Psychiatria Danubina, 2018; Vol. 30, No. 2, pp 230-232 *Letter to Editor*
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BUPRENORPHINE/NALOXONE IN THE TREATMENT OF OPIATE DEPENDENCY DURING UNINTENTIONAL PREGNANCIES – BOSNIA-HERZEGOVINA EXPERIENCES

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Dear Editor,

Despite the broader use of new opiate dependence treatment, the maternal and neonatal outcomes following buprenorphine/naloxone (Bup+Nal) exposure during pregnancy have not been documented enough. There are no controlled data in human pregnancy US FDA pregnancy category C: Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. Use is contraindicated in UK and US: This drug should be used during pregnancy only if the benefit outweighs the risk to the fetus. US FDA pregnancy category C Comments: Prolonged use of opiates during pregnancy can result in physical dependence in the neonate; women should be advised of the risk of neonatal abstinence syndrome (NAS) and ensure that appropriate treatment will be available. Infants born of mothers receiving this drug during pregnancy should be closely monitored for symptoms of withdrawal (e.g., hypertonia, neonatal tremor, neonatal agitation, myoclonus, apnea, and bradycardia); onset has ranged from 1 to 8 days following birth with most cases occurring during day 1 (Anonymous 2018).

There are limited prevalence data on substance abuse in pregnant women in Canada (Poon et al. 2014).

While little information exists about the incidence of treatment of opiate addiction in pregnant women, more than 550 000 women were admitted to US treatment programs in 2007, with roughly 4% being pregnant at the time of admission. In 8.6% of these pregnant women, opiats were the primary substance of abuse at admission (TEDS 2018). This makes opiate use and dependence in pregnancy an important health problem.

Although it would be ideal to abstain from taking opiates throughout the course of pregnancy, most opiate-dependent women are unable to do so even under close medical supervision and are at risk of relapse. The pressure from rapid detoxification might cause maternal stress, withdrawal, and fetal stress, which are associated with poor fetal growth, preterm delivery, and fetal death (Dashe et al. 1998).

Abrupt opiate withdrawal in pregnancy might also increase the likelihood of abortion, premature labor, miscarriage, and stillbirth (Kaltenbach et al. 1998).

The current criterion standard for managing opiate dependence in pregnant women is methadone maintenance (Wong et al. 2011).

The NAS associated with buprenorphine generally appears within 12-48 h, peaks at approximately 72-96 h, and lasts for 120-168 h. These results appear similar to or less than that observed following in uterus exposure to methadone. From a review of the literature, buprenorphine appears to be safe and effective in both mother and infant with an NAS that may differ from methadone both qualitatively and quantitatively (Johnson et al. 2003).

Bosnia-Herzegovina Experiences

We aimed to present retrospective chart review identified six opiate-dependent pregnant women treated with the Bup+Nal film product, so this is the first report about pregnant women treated with the Suboxone (Bup+Nal) film product from Balkan region.

Seven maternal outcome measures - weight gain, fetal presentation at delivery, Cesarean delivery, analgesia during delivery, urine drug screening results at delivery, number of days of maternal hospital stay, and began breastfeeding following delivery-and eleven neonatal outcome measures-gestational age at delivery, Apgar scores, head circumference, length, and weight at birth, and length of hospital stay-were extracted from medical records.

The opiate substitution therapy (OST) with Bup+Nal at the Psychiatry Department of University Clinical Center (UCC) Tuzla in the period 29 July 2009 to 1 August 2016 was used as treatment for 278 opiate addicts with average age 29.6±5.8, out of that number 258 (92.8%) were male of average age 29.7±5.9 and 20 (7.2%) female opiate addicts with average age 28.1±4.0, and there was no statistically significant difference in age (p=0.242) (Hasanović et al. 2017). From 20 female patients six (30%) became pregnant while in OST.

Three of them followed warning about possible embriotoxicity of Naloxone before they started OST and signed informed consent (Ivana, Sanela, Leona), due to that they left OST voluntarily after became pregnant and stayed “drug free” up today.

On the other side three of them (D.R. x 3 pregnancies, D.M x2 pregnancies and H.T. x 1 pregnancy) stayed in the OST program to the end of their pregnancies and delivered newborns.

