Case Report

Neurological Fetal Damage after Administration of Nalbuphine Hydrochloride in Antenatal Period: A case report

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ABSTRACT:

Introduction: *Nalbuphine Hydrochloride (NB.HCL) is a synthetic agonist and antagonist opioid analgesic available for use in severe pain management and during labor & delivery. It can also be used as a supplement to balanced analgesic for preoperative and postoperative analgesia. Though it is safe & potent analgesic but sometimes it causes respiratory depression at birth, fetal bradycardia, apnea, cyanosis, hypotonia, neurological damage and even death. NB.HCI should be used in antenatal period and during labor & delivery, only if clearly indicated and the potential benefit outweighs the risk to the infant. Newborns should be monitored for respiratory depression, apnea, bradycardia and arrhythmia. A case presentation is given of a persistent neurological damage of newborn appearing after NB. HCI administration in the antepartum period.* ***Methods:*** *This case report describes the neurological damage of fetus after several administrations of NB.HCL in the antenatal period.* ***Conclusion:*** *As fetal bradycardia occurs following the use of NB.HCI in antepartum period, so when it is used to pregnant mother in antenatal period, all the measures for monitoring and resuscitation must be available including attendance of pediatrician or neonatologist to reduce development of fetal neuronal damage and subsequent morbidity.*

Key words: *Nalbuphine HCl, pregnancy, antepartum hemorrhage, neonate, caesarean section*

(The Planet 2019; 3(2): 53-56)

INTRODUCTION:

Nalbuphine Hydrochloride (NB.HCL) is a synthetic agonist and antagonist opioid analgesic available for use in severe pain management and during labor & delivery. Other opioids' like morphine, pethidine has potent analgesic effect but causes severe

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respiratory depression. NB.HCI can also be used as a supplement to balanced analgesic for preoperative and postoperative analgesia.[1,2] Though it is safe & potent analgesic but sometimes it causes respiratory depression at birth, fetal bradycardia, apnea, cyanosis hypotonia, neurological damage and death. NB.HCI should be used in antenatal period and during labor & delivery only if clearly indicated and only if the potential benefit outweighs the risk to the infant. Newborns should be monitored for respiratory depression, apnea, bradycardia and arrhythmia if NB.HCI has been used.[3]

CASE HISTORY:

A 22 years old, primi 30 week's pregnancy admitted to UHC, Tanore, Rajshahi with the complaints of upper abdominal pain, radiating to right hypochondriac region. Patient was conservatively treated with anti-spasmodics and antiulcerants, but pain did not subside. So patient was referred to RMCH but patient got admitted in a private hospital and was diagnosed as 31 week's pregnancy with calculus cholecystitis. In spite of conservative treatment, patient's pain was not subsided & then she was treated by Inj. Nalbun-2 (inj. Nalbuphine HCI) & got it for several times (about 5 injections at different days) for her pain management. At that time patient developed tachycardia, raised BP, Semi consciousness. Fetus developed bradycardia with less fetal movement. At her 34 weeks' pregnancy she was admitted at UHC, Tanore, under my supervision. On physical examination her Pulse was 80b/m, BP-110/70mm Hg, patient's Resp. rate- 16-18 beats/m, no edema but with mild anemia. **P/A**: FH:34wks. FHS: 152 beats/m. Her Hb% was 11.2gm/dl, Urine for R/M/E was normal, S. creatinine:0.8 mg/dl, RBS-4.5 m. mol./L. She did not have any significant respiratory and cardiovascular abnormality, normal body temp. She was conscious & no neurological abnormality at presentation.

But unfortunately she developed premature rupture of membrane (PROM) for 14 hours, but labor did not progress simultaneously, fetal tachycardia developed and excess watery discharge continued. So LUCS was done under SAB, and she gave birth to a male baby weighing 2000 gram. Baby did not cry after birth. APGAR score was 3 at 01minute & 5 at 5 minutes and primitive reflexes were poor. Baby was managed by a physician and was referred to SCANU of Naogaon Medical College, where he was treated accordingly. Baby developed seizure due to perinatal asphyxia and was managed appropriately. Ultrasonogram of brain showed cortical atrophy with dilatation of ventricles. At follow up of the baby at three months, head control not yet achieved, and at six months' baby had motor delay and also developed seizure disorder which is under medication of a pediatrician.

