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Role of Buprenophine in Chronic Pain Management in Covid-19

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Abstract: *The suitable Management of chronic pain COVID-19 pandemic is the most demanding process, particularly with developing evidence that COVID-19 Infection analogous to pain,muscle ache, extended neuropathic pain. This review provides the relavant management of chronic pain patients during the COVID-19 pandemic.Buprenorphine is a schedule third semisynthetic opioid analgesic show distinctive pharmacokinetic & pharmacodynamic properties, & involves vital role in chronic pain management in COVID-19.Transdermal formulation of buprenorphine provide controlled delivery for sustained analgesic effectiveness. It's matrix system permitts for slow release of baprenorphine & damage does not construct dose dumping i.e provides predictable serum buprenorphine level over a prolonged period. Also, Buprenorphine show minimal level of adverse effects compared to other opioids like morphine, fentanyl involves respiratory depression, addiction, euphoria, etc.& show good patient acceptance.*

Keywords: Transdermal Buprenorphine,COVID-19, Pain management, Safety

I. INTRODUCTION

In December 2019, the highly contagious virus disease I.e COVID - 19 was found in China.In this pandemic condition, the pain complaints of patients are expanded and often be ignored.chronic pain is defined as pain that Continue or recurs for more than 3 months.for many patient with chronic pain,although opioid treatment may be the Only show effectiveness. Buprenorphine is a potent analgesic, has been available in parentral, sublingual & transdermal forms.Buprenorphine offers number of advantages over other opioids & its physicochemical properties make it suitable candidate for administration in transdermal preparation.The transdermal buprenorphine used for Control of chronic cancer and non-cancer pain, especially where non-opioid analgesics become ineffective.The main purpose of this review is to offering clinical guidance about dosing, Safety concerns of buprenorphine and treatment strategies for chronic pain during COVID time. This article is based on previously conducted studies.

1.1 Pharmacodynamics

Buprenorphine is Judge as partial μ opioid receptor agonist with pharmacodynamic properties that results from its unique structure, & its receptor bindinding occurence. Buprenorphine is a complex lipophillic molecule which obtained from thebaine & it is made from multiple chiral centers, morphine skeleton a distinctive cyclopropyl methyl group and morphine skeleton.Thebaine is the one of the opium alkaloid obtained from poppy palaver somniferum.The Special pharmacogical properties of buprenorphine permitts for its Analgesic activity, also it has ability to reduce intensity of various Opioid-related Adverse effects like respiratory depression, misuse liability in compare to the other full mu receptor agonists oxycodone, morphine & fentanyl,etc.The buprenorphine shows therapeutic effect by interacting with 4 various Opioid like receptor (mu, d, k and opioid receptor like 1[ORI-1], which are distributed various tissues in the body.Buprenorphine has a High affinity for the mu receptor and a lower Intrinsic activity than a full agonist mu opiard receptor agonist .(Cleeland et al 1994).It observes that the mu agonist effect of buprenorphine is most important to produce its required analgesic results. The Reserve buprenorphine affects the mu receptor, le it permits to the shift from another opioid to buprenorphine. Buprenorphine have the structure & special binding position which is grant for more molecular interactions between the molecule & μ-opioid receptor, producing a very high binding affinity (low ki value) contranst with that of other opioids.Buprenorphine exhibits slower dissociation from the mu -opioid receptor compared with other opioids which may give prolonged analgesia activity & loss possibility for removal when used properly for Chronic pain.Buprenorphine interact with orphanin FQ noniceptin receptor ORL-1 in the spinal cord & the brain stem. when buprenorphine binds & activates ORL-1 in the spinal card shows the analgesic effect. ORL-1activation in the brain

