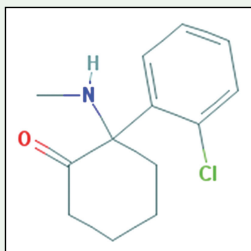


Ketamine Use in Pregnancy: Potential Life Long Effects on the Unborn Fetus

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BACKGROUND

The adverse effects on the newborn infant of the misuse of substances such as methadone during pregnancy are well documented over recent decades¹. Whilst the dangers of ketamine use are well described² very little is known about the potential effects on the fetus, infant and developing child.



AIMS

We report 3 recent cases of mother infant dyads with a history of maternal ketamine use and review the available literature on the subject.

METHODS

Retrospective case note review and literature search.

CLINICAL CASES

Baby B was born at term with a birthweight of 2.7kg (2nd centile). He was well at birth and did not require resuscitation. Mum had reported both cocaine and ketamine use during pregnancy and was under the care of the local addiction unit and liaison midwife. Baby B was observed for 3 days following delivery and was discharged home with mum. Prior to discharge he had a normal cranial ultrasound scan (routine practice for infants exposed to cocaine in utero).

He failed to attend the Neonatal Abstinence Syndrome (NAS) follow up clinic but is reported to be progressing well by his local health visitor.

Baby J was born at term with a birthweight of 3.1kg (9th-25th centile) following an uncomplicated delivery. Mum reported snorting 8g of ketamine per day and was known to have a somewhat chaotic lifestyle. Her previous children were in care and she had sporadic antenatal attendance with the liaison midwife. Urine screening did not demonstrate any other illicit drug use. Baby J was observed on the neonatal unit for 5 days prior to discharge to foster care. Baby J continues to reside in foster care and short term reports indicate she is progressing well.

Babies W1 and W2, a set of twins, were delivered at term with birthweights of 2.5kg and 2.6kg (0.4th-2nd centile). Mum reported ketamine use during the first 6 months of pregnancy but was abstinent from then on with no additional illicit drug use (proven by clear urine screening). She had a history of chronic urinary tract infection secondary to ketamine use. Mum engaged well in antenatal care with the liaison midwife throughout pregnancy. The twins were observed for 5 days and showed no signs of NAS, they were discharged with mother and have not yet been seen for follow up.

DISCUSSION

Ketamine, an anaesthetic drug has evolved as a popular drug of abuse. There is a paucity of research on the effects of maternal ketamine use during pregnancy and the consequences for the infant both in the neonatal period and in the long term.

Animal studies have shown that ketamine interferes with the critical developmental processes occurring during the brain growth spurt³. This period of peak vulnerability to ketamine encompasses the interval from the third trimester to the first several years after birth⁴. This detrimental effect of ketamine is related to its ability to induce acute patho-morphological changes in brain neurons by triggering widespread neuronal brain apoptosis⁵. Research using the rat model has shown that a combination of cocaine and ketamine reduced fetal birth weight but not ketamine alone³. These studies raise the possibility of ketamine use in pregnant women causing long term neurodevelopmental consequences in their infants.

In addition to the neurodevelopmental effects, chronic ketamine use in adults is known to cause ulcerative cystitis² and papillary necrosis⁶, these urological effects have not been studied in the ketamine exposed neonatal population.

One observational report has suggested that *in utero* ketamine exposure can cause growth retardation, hypotonia and poor reflexes⁷. However, these conclusions were based on a single case report.

None of the infants in our series demonstrated any acute effects which could be directly ascribable to ketamine, although 3 of the 4 were small for gestational age. None of the infants showed any signs of NAS, this finding is not surprising given ketamine is not known to be physically addictive. Other illicit substances used during pregnancy, known not to be physically addictive (namely cocaine) have been described to worsen NAS in infants with opiate withdrawal⁸. Given that ketamine and cocaine together have been shown to have detrimental brain effects in the animal model, ketamine may have the potential to have similar detrimental effects on severity of NAS.

Given the animal research and clinical adult evidence close long term follow up of our series, and any subsequent ketamine exposed infants is essential.

CONCLUSION

A recent review on behalf of the Independent Scientific Committee on Drugs (ISCD)² highlighted the increasing use of ketamine as a recreational drug, many of these users will be women of child bearing age. Whilst animal and long term adult studies have clearly demonstrated the worrying detrimental effects of ketamine use, there is a significant lack of evidence on the effects in the neonatal and infant population. A thorough review of the literature revealed only a single case report⁶.

Further research focussing on both short and long term effects of ketamine use on the fetus and the neonate is urgently required. Of particular concern are both the potential bladder and more worryingly the neurocognitive effects of chronic ketamine exposure on the developing fetus.

The ICSD review clearly highlights the need for prevention and harm minimisation campaigns, these campaigns must include information about potential harm to the unborn fetus and in the long term.

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