DISCUSSION:

For pain management, Opioid analgesics like morphine is an active alkaloid excreted from the opium poppy plant in German in 1804 by Friedrick Serturner and pethidine was discovered in 1937.[4] Both the drugs have excellent pain killing effect but were abuse & adverse effect like respiratory depression &

anti cholinergic effect. NB.HCI is a potent analgesic and essentially equivalent to that of morphine used in pregnancy (other than labor). Severe fetal bradycardia has been reported when NB.HCI was administered during labor, Naloxone may reverse this effect.[5]

NB.HCI was first synthesized in 1965 and was introduced for medical use in the united states in 1979. In the search for opioid analgesic with less abuse potential than pure morphine. NB.HCI is a mixed agonist/antagonist opioid modulator. (Morphine--moderate efficacy partial agonist/antagonist of in opioid receptor).[5,6] NB.HCI is used in the severe pain management during labor & delivery as a supplement to balanced anesthesia for preoperative & postoperative analgesia. It has potent & safe analgesic effect but exerts some adverse effect like severe respiratory distress, bradycardia, apnea, cyanosis, hypotension, neurological fetal damage if it used in the antepartum period. Prolonged use in antepartum period leads to NAS (Neonatal abstinence syndrome or NOWS (Neonatal opioid withdrawal syndrome) presented as irritability, hyperactivity, increased startle reflex and abnormal sleep pattern, high pitch cry, tremor, vomiting, diarrhea and failure to gain weight.[6,7,8]

This is the job of pediatrician who was unware of maternal group assignment in this case, more over Naloxone was not available at the time of delivery. The APGAR score at one minute 3 and five minutes 5 after delivery. Primitive reflex poor even after resuscitation as per HBB protocol. Umbilical venous or umbilical arterial blood samples were not taken for measurement of blood gases due to lack of facilities,

So which factor triggering the neurological damage of fetus is not clear. The possibilities may be that, it was due to bradycardia, arrhythmia, apnea, cyanosis and eventually prolonged hypoxia to the brain due to NB.HCL use in antepartum period. Another possibility is preterm labor. Infections like CMV & Toxoplasma, Syphilis were excluded by TORCH screen and VDRL of the mother.

CONCLUSION:

As fetal bradycardia occurs following the use of NB.HCI in antepartum period and before Caesarean section, reduces maternal stress response related to intubation of surgery but decrease the APGAR score at one minute after delivery. So when NB.HCI is used to pregnant mother in antenatal period, all the measures for monitoring and resuscitation must be available including attendance of pediatrician.

REFERENCE:

1. Podlas J, Breland BB. Patients controlled analgesia with Nalbuphine during labor. Obstet Gynacol. 1987; 70:202-4.
2. Errick JK, Hee RC. Nalbuphine: A preliminary review of its pharmacological properties and therapeutic efficacy. Drugs. 1983; 226:191-211.
3. Littleford J, Effects on the fetus and newborn of maternal analgesia and anesthesia: A review. Can J Anesth. 2004; 51(6):586-609.

4. Schmitz R. Friedrich Wilhelm Sertürner and the discovery of morphine. Pharm Hist. 1985; 27(2):61-74.
5. Amin SM, Amr YM, Fathy SM, Alzeftawy AE. Maternal and Neonatal effects of Nalbuphine given immediately before induction of general anesthesia for elective caesarean section. Saudi Journal of Anesthesia. 2011;5(4):371-75.
6. Amin OAI, Ibrahem MA, Salem DAE. Nalbuphine versus midazolam as an adjuvant to intrathecal Bupivacaine for postoperative analgesia in patients undergoing caesarean section. J Pain Res. 2020; 13:1369-76.
7. Nicolle E. Devillier P, Delanoy B, Durand C, Bessard G. Therapeutic monitoring of Nalbuphine: Transplacental transfer and estimated pharmacokinetics in the neonate. Eur. J. Clinical pharmacology. 1996; 49:485-89.
8. Dadabhoy ZP, Tapia DP, Zsigmond EK. Transplacental transfer of Nalbuphine in patients undergoing caesarean section. Anesth. Analg. 1985; 64: 205-10.