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stem Stop opioid analgesic responses & show to the partial agonist property of buprenorphine. The opioid binding at mu-opioid receptor causes phosphorylation which assists the the release of G-protein subunits, inhibition of adenyl cyclase, regulation of ion channel & decreases the cAMP levels.These signalling process slow down neurotransmitter release which results in Hyperpolarisation of cell membare.In that way, it stops noniceptor activation & affording phosphorylation.But phosphorylation at specific amino acid residues on the receptor cytoplasmic domain may carry out B-arrestin recruitment. B-arrestin has connected with respiratory depression, constipation & abuse liability.Buprenorphine is unique that compared to other opioids, it stimulate sufficient G-protein signalling but restrict the B-arrestin recruitment to the receptor. Buprenophine shows lower phosphorylation at mu opioid receptor compared to full u receptor agonists.It also shows phosphorylation of amino acid, serine 375 at μ-opioid receptor, although other opioids also produce substantial phosphorylation in at additional amino acids, ie, threaping 340, 376and 379.Buprenorphine limit the B-arrestin recruitment to the receptor because absence of threonine phosphorylation, which could grant to buprenorphine potentially favourable Safety profile.

1.2 Pharmacokinetics

Buprenorphine have High potency ,low weight & High lipophilicity.Buprenorphine orally shows 1st pass metabolism, therefore its oral absorption is poor.Buccal route shows effective administration or currently the more effectual delivery system because it has highest observed non- intraverous bioavailability range compare to other routes. Sublingual route is also effective. Administration by transdermal routes has low absorption, but it is overcome by designing for various formulations. Buprenorphine shows High protein binding (ie: 96% protein bound), basically to alpha& beta- globulin and exhibits a large Volume of distribution because of its High lipophilicity, which may also permits, analgesic activity.

Metabolism

The Hepatic cytochrome P (CYP) 450 system metabolises buprenorphine to nor buprenophine by N-dealkylation of the cyclopropylmethyl group.Nor-buprenorphine is 10 times more potent than buprenorphine in causing respiratory depression effect antagonized by nalaxone(Gal 1989).According to In-Vitro studies, indicate that nor- buprenorphine show high affinity to μ,delta and k-opioid receptors low affinity for ORL-1 & preclinical studies show confirm its slight contribution to analgesia.

Excreation

The buprenorphine & its metabolites excreated 70% by biliary system & same small partion also follows elimination from urinary system. Therefore buprenorphine is suitable for the patients with renal & hepatic impairement due to this made of excretion.

Side-effects-Buprenorphine can cause nausea, vomiting, sedation, papillary constriction, delayed gastric emptying and respiratory depression. Buprenorphine at high doses can increases liver enzymes due to accumulation within mitochondria.Buprenorphine have its respiratory effects are limited, compared to morphine & fentanyl which have been shown to have no ceiling effect for analgesia but which can cause severe respirating depression apnea in high doses.

II. TRANSDERMAL PATCHES OF BUPRENORPHINE IN PAIN MANAGEMENT

The risk of respiratory depression due to with buprenorphine is low, unless used with other CNS depressants. Especially, the EU Summary of product characteristics mentions that transdermal buprenorphine show respiratory depression with a rare event, Occuring in >/ 0.01% but < 0.1%of patients.The application of the transdermal patch, buprenorphine diffuses from the patch through the skin into the circulation, show a controlled constant delivery of buprenorphine over the 7-day dosing interval.The Buprenorphine patches with 7-days application is available with flux rate of 5,10, and 20 ug/h. Anyway of the dosage level (5, 10 or 20 ug/h), the steady state concentration is reached during the it's first application & Buprenorphine concentration in plasma remain relatively constant during each subsequent 7-day patch application. When the patch is removed, plasma drug concentration decrease by approximately 50% in the first 12 hours (range 10-24 hours)after removal. The suggested sites for application are the upper outer arm, upper chest, upper back & the side of chest.It is a special interest because of its long period of action, antihyperalgesic effects & free renal involvement. It is normally started on a small dosage and gradually increasing it after 3 days. There are 2 forms of patch are available:a)The

