

# Current status and challenges in the development and regulation of gene therapy in Japan

Uchida, E.<sup>1</sup>

Department of Psychiatry, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaakob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia<sup>1</sup>



**ABSTRACT**— Failure in achieving abstinence in methamphetamine dependence population is a common scenario. The use of methamphetamine in pregnancy however, was not so often brought to attention. This report highlights the challenges and issues encountered in the management of a pregnant lady with the problem of methamphetamine dependence, who presented with psychosis. Among the areas outlined were issues in commencing treatment for methamphetamine psychosis, presence of psychosocial conditions that impeded total abstinence and the risks of methamphetamine use during pregnancy.

**KEYWORDS:** Methamphetamine, Dependence, Pregnancy, Psychosis

## 1. INTRODUCTION

Data from the Malaysian National Drugs Agency December 2013 Report, showed that among 7864 drug users, 632 were abusing Amphetamine Type Stimulant. Rates of admission due to Methamphetamine abuse in pregnancy are higher compared with men and non- pregnant lady in the United States [1]. A number of issues may complicate the management of pregnant women who abused methamphetamine such as the low motivation for them to come forward voluntarily for treatment, the high rates of fetal and maternal complications due to methamphetamine abuse [2], [3] and the inavailability of effective treatment for methamphetamine dependence.

## 2. CASE REPORT

NZ, a 32-year-old Malay lady was brought to the Emergency Department by her boyfriend for further management of psychosis. She was noted to be talking to herself irrelevantly and neglecting her hygiene for a week. Further examination and investigation showed pregnancy of 32 weeks, and positive urine drug test for Methamphetamine. NZ was admitted to the psychiatric ward and referral was made to the Obstetrics and Gynaecology (O & G) team. She attributed the delay in pregnancy checkup due to being unaware of her unplanned pregnancy. Patient's drug use started since adolescent, with glue sniffing and later converted to methamphetamine abuse. She experienced desirable effects such as euphoria, reduced appetite, increased energy and less need for sleep after she took methamphetamine, which would last from hours to days. She also admitted of feeling anxious, sleepy, with increased appetite and fatiguability if she did not use the drug for a few days. Over the years there was a need to increase the methamphetamine intake to achieve similar desirable effects. NZ previously worked as a sexual worker before working together with her boyfriend packing and distributing methamphetamine which also led to a marked increase in methamphetamine usage and a luxurious income. Her boyfriend was her sole support after being estranged from her family for many years. During her admission to the psychiatric ward, the patient was commenced on Tablet Olanzapine 5mg daily and an intensive psychoeducation and counseling regarding drug use in pregnancy was given which include prevention of risk behaviors such as protected sexual intercourse, avoiding intravenous drug use and the need for proper contraception. A detailed ultrasound scan was also done by the O & G team which yielded normal findings. Referral to the social welfare officer to help locate the patient's family members for further pregnancy support was also initiated. NZ's psychotic symptoms markedly improved after one

week. She was discharged after 12 days of admission under the care of her family. 2 weeks after discharged, NZ was brought back to the Emergency Department after a hotel staff found her in a very psychotic state just after delivering her baby in a hotel room. She was at the 36 weeks' period of amenorrhea.

