The WindowPain

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Risk of Coumadin & Acetaminophen

Pain Management nurses are acutely aware patients who are taking blood anticoagulants (blood thinners) should not be taking NSAIDs at the same time due to increased risk of bleeding. Aspirin and other nonsteroidal anti-inflammatory drugs inhibit platelet function and can cause injury to gastric mucosa, etc. An alternative analgesic choice is acetaminophen. Are you aware increased doses of acetaminophen can temporarily increase INR when patients are on coumadin (warfarin)?

In one study, 54% of patients who were taking acetaminophen and warfarin had exceeded their therapeutic range by 0.3 or more versus the placebo group (17% exceeded therapeutic range). Studies have investigated whether acetaminophen or its metabolites (N-acetyl-p-benzoquinone-imine, NAPQ1) affect warfarin pharmacokinetics.. Its may potentiate the inhibition of components of the vitamin K cycle. Effects of NAPQ1 may inhibit components of mitochondrial transport. Serial INRs and investigation of current OTC acetaminophen consumption should be evaluated

Paauw, Douglas S (2015, January 15), Warfarin and OTCs: An Unrecognized Risky Combination Medscape.com

Renato DL et al (2011). Warfarin and acetaminophen interactions: A summary of the evidence and biologic plausibility. Blood, 118(24): 6269-6273

Submitted by
Sandra Kuefner, ANP-C

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Newsletter Committee Editor:

Donna Sipos Cox, FNP

Contributors:

Sandra Kuefner, ANP

ZOOM CE Meeting with NYC Chapter

The ASPMN NYC Chapter held its first ZOOM CE offering on Thursday, April 30th. There were over 20 participants to listen to Robert Montgomery, CNP, RN-BC, ACNS-BC presentation "Perioperative Buprenorphine: To Continue or Not to Continue? That is the Question".

Dr. Montgomery reviewed the pharmacology of buprenorphine, including it's affinity for the mu receptors and the long half-life which is why it takes so long to dissipate. The intravenous formulation of buprenorphine is no longer available. Subliguinal tablets and film are utilized for opioid use disorder. Sublingual buprenorphine has more bioavailability than transdermal. Transdermal and buccal forms are utilized for moderate to severe chronic pain.

Dr. Montgomery stated the equianalgesic conversion for 24mg buprenorphine is 1000mg morphine. Buprenorphine is an agonist at the delta receptor and antagonist at the kappa receptor. The kappa receptor antagonism blocks dynorphine. In experimental studies this mechanism: reduces anxiety and depression, reduces the unpleasantness of opioid withdrawal and attenuates opioid induced hyperalgesia.

Patients who are on buprenorphine for chronic pain may have higher doses than patients using for substance use disorder.

Historically consensus was to discontinue suboxone five days prior to surgery. This method was never scientifically evaluated and was based on pharmacology

principles. The issue with stopping early included relapse. The next preoperative consensus involved discontinuing buprenorphine one day prior to surgery and initiation of the Stamford Protocol.
Currently preoperative recommendations for patients on >12mg/day is to decrease the buprenorphine dose to 12mg or less per day. For patients currently on 12mg/day dosing or less is to continue the same dosing preoperatively and postoperatively. Patient on buprenorphine patch is to continue since it is very low dose compared to the other preparations.

Patients should have multimodal pain management; utilizing anesthesia blocks, intraoperative ketamine, lidocaine and avoid opioids which were the choice of overuse for the patient. Fentanyl can be utilized for these patients immediately postoperatively since fentanyl has a higher affinity. Then opioids may be used for pain management.

The 2019 HHS Pain Management Best Practice Report has the following recommendations.

- Buprenorphine treatment for chronic pain should be available and include third-party payment and hospital formularies availability.
- CMS and private payers to provide coverage and reimbursement for buprenorphine treatment for both opioid use disorder and chronic pain management.
- Encourage primary use of buprenorphine rather than use only after failure of standard mu agonist opioids, if clinically indicated.
- Encourage clinical trials using buprenorphine for chronic pain to better understand indication, usage and dosing.

Submitted by
Donna Sipos Cox, FNP-C, AP-PMN
and Sandra Kuefner, ANP-C

Acetaminophen, an Endocannabinoid?

Acetaminophen has been around since the late 1800s as phenacetin. In the 1950s, research determined the active metabolite was N-acetyl-para-aminophenolo (APAP). At that time, phenacetin was discontinued due to nephrotoxicity. Acetaminophen, the analgesic and antipyretic effects, historically was thought to be attributed to the inhibition of prostaglandins in the central nervous system as it lacks peripheral anti-inflammatory properties. APAP crosses the blood brain barrier and has been categorized within the NSAID family. The anti-inflammatory effect is attributed to the inhibitions of cyclo-oxygenase activity, decrease in nitric oxide synthesis and facilitation of the serotonergic system.

Acetaminophen metabolized to N-arachidonoylphenolamine (AM404) which inhibits the cellular uptake of anandamide, which is an endocannabinoid. AM404 and anadamide are reported to produce anxiolytic-like effeccts. A literature search has found a newer mechanism of APAP involving the modulation of the endogenous cannabinoid system. The endocannabinoid (eCB) system has receptors, endogenous ligands and ligand metabolic enzymes. AM404 increases tissue concentration of endocannabinoid arachidonoyl ethanolamide; an anandamide. AM404 and anadamide have been noted to exhibit antinociceptive and hypothermic effects on rodents in addition to anxiolytic effects. Anxiolytic effects can be related to the activation of cannabinoid receptor type 1.

Interestingly, some diseases are associated with clinical endocannabinoid deficiency syndrome. These range from failure to thrive, schizophrenia, migraine, multiple sclerosis, Huntington's disease, Parkinson's disease, Irritable Bowel Syndrome to motion sickness.

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Submitted by
Sandra Kuefner, ANP-C