence and substance abuse are also often used interchangeably with the above terms; the broad group of ''chronic opioid-consuming patients'' or "opioid dependent patients" encompasses all patients who have been consuming opioids on a daily basis before surgery

ANESTHETIC CONSIDERATIONS:

- Increased risk of aspiration (decreased LES tone, delayed gastric emptying, and increased risk of N+V)
- Tolerance to opioid effects, including analgesia
  - Anesthetic requirements vary according to acute or chronic exposure
- Risk of withdrawal, manifesting with excess sympathetic tone
- Potential IVDU: co-morbid disease more prevalent, including HIV, HCV, endocarditis, and malnutrition
- Increased incidence of co-morbid illnesses and conditions
  - Pain syndromes (CRPS, neuralgias)
  - Malignancy (with its attendant considerations)
  - Infectious diseases (HIV, HCV, HBV)
  - Cardiac and respiratory insufficiency
- Difficult postoperative pain control, requiring multidisciplinary and multimodal therapy
  - Early involvement of the acute / chronic pain service
  - Ensure adequate maintenance doses of chronic opioid plus analgesia for perioperative period, recognizing that these patients are still at risk for respiratory depression
  - Consider co-analgesics/multimodal analgesia

ANESTHETIC GOALS:

- Ensure pain management peri-operatively, bearing in mind that these patients may need very large doses of opioids
- Remember PO to IV conversions and adjust accordingly
- Monitor closely postoperative as often these patients have increased complaints of pain, while often having increased evidence of post operative sedation (compared to opioid-naive controls)

HISTORY & PHYSICAL

- Drug, dose, route, frequency, duration, and time last used
- Indication for opioid (if any), and appropriate pain history
- History and investigations appropriate to co-morbidities
  - Many organ systems may be affected, and a thorough review of systems is appropriate

OPTIMIZATION

- Should surgery go ahead?
  - The acutely intoxicated addict may not be appropriate for elective surgery
- Schedule as an early case of the day, so there will be time monitor the patients and adjust analgesic requirements in the PARR
- How much opiate of a given type should be given to meet the patient's baseline use to avoid withdrawal?
- How will postoperative pain be managed?
  - The perioperative period is not a suitable time to attempt withdrawal of opiates
  - Have the patient take their regular dose of opioid prior to surgery, or supply them with equivalent
  - Utilize analgesic adjuncts such as acetaminophen, NSAID, gabapentin, clonidine, ketamine, COX-2s etc.
    - No clear evidence as to which is best
    - **Use of ketamine perioperatively is well supported** as the NMDA system has a role in the development of both acute and chronic tolerance
  - Involvement of ancillary resources, such as addictions specialists, if appropriate
    - This includes preoperative referral to such resources
- **Regional blocks should be offered whenever feasible**
- LA infiltration may be helpful
- **Avoid opioid agonist-antagonists** (i.e. nalbuphine, butorphanol, pentazocine) due to risk of withdrawal symptoms

ANESTHETIC OPTIONS

- Consider adjuncts to pain management, including regional anesthesia
- Texts advocate inhalational anesthesia for GA, due to the ability to rapidly adjust dose and depth, as requirements are unpredictable

ANESTHETIC SETUP

- **Drugs**
  - Standard
- **Equipment**
  - Standard CAS monitors

MANAGEMENT OF ANESTHESIA

- **Induction**
  - Perioperative management of opioid-dependent patients begins with preoperative administration of their **daily maintenance or baseline opioid dose before induction** of any type of anesthesia
  - Likewise patients should be instructed to take their morning dose of co-analgesics (gabapentin, NSAIDs etc.)
    - If the patient forgets their a.m. dose it should be given in the preoperative area either PO or IV

        - Continue transdermal patch opioids, if removed for the OR it may take up to 6-12 hours to re-establish baseline analgesic effects
- **Maintenance**
    - Nothing
- **Emergence**
    - Comfortable prior to extubation

DISPOSITION & MONITORING

- Post-operatively baseline opioids need to be incorporated into the PCA dose for the patient (or as a background infusion)
    - Many guidelines exist for this background requirement, but, **50-60% of the patients preoperative dose is a good place to start with PCA** and other analgesia in addition
- In the patient with a previous history of opiate dependence, opiates should not be withheld for treatment of postoperative pain, although **adjunctive medications and regional techniques should be maximized**
- Postoperatively, monitor for withdrawal symptoms (diaphoresis, mydriasis, hypertension, tachycardia, anxiety, lacrimation, rhinorrhea, yawning, tremors, diarrhea, hyperthermia)

