Transdermal Buprenorphine Induced Respiratory Acidosis in a Post TKR Patient -A Rare Case

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Abstract

Abstract- Post-operative pain management consists of a cocktail of drugs ranging from Nsaids, Opioids and Nonopioids. Transdermal Buprenorphine patch is commonly used in pain management of post-operative cases, musculoskeletal pain, cancerous and non-tumorous conditions. Buprenorphine is safely used because of its partial intrinsic activity and slow dissociation on Mu (?) receptor causing prolonged analgesic effect with a ceiling for respiratory depression. Buprenorphine is commonly used in elderly patients and in patients with chronic renal failure. We report a probable case of buprenorphine patch induced respiratory depression and sedation leading to respiratory acidosis. Respiratory acidosis was managed symptomatically with oxygen therapy and removal of transdermal buprenorphine patch lead to the reversal of clinical condition. Awareness of this possible side effect of buprenorphine patch and unwarranted use should be avoided.

Index terms— respiratory acidosis, buprenorphine, transdermal patch, respiratory depression.

1 Introduction

pioid analgesics play a vital role in pain management. Post-operative analgesia involves a cocktail of drugs like NSAIDS, Anaesthetic blocks, Opioids and non-Opioids. Post-operative analgesia is also administered through various routes of oral, Intra-muscular, Intravenous, Epidural catheters, Anaesthetic blocks, infiltrations and latest one being the transdermal drug formulations [1]. Transdermal drug formulations provide a stable plasma drug concentration ensuring long lasting and adequate pain relief. These formulations are long acting, non-invasive, reduce morbidity and increased quality of life in patients [2].

Buprenorphine is a semi-synthetic derivative of the baine with a reactive alkaloid of morphine in it. It has a molecular weight of 467 and chemically an opioid because of the inclusion of a C-7 side chain containing a t-butyl group.

Pharmacological effects of buprenorphine are brought about by the binding of the molecule with µ (Mu), k (Kappa) and ? (Delta) receptors. [3]. Antagonist action on k and delta receptors shows less sedation, spinal analgesia and psychomimmetic effects than morphine or fentanyl [4]. Pharmacokinetic profile of buprenorphine is lipophilic and exhibits multiphasic clearance. It is highly protein bound mostly to alpha-globulin and betaglobulin fractions. Since most drugs bind to albumin there is no competition for binding proteins with less drug interactions. Oral Buprenorphine has low bioavailability of 15%. Buprenorphine has extensive first pass metabolism in GI mucosa and liver, it is conjugated with glucuronic acid and metabolised by CYP3A4 into buprenorphine and nor-buprenorphine. Nor-Buprenorphine which exerts a week analgesic action of minimal significance. End stage renal failure doesn't affect the excretion of drug [5].

Transdermal delivery systems which comes in various dosages and company brands. They have many advantages which primarily includes non-invasive administration and rate controlled delivery of drug [6]. They maintain a steady state of plasma concentration of drug. They have good patient tolerability and efficacy, commonly used in chronic pain states as cancer, noncancerous conditions, chronic musculoskeletal pain conditions

like osteoarthritis knee and low back ache. Clinical studies suggest that transdermal patch has increased the odds of more than 10 in functional improvement after buprenorphine patch in chronic musculoskeletal pain scenario. These transdermal systems have been designed to overcome the pharmacokinetic dis-advantages of oral and parenteral administration of drug which include poor gastrointestinal absorption, first pass metabolism and low bio-availability.

The increased analgesic potency of buprenorphine, lipophilic nature, low molecular weight and low addictive potential makes it an ideal drug of choice through transdermal route in management of O post-operative analgesia [7]. Transdermal buprenorphine doesn't have immunosuppressant effect at therapeutic analgesic doses unlike morphine and fentanyl.

Transdermal buprenorphine patches are advocated in the elderly population by the American Geriatric society for chronic pain conditions [8]. Society suggests buprenorphine patches as a first line management in chronic pain conditions followed by NSAIDS only when acute exacerbations are present. Buprenorphine can be used in renal failure and dose adjustment is not needed [9].

Transdermal patches use matrix technology which homogenously incorporates the drug in a solid matrix patch when applied to the skin and remained effective for a minimum duration of 72 hours to seven days [10].

