Case Report / Olgu Sunumu

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Serotonin Syndrome in a Toddler from Sibutramine Adulterant

Sibutramin Adulteran Nedeniyle Bir Çocukta Serotonin Sendromu

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Abstract

Serotonin syndrome (SS) is a rare yet potentially life-threatening condition resulting from excessive serotonin activity in the nervous system. This case report describes a 3-year-old girl who developed severe agitation and chorea following the accidental ingestion of three tablets of slymochoco, an unregulated dietary supplement containing sibutramine—a banned serotonin-norepinephrine reuptake inhibitor. The child presented with agitation, hypertonia, and generalized involuntary movements eight hours post-ingestion. Emergency treatment included intravenous diazepam, followed by oral chloral hydrate, leading to gradual symptom resolution within 48 hours. Sibutramine toxicity in children is uncommon, but can present SS with neuromuscular abnormalities, autonomic dysregulation, and altered mental status. Pediatric SS presents diagnostic challenges due to variability in symptoms, requiring vigilant assessment for neuromuscular findings such as clonus and hyperreflexia. Supportive care, including benzodiazepines for agitation, forms the cornerstone of management, whereas cyproheptadine may be used in severe cases. This case underscores the diagnostic challenges of SS in children, exacerbated by the continued presence of sibutramine in unregulated slimming agents. Clinicians should inquire about herbal and unregulated weight loss products when evaluating pediatric patients with unexplained autonomic or neuromuscular symptoms.

Keywords: Serotonin syndrome, pediatric, chorea, sibutramine toxicity

Öz

Serotonin sendromu (SS), sinir sisteminde aşırı serotonin aktivitesinden kaynaklanan nadir ancak potansiyel olarak yaşamı tehdit eden bir durumdur. Bu olgu raporu, yasaklanmış bir serotonin-norepinefrin geri alım inhibitörü olan sibutramin içeren, düzenlenmemiş bir besin takviyesi olan slymochoconun üç tabletini kazara yuttuktan sonra şiddetli ajitasyon ve kore gelişen 3 yaşındaki bir kız çocuğunu tanımlamaktadır. Çocuk, ilacı yuttuktan sekiz saat sonra ajitasyon, hipertoni ve genel istemsiz hareketler sergilemiştir. Acil tedavi, intravenöz diazepam ve ardından oral kloral hidrat uygulanmasını içermekteydi ve 48 saat içinde semptomların kademeli olarak düzeldiği görüldü. Sibutramin toksisitesi çocuklarda nadir görülür, ancak nöromüsküler anormallikler, otonomik düzensizlik ve değişmiş zihinsel durum ile birlikte serotonin sendromuna yol açabilir. Pediyatrik serotonin sendromu, semptomların değişkenliği nedeniyle tanı koymada zorluklar yaratır ve klonus ve hiperrefleksi gibi nöromüsküler bulguların dikkatli bir şekilde değerlendirilmesini gerektirir. Ajitasyon için benzodiazepinler içeren destekleyici bakım, tedavinin temelini oluştururken, şiddetli olgularda siproheptadin kullanılabilir. Bu olgu, kontrolsüz zayıflama ajanlarında sibutraminin varlığının devam etmesiyle daha da kötüleşen, çocuklarda SS'nin tanı zorluklarını vurgulamaktadır. Klinisyenler, açıklanamayan otonomik veya nöromüsküler semptomları olan pediatrik hastaları değerlendirirken, bitkisel ve düzenlenmemiş kilo verme ürünleri hakkında araştırma yapmalıdırlar.

Anahtar Kelimeler: Serotonin sendromu, pediatrik, korea, sibutramin toksisitesi

Introduction

Sibutramine, a serotonin-norepinephrine reuptake inhibitor, was once widely prescribed for managing obesity. However, its use has been discontinued globally because of significant cardiovascular risks. Despite this, sibutramine is often found as an adulterant in many counterfeit weight-loss products, leading to potential toxic exposures, particularly to vulnerable populations such as children. This report describes a case of

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a 3-year-old child who developed severe agitation and chorea after accidentally ingesting three tablets of the product. This case highlights the critical need for stringent regulatory enforcement, heightened public awareness, and early recognition of serotonin syndrome (SS) to prevent adverse health outcomes.

