In Utero Synthetic Cannabinoid Exposure

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ABSTRACT

Synthetic cannabinoids (SCs) are abused substances similar to cannabis (marijuana). These products are psychoactive herbal blends coated with different SC drugs. The chronic use of SCs causes addiction, withdrawal symptoms, and psychiatric symptoms, which are similar to cannabis. Different brands comprise different SCs with different amounts; therefore, it is difficult to presume the clinical effects of these illegal products. It is important for pediatricians, especially neonatologists, because of its increasing use among adolescents in the past few years; it will not be surprising to experience more and more exposed neonates and neonatal abstinence syndrome in the near future. Here we present a neonate who was exposed to SCs, which is marketed as "bonsai" in Turkey, during the whole pregnancy. We aim to warn physicians regarding the withdrawal symptoms of SCs.

Keywords: Synthetic cannabinoid, bonsai, neonatal abstinence syndrome

INTRODUCTION

Synthetic cannabinoid products (SCPs) have been increasingly used worldwide, especially among adolescents. They are marketed under different names in different countries such as "K2," "Spice," "Aroma," and "Dream." It is called as "Bonsai" in Turkey. These products are herbal blends that are coated with psychoactive ingredients. The euphoric and psychoactive effects of SCPs are not because of the herbal ingredients but result from SCs. SCPs have similar psychoactive effects to delta-9-tetrahydrocannabinol (Δ-9-THC), which is the psychoactive compound in natural cannabis (marijuana); however, the structure of the molecule is completely different. Most SCPs are more potent than Δ-9-THC. SCPs have become very popular because of its cannabis-like effects, easy accessibility, and lack of reliable detection method (1).

Here we report a neonate who was exposed to SCPs during the whole pregnancy and who exhibited withdrawal symptoms after delivery.

CASE PRESENTATION

The female neonate who was vaginally delivered at home was taken to the hospital by healthcare team. She was 38 gestation, had a birth weight of 2100 g, head circumference of 33 cm, and length of 49 cm. She was small for her gestational age. The mother called the healthcare team after delivery because she was addicted to SCPs, which is labeled as "Bonsai" in Turkey. She was using it since 3 years and continued to use it during the whole pregnancy, including the embryonic stage, along with smoking 1 pack of cigarette per day. She also reported that she smoked "bonsai" just before delivery. The baby was evaluated 4 h after delivery. She was agitated and irritable and had tremors and jitteriness, which increased by touch, light, and sound (Video 1). Blood count, blood glucose level, kidney function tests, liver and cardiac enzyme levels, and blood gas parameters were all within the normal range. The mother was an active user; therefore, the baby was fed a formula instead of breastfeeding. During follow-up, irritability, exaggerated moro reflex, jitteriness, and sinus tachycardia were the only pathological findings. Thoxoplasma, Rubella, Cytomegalovirus and Herpes Simplex virus Ig M and Ig G TORCH IgM and IgG test results, electrocardiography, and echocardiography were normal. Transfontanelle and abdominal ultrasonography did not demonstrate any pathology. On seventh day of life, jitteriness and irritability began to gradually decrease, and on the 10th day of life, the symptoms disappeared. The baby was discharged from the hospital at the end of the second week, and a written consent was taken from the parents before the discharge.

DISCUSSION

Here we report a neonate who was exposed to SCPs in utero throughout pregnancy. Addiction to SCPs among adolescents is increasing in Turkey, similar to many other countries; thus, the number of neonates who are exposed to SCPs in utero may increase in the next few years. Cannabis use in the gravid population and in utero cannabis exposure are common; however, to the best of our knowledge, our case is the first neonate in the literature who was exposed to SCPs in utero and who demonstrated withdrawal symptoms after delivery.