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96 hrs Transtec and the 7 day Butrans patch both are use matrix design.Matrix design it is provides controlled delivery of buprenorphine for sustained analgesic efficacy with reduced Adverse effects.The transdermal Buprenorphine Patch can significantly enhance the extent & duration of pain relief while maximizing safety. Although oral or parental formulations of buprencaphine gives effective analgesic activity, But frequency of dosing can` increase the fluctuation of plasma buprenorphine concentration potentially results in pain relief of in more adverse effects.The extended transdermal buprenorphine delivery can increase in duration and consistency of drug exposure & analgesic effectiveness with small frequent dosing, mainly in patients with altered metabolism and pharmacokinetics. Buprenorphine transdermal formulation can Improve compliance with drug therapy.Also trasdermal patch offers advantages in treatment of pain management in patient have disability to swallowing ,already suffering from gastrointestinal disorders, or discomfort with aral dosing or impaired memory.

III. ROLE OF BUPRENOPHINE IN CHRONIC PAIN MANAGEMENT IN COVID-19

The COVID-19 pandemic has brought new problems to already struggling patients with chronic pain. Powerfully, increase in inactivity due to government lockdown & quarantine orders have resulted in deconditioning, affects patients who depend on PT or exercise programmes as part of them pain management. Immunosuppression as a result of a medication whether chronic opioid therapy or the use of oral or injectable steroids is mainly concerning during time of global pandemic. Buprenorphine use as treatment for moderate-to-severe pain & both cancer & non-cancer pain. It is also used for a wide range of painful conditions including both nociceptive and neuropathic pain. Opioid use is indicated to provide suitable analgesia should be achieved without Significant Adverse effects. Here, Buprenorphine is Highly recommended while fentanyl & morphine are not suggested due to their dependence potential & side effects. Pain is an early sign of infection, a return of infection in COVID-19. Even after recovering from the coronavirus infection, a large number of people are struggling with post-covid symptoms, like chronic muscle pain, joint pain. According to Dr. Vishal Nigam, orthopedic and spine surgean at the Moolchand Hospital," Back pain and joint pain after covid could have been the most common present in orthopaedic clinics. Almost 15 per cent patient present with joint pains or arthralgia and 45 per cent patients present with muscle pains or myalgia".this pain can be temporary or can last longer. One of the wrong steps that patients takes is to try to get back to normal routine quickly despite weakness This leads to injury rather than recovery. Mild pain associated COVID-19 symptoms treated by paracetamol & other NSAIDS. But In case of moderate to severe pain, opioids mainly Buprenorphine recommended. Because buprenorphine show minimal immunosupression compared to other opioids.It is necessary to avoid corticosteroids by the practioner, if a patient has COVID-19 Infection, although asymptomatic at the time of presentation.

IV. OTHER USES OF BUPRENORPHINE

1. Buprenorphine with the combination of naloxone used to treat opioid deperdere or addiction.
2. Buprenorphine can be used in patients suffering with impaired renal function and chronic renal insufficiency and also in haemodialysis patients in whom its pharmacokinetics are unchanged.
3. When the Buprenorphine patch is applied before surgery and left in place for several days after surgery ,it helps to control pain.

V. CONCLUSION

The unexpected issues in the field of chronic pain has brought by the COVID-19 pandemic. The COVID - 19 having a intense effect on health care & patients with Chronic pain. Improper , delayed or stopping of treatment for patients may be creates consequences with patients like Increase in pain, disability.Buprenorphine does not produce dose dumping, it is become advantage specially in elder patients (Ref. Budd 2003), because the existing diseases like diabetes, cardio-vascular & neurological diseases in the elderly raises in care of drug interactions with multiple medications.transdermal buprenorphine become charming choice for older patients which suffer with renal insufficiency, due to the safe & effectuall use in renal failure. The transdermal administration route is an advantage for long-term use in ease of handling & Increased patient compliance and cost-effectiveness of treatment.

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