PREGNANCY

- Pregnancy is associated with greater methadone metabolism and reduced methadone bioavailability b/c of greater maternal blood volume and GFR
- Methadone maintenance therapy in heroin-addicted pregnant women is beneficial for both mother and infant
    - Better medical and prenatal care, lower incidence of unplanned pregnancies, and decreased neonatal abstinence symptoms
- Heroin use during pregnancy is associated wit 1st trimester spontaneous abortion, preterm delivery and IUGR
- Neonatal abstinence syndrome occurs in neonates repeatedly exposed to opioids in utero
    - Characterized by irritability, poor feeding, abnormal sleep patterns, diarrhea, fever, and seizures
    - Can result in death
- Opioid-dependent patients may have end-organ damage and infectious diseases
    - They are more likely to report inadequate analgesia during labour, vaginal or cesarean delivery and postpartum
- No difference in proportion of opioid-dependent women who required GA for C-section
    - However, there is a significant incidence of pain management problems post-op
- → **Neuraxial analgesia or anesthesia is the technique of choice** for a methadone-maintained or other opioid-addicted patient undergoing vaginal of cesarean delivery
    - They had similar pain scores and analgesia requirements during labour, but methadone-maintained patients required about 70% more opioid analgesia after C-section
    - If neuraxial contraindicated, PCA may be used but opioid dose requirements may be 30-100% higher than those of opioid-naïve patients

PATHOPHYSIOLOGY

- **Physical dependence** can be described as "an adaptive state that manifests itself by intense physical disturbance when the administration of drug is suspended"
- **Tolerance** describes the need for progressively larger doses to achieve the desired effect
- **Addiction** is compulsive use of a substance despite negative consequences which can be severe
- Mechanisms of tolerance are not fully understood
    - May have to do with the down regulation of the locus ceruleous (more so than the up regulation of peripheral mu receptors)
- Tolerance can develop after the acute administration of opioids, although there is controversy as to how quickly it can develop and with what doses (reasonable evidence that with remifentanil doses > 0.3 mcg/kg/min will cause this phenomenon)
- Also is a concern with opioid induced hyperalgesia after infusions, which seems to be related to dependence
    - Mechanism is not fully understood, but, may involve upregulation of excitatory neurotransmitters (glutamate and substance P) along with increased NMDA activity
- The development of tolerance is very patient specific

Opioid effects by receptor		
Traditional*	**IUPHAR***	**Clinical Effects**
1	MOP	Supraspinal analgesia
		Peripheral analgesia
		Sedation
		Euphoria
		Prolactin release
2		Bradycardia Urinary retention Spinal analgesia
		Respiratory depression
		Physical dependence
		Gastrointestinal dysmotility
		Pruritis
		Bradycardia
		Growth hormone release
1	KOP	Sedation Spinal analgesia
		Miosis
		Diuresis
2		Psychotomimesis
		Dysphoria
3		Supraspinal analgesia
	DOP	Spinal and supraspinal analgesia
		Modulations of -receptor function
Nociceptin / orphanin	NOP	Anxiolysis
		Analgesia

* International Union of Pharmacology Committee on Receptor Nomenclature has recommended new naming schema to replace traditional Greek nomenclature

- **Conversion Between Opioid Analgesics** - A practical guide from the University of Alberta Multidisciplinary Pain Centre
    - Make a list of the total amounts of each opioid drug currently being taken **orally, rectally or transdermally** in a 24 h period
        - Count milligrams of each drug, whether being given as long- or short-acting preparations, scheduled or breakthrough
        - Injectable opioids get added in later
    - Look at the table and multiply the amount of each oral drug by its bioavailability (column 4), to get a smaller number
        - This is the number of milligrams that actually gets into the bloodstream
        - Remember that a 100 mcg fentanyl patch is 0.1 mg of fentanyl PER HOUR
    - Convert each number in your list to IV morphine equivalents, by using column 2
    - If any opioids are being given parenterally, add them to the list at this point, and convert them to IV morphine equivalents as well
    - Add up the IV morphine equivalents (should now have a single number in milligrams)
    - **Reduce this number by 30%**
    - Select your new drug
        - Use column 2 to obtain the equivalent parenteral dose of the new drug
        - Divide this number by the bioavailability of the new drug to get a bigger number, that being the oral 24 hour dose of the new drug
        - Divide this dose into long- and short-acting fractions as you see fit
    - **Use these steps as only a** starting point
    - **Apply careful clinical judgement and be prepared to adjust the dose** of the new drug according to response

Drug	IV dose (mg) = 10 mg IV morphine	PO dose = 30 mg PO morphine	Bioavailability of oral dosage form	Dosing interval (hrs)
Morphine	10	30	0.3	3
Anileridine (leritine)	25	75	0.3	3
Codeine	100	300	0.3	3
Diamorphine (heroin)	5	12.5	0.4	3
Fentanyl	0.1	-	-	1
Hydromorphone (dilaudid)	2	3	0.6	3
Levorphanol	2	4	0.5	6-12
Meperidine (demerol)	80	250	0.3	3
Methadone	2-10	2-10	1.0	8-12
Oxycodone (percocet, oxycontin)	10	12	0.8	3
Propoxyphene (darvon)	50	100	0.5	4
Sustained release morphine (ms-contin)	-	60	0.5	8-12

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