Common side effects of transdermal buprenorphine are nausea, vomiting and less incidence of constipation compared to other opioids [11]. Respiratory depression is a potential complication of opioids which commonly includes Morphine, Methadone, hydromorphone, oxycodone and transdermal fentanyl [12]. Buprenorphine since having partial Mu receptor agonist activity, respiratory depression can occur. Respiratory depression due to buprenorphineis a rare complication which will have a slow onset and a longer duration compared to full Mu agonists like morphine, hence reversal with naloxone is difficult and also requires higher doses of naloxone for reversal. Buprenorphine has a ceiling effect or a bell shaped curve with regards to respiratory depression and analgesia at doses >1mg/kg and 0.1mg/kg. Ceiling effect on respiratory depression is not dependent doses used for analgesic action and recent literature suggests a linear dose response without any evidence of a ceiling effect in the therapeutic drug window. Ceiling effect provides safety profile for the drug which is not present with morphine or fentanyl. Reports of fatal respiratory depression have been rarely reported in literature mostly occurring in drug addicts [13].

In case of respiratory depression, management is to discontinue the drug delivery of buprenorphine, give oxygen mask, IV naloxone 2 mg stat over 90sec, commence naloxone 4mg/hour intravenously, continue monitoring till 90 min, monitor patient for next 24 hour and restart dose when the patient condition is satisfactory at a reduced dose [14].

Pharmaco -kinetically buprenorphine is metabolised in liver and its metabolism is not affected in patients with renal failure. The major metabolite being nor-buprenorphine which has low potency and low affinity of this metabolite to receptors and is less likely to cause toxicity in renal failure [15].

2 II.

3 Case Report

We describe a case of a 78 year old female with a weight of 72 kg and 146 cm in height. The patient was posted for elective right total knee replacement. Preoperative her blood parameters were Hb-12.3 g/dl, urea-32 and creatinine-1.1. She was a known hypertensive on Tab. Calcigard 10 mg OD with ASA grade 2. Her spirometry report was in normal range.

She was operated for right total knee replacement and intra-operative period was uneventful. On post-operative day-1, she was shifted to general wing from surgical ICU and was put on buprenorphine patch of strength 10 µg/h for pain management near the incision site after dressing the wound. On POD-2, she became drowsy and was talking irrelevantly. Her saturation in room air was 84%. Her blood parameters showed sodium-138mmol/l and potassium-4.6mmol/l. Arterial Blood gas analysis from the femoral artery showed elevated PCo2 suggesting respiratory acidosis due to sedation effect and her respiratory inhalation wasn't strong. Patient was started on oxygen mask with 4L of oxygen and serial values of Arterial blood gas analysis were measured. The buprenorphine patch also was removed in view of suspicion of buprenorphine induced respiratory depression and respiratory acidosis.

The patient had a back ground of chronic renal failure with elevated creatinine with a value of 1.1-1.3 which could have added a metabolic component to the respiratory acidosis. Patient improved after the removal of patch. After two days, patient was mobilised and started on chest physiotherapy with deep breathing exercises. She was shifted to ward and discharged on day 5. The serial blood gas analysis values are showed in Table 1.

4 Discussion

Transdermal buprenorphine patches are commonly used in the post-operative period for pain management along with other analgesics [8]. In our patient, in view of her pre-operative elevated borderline creatinine values, she was only put on paracetamol injection through intra-venous route for pain. Her pain wasn't relieved and started on Buprenorphine patch. Buprenorphine being a semi-synthetic analogue of morphine have a partial mu receptor action causing analgesia with a ceiling effect for respiratory depression [9]. Transdermal buprenorphine patch causing respiratory depression in an adult is rarely reported in English literature.

We report a probable case of buprenorphine patch induced sedation and mild respiratory depression with a background of underlying chronic renal pathology. Old age with pain adding as a catalyst to the base line situation leading to respiratory acidosis and falling oxygen saturation values. The patient returned back to her physiological state after starting on oxygen, IV fluids, Input-output monitoring and removal of buprenorphine patch.

Awareness of such a pharmacological side effect of buprenorphine patch when used as a modality of pain management in elderly population. Buprenorphine patch induced respiratory depression has been reported in paediatric age but not in adults. We want to emphasize in our report, the careful use of morphine or buprenorphine patches in elderly population to avoid complications.

1

Parameter	Arterial Blood gas values at Admission(ICU)	Arterial Blood Gas Values at discharge(Ward)	Normal Values
PH	7.19	7.30	7.350-7.450
PCO2	55	40	32.0-48.0 mmHg
PO2	88	95	83.0-108 mmHg
HCO3-	20.9	24.3	21.0-28.0mmol/L
SPO2	84%	98%	98%

Figure 1: Table 1 :

.1 Consent: Obtained

Conflict of interest: None Acknowledgements: None

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