Smoking and oral ingestion are the most common methods of consumption. The mother of our case used the method of smoking. SCPs demonstrate their effects by cannabinoid re-

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ceptors. The two known cannabinoid receptors are CB1 and CB2. CB1 receptors are found in many vital organs, including the heart, liver, kidney, and immune system, but mainly in the central and peripheral nervous systems. CB2 receptors are mainly expressed in lymphoid organs. CB1 receptors cause psychotropic effects of cannabinoids. SCPs are agonists of CB1 receptors and are more potent than Δ-9-THC, which is a partial agonist of CB1 receptors. Therefore, SCPs have more adverse effects than natural cannabis (2). Each SCP is different, and the ability of binding to CB1 and CB2 receptors changes with respect to the drug. This situation causes a wide range of physiological effects (2). Adverse effects of SCPs are similar to those of high dose of natural cannabis, but there are also unique symptoms such as vomiting, prominent agitation, seizure, acute myocardial infarction, and kidney damage (2). Altered mood and perception, listlessness, red eyes, nausea, vomiting, fever, and sweating are most common findings among adolescents and adults (2). Common cardiac adverse effects of SCPs are tachycardia and high blood pressure, but bradycardia and hypotension have also been reported (2, 3). The present case had tachycardia and normal blood pressure. She was agitated and had tremors, exaggerated moro reflex, and jitteriness without any stimulus, and, these movements were exaggerated by touch, sound, and light. She also had a high-pitched cry. SCPs comprise different herbal compounds, vitamin E, amides of fatty acids, clenbuterol (potent β2-agonist), and preservatives. Different SCPs contain different concentrations of these additives and chemicals. Thus, it is not easy to determine the exact content of these products and exact symptoms. There is a wide range of presenting symptoms because of the possibility of multiple drug use. SCPs may induce different metabolic effects such as hypokalemia, hyperglycemia, acidosis, and increased creatinine kinase (CK) levels (3). Serum glucose, potassium, and CK levels and blood gas parameters of the present case were all normal. Electrocardiography and echocardiography were also normal. Transient acute renal insufficiency because of acute tubular necrosis has also been reported (4). In our case, renal function test results were all normal. SCPs may usually not be detected by the standard urinary drug screening tests because there are many types of SCPs, and their effective dose and excreted metabolites are small. Therefore, expanded urine toxicology screening tests should be performed to detect these products (5). In our hospital, we did not have a chance to perform expanded urine toxicology screening tests; thus, we did not prove the use of the drug. We knew that the baby was exposed to SCPs during the whole pregnancy by the self-report of the mother. Δ-9-THC has various inhibitory effects on γ-aminobutyric acid (GABA) in the brain. Hence, SCPs may cause anxiety, agitation, and seizures by inhibiting GABA (6). SCPs may also include β_1 agonists, which may be responsible for hypertension, palpitations, tachycardia, anxiety, and irritability (6). The infant was agitated and had jitteriness and exaggerated moro reflex, but we did not notice any seizure activity. There is no antidote for cannabinoid intoxication, and the symptoms are usually self-limited and short acting. Treatment of agitation and restlessness with benzodiazepines is effective (6). We did not use any medications for calming the infant. However, we noticed that swaddling, limiting exposure to light and sound, and non-nutritive sucking were helpful.

It is difficult to determine the effects of SCP use on the developing fetus because addicted mothers often simultaneously use other drugs, including tobacco. To date, there has been no information about the fetal effects of SCPs. However, in a large population-based prospective cohort study, maternal cannabis use during pregnancy was associated with growth restriction during mid and late pregnancy (7). There is no precise information about the teratogenic effects of cannabis, but one study reported that intrauterine cannabis exposure increased the risk for neonatal intensive care unit (NICU) admissions, predominantly for prematurity (8). The present case had restricted growth and stayed in NICU for 2 weeks because of withdrawal symptoms similar to those of intrauterine cannabis exposure.

In conclusion, the addiction to SCs is very common worldwide and also in Turkey. The clinicians may experience more and more SCP-exposed neonates in the next few years. Hence, this study may warn clinicians about the possible symptoms of intrauterine SCP exposure.

Informed Consent: Written informed consent was obtained from the parents of the patient who participated in this study.

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Video 1. The symptoms of the infants is demonstrated

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