### 3. DISCUSSION

Till date there has been no approved medication as treatment for methamphetamine dependence. Current management for the problem mainly relies on outpatient behavioral therapies and contingency management which has shown some short term benefit [4] but not for long term [5], [6]. The search for the ideal long term treatment that can reduce methamphetamine craving for both short term and long term, as well as medication that improve the cognitive deterioration due to chronic methamphetamine abuse is still ongoing. Most methamphetamine dependence cases remain undetected and only in a few cases the individual comes forward voluntarily to seek treatment. As for NZ, the sole reason why she was brought by her partner for admission was to manage her uncontrolled psychosis; not for seeking treatment for her methamphetamine use problem. Her antenatal care was markedly delayed to the third trimester, thus increasing the risk of maternal and fetal morbidity. It is often a challenge to delineate a primary psychotic episode from a psychotic experience induced by methamphetamine [7] mainly because of the overlapping symptoms presentation which may include delusions of persecution, auditory hallucinations and disorganized thoughts. The picture is further complicated by the fact that the symptoms of psychosis in methamphetamine dependence patient can still be present up to six months of drug abstinence. Pregnancy itself puts these substance abusing women in a great risk; hence intrapartum psychosis as in NZ was a major issue in her management. Data pertaining to the best treatment approach for methamphetamine induced psychosis is still lacking. However, antipsychotics have been shown to be effective in reducing symptoms of psychosis caused by methamphetamine [8], [9] and has also been used for acute management of methamphetamine psychosis in emergency departments [10]. Although there is little evidence on atypical antipsychotic associated with increased risk of teratogenicity, the risks and benefits of starting any antipsychotic in pregnancy need to be properly judged. All antipsychotics fall under Category C of the FDA Pregnancy Categories, without adequate and well controlled studies in humans. Among the outcomes noted on Olanzapine exposed pregnancy are higher rate of placental passage, spontaneous abortion, prematurity and still birth [11]. Olanzapine [12]. Risperidone [13] and Quetiapine [14] have shown good responses for methamphetamine induced psychosis.<sup>15</sup> However, the duration of treatment required with antipsychotic in methamphetamine induce psychosis remains controversial. In this patient, Tablet Olanzapine was commenced after careful evaluation on the marked psychosis she was having and the risk of psychosis towards the pregnancy. Exposure to methamphetamine in pregnancy itself is also associated with a number of adverse fetal and neonatal outcomes, including preterm birth, low birth weight, small for gestational age, cardiovascular and musculoskeletal anomalies. This is where a combined approach with the O & G team for psychoeducation towards prevention of risk behavior related to drug use, the importance of regular antenatal check-up and engagement with a suitable contraceptive plan will optimize patient's care. Despite NZ's awareness of the numerous consequences, getting her towards reducing her drug use is a main challenge in the management. Even after being given an intensive counseling during her inpatient stay, she resorted back to drug use on the same day she was discharged from the ward. One of the factors that leads to the poor treatment engagement for methamphetamine abusers is craving and cue induced craving. Craving is described as an intense urge to use drug, even after a period of abstinence, triggered by drug related environmental cues. Cue induced craving may increase in the first 3 months of abstinence from methamphetamine<sup>16</sup> hence making it more difficult for patients to achieve abstinence. The presence of NZ's substance abusing partner and the conducive environment for continued drug use as she packed the drug continued to be persistent cues that impede abstinence from the drug.

#### 4. REFERENCES

- [1] Terplan M, Smith E J, Kozloski M J, & Pollack H A. Methamphetamine use among pregnant women. *Obstet & Gynecol* 2009;113(6): 1285-1291.
- [2] Smith L M, LaGasse L L, Derauf C, Grant P, Shah R, Arria, A & Lester B. M. Prenatal methamphetamine use and neonatal neurobehavioral outcome. *Neurotoxicol Teratol* 2008; 30(1): 20-28.
- [3] Eriksson M, Larsson G, Winbladh B, & Zetterström R. The influence of amphetamine addiction on pregnancy and the newborn infant. *Acta Paediatr* 1978; 67(1): 95-99.
- [4] Shoptaw S, Reback C J, Peck J A, Yang X, Rotheram-Fuller E, Larkins S & Hucks-Ortiz C. Behavioral treatment approaches for methamphetamine dependence and HIV-related sexual risk behaviors among urban gay and bisexual men. *Drug Alcohol Depend* 2005; 78(2):125-134.
- [5] Rawson R A, Marinelli-Casey P, Anglin M D, Dickow A, Frazier Y, Gallagher C & Zweben J. A multi-site comparison of psychosocial approaches for the treatment of methamphetamine dependence. *Addiction* 2004; 99(6): 708-717.
- [6] Roll J M, Petry N M, Stitzer M L, Brecht M L, Peirce J M, McCann M J & Kellogg S. Contingency management for the treatment of methamphetamine use disorders. *Am J Psychiatry* 2006; 163(11)
- [7] Srisurapanont M, Arunpongpaisal S, Wada K, Marsden J, Ali R & Kongsakon R. Comparisons of methamphetamine psychotic and schizophrenic symptoms: a differential item functioning analysis. *Prog Neuro-Psychoph* 2011; 35(4): 959-964.
- [8] Leelahanaj T, Kongsakon R, & Netrakom P. A 4-week, double-blind comparison of olanzapine with haloperidol in the treatment of amphetamine psychosis. *J Med Assoc Thai* 2005; 88: S43-52.
- [9] Srisurapanont M, Jarusuraisin N & Kittirattanapaiboon P. Treatment for amphetamine psychosis. *Cochrane Lib* 2001.
- [10] McIver C, McGregor C, Baigent M, Spain D, Newcombe D, Ali R. Guidelines for the medical management of patients with methamphetamine-induced psychosis. South Australia: Drug and Alcohol Services; 2006.
- [11] Brunner E, Falk D M, Jones M, Dey D K & Shatapathy C C. Olanzapine in pregnancy and breastfeeding: a review of data from global safety surveillance. *BMC Pharmacol Toxicol* 2013; 14, 38.
- [12] Misra L K, Kofoed L, Oesterheld J R & Richards G A. Olanzapine treatment of methamphetamine psychosis. *J Clin Psychopharmacol* 2000; 20(3): 393-394.
- [13] Misra L & Kofoed L. Risperidone treatment of methamphetamine psychosis. *Am J Psychiatry* 1997; 154(8): 1170-1170.



This work is licensed under a Creative Commons Attribution Non-Commercial 4.0 International License.