D.R., (born 1987): mother who delivered three girls during OST with Bup+Nal, previously, she never had any abortion, and during OST (Bup+Nal) menstrual cycles were regular. When she misused heroin, she experienced breaks of the menstrual cycles and up to 8 months.

Patient reported the first pregnancy 2011 in the fifth month of pregnancy, she was faced with the consequences of too late reporting of pregnancy and she was suggested to remove the OST (Bup+Nal) and translating the alternative (buprenorphine monotherapy or methadon).

She refused any possible thought of interrupting OST (Bup+Nal) and signed to continue treatment on her personal responsibility. Her mother who is partner in the therapy (Hasanović et al. 2012) signed too, that she agreed with her daughter. The daily dose was reduced from 8 mg to 4 mg.

The same behavior of patient and her mother repeated in the following two pregnancies more. She reported pregnancy late, in fifth month of it's duration and insisted to continue with the OST (Bup+Nal), but she did not want to reduce dose, the dose remained 8 mg, as during period when she was not pregnant.

The first 2011 and the second 2012 pregnancy as well as delivery of newborns realized regularly. Babies were born at term, weighed 2650 gr/48cm first and 3600 gr/56 cm second.

The third pregnancy 2013 was complicated by bleeding because the patient caught a cold several days after the exposure to cold during her working in the field. Due to the threat of miscarriage, birth completed operational "Caesarean section" for precedence breech. The baby was born prematurely in 7 months, weight 1.050 gr, briefly stayed in the incubator. Today this girl is properly developing like her sisters.

During all three pregnancies the patient did not have problems with blood pressure or any other complications. During each pregnancy she gained contemporary10 kg of body mass.

The patient was IVU and Virus Hepatitis „C" positive, so she was successfully treated with interferon therapy.

There were no any sign of Newborn Abstinence Syndrom (NAS). Patient nursed the first baby 40 days, lactation ceased spontaneously, the babies of the second and third pregnancy were not breastfed.

D.M. born 1985 she was heroin addict for 6 years, before started OST program (Bup+Nal). During the OST became pregnant. It was her third pregnancy. From the previous two pregnancies when she was not on the OST, she delivered a son and a girl who were 11 and six years. The third child, a son M. she delivered in her second marriage with our OST (Bup+Nal) patient who is also a former heroin addict with criminal behavior who served in prison before they were married. Before they married he had one son from his first marriage.

She has no Hepatitis B nor C. She delivered the baby regularly, it lasted 2 hours. The boy was born 10 days later than the term, weighed 3600 gr. There was no signs of newborn abstinence syndrome (NAS). Daily dose Bup+Nal during childbirth was; 6 mg (and now she is at the same dose).

OST with Bup+Nal started with 10 mg, but the dose gradually decreased 8mg than 6 mg nowadays according the prescribed Doctrine of Health Care Institution and Cantonal Ministry of Health. The boy developed normally, he began to walk, now weighs about 14 kg. The gynecologist advised her that the baby can not breastfeed and she did not.

The second OST pregnancy with the same (second) husband (her fourth pregnancy) was hiden during the whole period of its' duration. Three days before childbirth she visited us for regular OST control, as always accompanied with her mother who is partner in the treatment. She was wearing loose clothing; there were no any sign which could reflect that she was pregnant. The knowledge that she gave birth of this baby have been given to us by phone call from doctors of the Clinic of Gynecology and Obstetrics.

She stated: The fear that she would be excluded from the OST program, was the reason to hide this pregnancy.

H.T. born 1987 is our third pregnant patient on the OST with Bup+Nal. She is five years in OST with Bup+Nal. She was married for a heroin addict who, was in prison, when he went out the prison, he forced her to misuse heroin again. She divorced, than married again but in Germany. She decided to continue with OST, became pregnant and decided to keep pregnancy and to continue with OST.

She delivered healthy son in the beginning of 2016, without any complication for her or baby during pregnancy, during childbirth and after delivering baby.

To conclude, our findings suggest no obvious significant adverse maternal or neonatal outcomes related to the use of buprenorphine+naloxone for the treatment of opiate dependence during pregnancy.

Limitation of our report is a small number of subjects we included in.

Acknowledgements: None.

Conflict of interest: None to declare.

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