Case Report

A 3-year-old girl, previously well, was brought to the emergency department by her mother after accidentally ingesting an unregulated dietary supplement (slymochoco) that belonged to the mother. The child consumed three tablets approximately eight hours before presentation. Two hours post-ingestion, the mother noted involuntary movements involving the upper and lower limbs, and smacking of the lips. As the symptoms worsened, the mother immediately sought medical attention. There was no history of fever, vomiting, diarrhea, or seizures. The child was unable to control abnormal movements and had no history of falls or trauma.

On examination, the child was conscious, pink, and not tachypneic, but appeared agitated. Her vital signs were stable, with a blood pressure of 86/56 mmHg, heart rate of 128 bpm, and SpO of 100% on room air. She was afebrile. Neurological examination revealed chorea-like movements of the bilateral upper and lower limbs with hypertonia and normal reflexes. We didn't observe any specific type of rigidity or tremor in this child. Neither ocular clonus nor clonus of the extremities was observed. Other systemic examinations were unremarkable.

Initial blood work revealed no evidence of infection. The full blood count, renal profile, liver function test results, and electrolytes were within normal ranges. Her electrocardiography shows sinus tachycardia. Intravenous diazepam 2.5 mg (0.2 mg/kg) was administered 9 hours post-ingestion in the emergency department to reduce involuntary movements as the child became increasingly restless and agitated. The involuntary movements persisted but decreased in intensity.

While admitted to the ward, the child was initiated on chloral hydrate syrup (regular) 130 mg, TDS (10 mg/kg) to manage her agitation. She was treated conservatively, and the abnormal movements gradually resolved over 48 hours. A urine sample was taken on the day of admission and stored at the hospital laboratory for 48 hours before being sent to the state chemical laboratory for testing. The results of the urine sibutramine tests were negative on day three after admission. By day three, the child was completely symptom-free and able to sleep throughout the night. She was discharged in good condition. The child's parents permission was obtained for publication of this case.

Discussion

SS is a potentially life-threatening condition caused by excess serotonin in the nervous system, often due to drug ingestion. It presents with a triad of symptoms: Altered mental status, autonomic dysregulation, and neuromuscular abnormalities. While SS is well documented in adults, cases in children are rare. However, a recent literature review revealed that the prescription of selective serotonin reuptake inhibitors is on the rise due to an increase in pediatric mental health issues.[1]

Symptoms of SS can vary widely among pediatric patients, with some children exhibiting mild symptoms such as restlessness and others presenting with severe complications such as rhabdomyolysis and seizures. The most common presenting symptoms are confusion, agitation, tachycardia, hypertension, hyperreflexia, rigidity, and tremor.[1] None of the patients presented with involuntary movement. In a case described by Phan et al.,[2] a single 50 mg dose of sertraline triggered SS in a child, underscoring the heightened sensitivity of pediatric populations to serotonergic agents.

Sibutramine overdose is rare but potentially severe, especially in children. Its clinical presentation often mimics SS, with symptoms such as tachycardia, hypertension, agitation, and hyperthermia. In a report by Bucaretchi et al.,[3] a 4-year-old girl exhibited severe agitation, hallucinations, and autonomic dysfunction after ingesting a significant amount of sibutramine. Another case highlighted psychomotor disturbances and chorea-like movements following sibutramine ingestion in a 26-year-old woman. She responded well to haloperidol therapy.[4] Although this case did not meet the Hunter Criteria due to the absence of clonus or hyperreflexia, the clinical picture remained highly suggestive of SS, particularly in the pediatric population where atypical presentations are documented. The presence of chorea-like movements further complicated the assessment, as it may obscure or mimic classic neuromuscular findings such as clonus or tremor, which are key components of diagnostic criteria like the Hunter Criteria.

The management of sibutramine toxicity focuses on supportive care and symptom control. The initial steps include stabilizing the airway, breathing, and circulation, followed by interventions to manage agitation and autonomic symptoms. Benzodiazepines are commonly used to control agitation and seizures, whereas cyproheptadine, a serotonin antagonist, can be effective in cases of SS. In cases described by Bucaretchi et al.,[3] symptomatic treatment included sedation to manage severe agitation and hypertension. Our patient was managed with benzodiazepines to alleviate her agitation. In this case, while benzodiazepines are the standard first-line agents for managing agitation in SS, chloral hydrate was used to manage the child's persistent restlessness. This decision was influenced by several contextual factors. Firstly, SS is rare

in the pediatric population, contributing to limited clinical familiarity among treating physicians. Additionally, local practice in our setting commonly advocates the use of chloral hydrate as an oral sedative in pediatric patients, particularly when intravenous sedation is not immediately necessary. Given the child's stable cardiorespiratory status and the need for a sedative with a predictable oral administration profile in a non-intensive care unit setting, chloral hydrate was deemed a practical and safe interim measure.[5] The patient's favorable clinical course and resolution of symptoms within 48 hours further supported the appropriateness of this individualized, context-specific management approach. Cyproheptadine is indeed recognized as a safe and effective oral serotonin antagonist in managing mild-to-moderate SS. However, in our setting, cyproheptadine is not readily available in the state hospital formulary, limiting its accessibility for acute use. Additionally, given the child's stable vital signs and progressive improvement following benzodiazepine administration and supportive care, we opted for close clinical observation rather than escalation to cyproheptadine. The decision was based on the mild-to-moderate severity of symptoms, the absence of complications such as hyperthermia or severe autonomic instability, and the child's favorable trajectory within 48 hours. While cyproheptadine may have been a therapeutic consideration under different circumstances, our conservative approach was guided by resource availability and clinical response.

The long-term effects of sibutramine ingestion in children are not well documented. Waszkiewicz et al.[6] reported that sibutramine exposure could trigger manic episodes in predisposed individuals, highlighting the need for careful psychiatric evaluation in affected children.[6]

Diagnostic confirmation often involves urine toxicology testing for sibutramine and its active metabolites, mono-desmethylsibutramine and di-desmethylsibutramine. Sibutramine has a short half-life of approximately 4 hours. Active components such as desmethylsibutramine are metabolized within 24-48 hours of ingestion.[7] Some urine tests for sibutramine levels are designed to detect only certain metabolites and have lower limits of detection. A study utilizing gas chromatography/mass spectrometry reported limits of detection for sibutramine metabolites in the range of 10 to 50 ng/mL, indicating that concentrations below this threshold might not be reliably identified.[7] Another reason for obtaining negative results is improper handling of samples. Delays in testing or improper storage can also lead to the degradation of detectable substances, resulting in false-negative findings. Gastric decontamination with activated charcoal may be considered if ingestion occurs within a short timeframe, although its efficacy diminishes over time.[8]

The recurrent adulteration of unregulated weight loss products with sibutramine presents a critical public health threat, necessitating urgent intervention. Raising awareness among both the public and healthcare professionals about the associated cardiovascular and neurological risks is imperative. Strengthening regulatory frameworks and enforcement mechanisms is essential to curtail the distribution of counterfeit slimming agents. Clinicians should maintain a high index of suspicion for the use of herbal or unregulated weight loss products when assessing pediatric patients with unexplained autonomic or neuromuscular dysfunction, ensuring timely diagnosis and intervention.

Conclusion

This case highlights the ongoing public health risk posed by counterfeit weight loss products adulterated with sibutramine, a serotonin-norepinephrine reuptake inhibitor which was withdrawn due to its cardiovascular risk. Despite SS's rare occurrence in children, it should be considered in cases of unexplained neurologic and autonomic symptoms, with early recognition and supportive management being crucial. This case underscores the limitations of toxicology testing, the need for thorough clinical evaluation, and the importance of strengthening regulatory measures to prevent the distribution of such harmful products.

Ethics

Informed Consent: Informed consent was obtained from the patient's parents.

Footnotes

Authorship Contributions

Concept: S.M., D.G.B., M.K., K.A.B., Design: S.M., D.G.B., M.K., K.A.B., Data Collection or Processing: S.M., D.G.B., M.K., K.A.B., Analysis or Interpretation: S.M., D.G.B., M.K., K.A.B., Literature Search: S.M., D.G.B., M.K., K.A.B., Writing: S.M., D.G.B., M.K., K.A.B.

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