

## 4-yaşında bir çocukta fatal eroin ve metadon intoksikasyonu: Olgu sunumu

### Fatal heroin and methadone intoxication in a 4-year old child: A case report

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#### ÖZET

Tüm dünyada psikoaktif madde kullanımı nedeniyle zehirlenme olguları gün geçtikçe artmaktadır. Bu maddelere kaza ile maruz kalmak da zehirlenmeye hatta ölüme neden olabilmektedir. Bu olguda, kaza sonucu antihipertansif ilaç içtiği iddiasıyla hastaneye kaldırılan 4 yaşındaki yabancı bir kız çocuğuna ait bir olgu sunulmaktadır. Histopatolojik incelemede pulmoner ödem dışında patolojik bulgu gözlenmemiş ancak toksikolojik tarama analizlerinde metadon, eroin ve bunların metabolitleri ile birlikte eroin safsızlıkları tespit edilmiştir. Biyolojik örneklerinde herhangi bir antihipertansif ilaç tespit edilmeyen olgu, eroin ve metadonun birlikte alınmasına bağlı çoklu psikoaktif madde intoksikasyonu olarak bildirilmiştir. Olgu ile bağımlı ebeveynlerin çocuklarının içinde bulunduğu tehlikeye karşı yetkililerce tedbir alınması gerekliliği bir kez daha ortaya çıkmıştır.

**Anahtar Kelimeler:** Metadon, eroin, çocuk, intoksikasyon.

#### ABSTRACT

Intoxication cases due to drug abused have been increasing dramatically worldwide. Accidentally exposure to abused drugs also causes intoxication even death. In this report we describe an autopsy case pertaining to a 4-year old foreign girl who was taken to hospital for accidental intake of antihypertensive drugs. No pathological significance was observed except pulmonary edema in histopathological examination. Methadone, heroin, their metabolites and heroin impurities were found in biological samples with toxicological screening. Antihypertensive drugs were not detected in the samples. The case declares drug intoxication due to heroin and methadone intake together. In addition reveals children of drug-dependent parents are in danger and essential precautions should be taken by government.

**Keywords:** Methadone, heroin, child, fatal intoxication.

## INTRODUCTION

Heroin is a commonly abused semi-synthetic opiate drug that is synthesized from morphine. It is rapidly converted to 6-acetylmorphine and then to morphine and causes many short term and long term effects to the body including euphoria, nausea, vomiting, hypoventilation, respiratory arrest, pulmonary edema, hypotension and bradycardia even death.

Methadone, is a synthetic opiate agonist with long-acting effects. The effects of methadone are

similar to heroin, although they are less intense and last longer. Therefore, methadone abuse is common among opiate addicts. It is used as a maintenance therapy for heroin addicts in several countries, however buprenorphine is used for this purpose in Turkey. Methadone is a controlled substance and available on the illicit market in Turkey.

Multiple intoxication cases reported in children are related to methadone or other illegal drugs (1-16). We report a case of a child who died due to a combined exposure to methadone and heroin.

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## CASE HISTORY

We encountered a case of fatal methadone and heroin poisoning in a 4-year old foreign girl. The girl was admitted to the emergency department with cardiopulmonary arrest. Fixed pupillary dilatation was observed on examination and accepted exitus after appropriate cardiopulmonary resuscitation. Her parents claimed that she had taken her father's antihypertensive drugs containing lisinopril and metoprolol accidentally.

She was referred to Morgue Department of Council of Forensic Medicine (Istanbul) to determine the accurate reason of death by autopsy. Yellow-brown ecchymosis in an area of between 0.1-1 cm on the anterior left cruris, 0.6x0.5 cm abrasion area on the left earlobe, 0.3x0.2 cm abrasion area on the inside of the left elbow, ecchymosed injection trail on the inside of the right elbow, periorbital purple discoloration and a normal genital-perianal region was observed by external examination.

Right (134g) and left (148g) lungs were weighted. Both lung surfaces appeared as mottled, swollen, tense with subpleural petechial bleeding. Other organs and the skeletal system were observed to be normal. Samples of heart, brain, cerebellum, brainstem, lung, liver, kidney, thymus and cervical medulla spinalis were taken for histopathological examination. Samples of femoral arterial blood, bile fluid, vitreous fluid, stomach content, kidney and liver were collected for toxicological examination. No pathological significance was observed except pulmonary edema in histopathological examination.

A screening for abused drugs (opiates, cocaine, cannabis, amphetamine, barbiturates, benzodiazepines, methadone, buprenorphine, tricyclic antidepressants and K2) in blood was performed by a cloned enzyme donor immunoassay (CEDIA; Thermo Fisher Scientific, Finland) and positive results for opiates and methadone were obtained. Subsequently, a liquid chromatography-tandem

mass spectrometry (LC-MS/MS) blood analysis confirmed the presence of methadone, heroin metabolites and impurities. However, neither lisinopril nor metoprolol was detected in the blood. Blood alcohol result (analyzed by a headspace GC/FID technique) was negative in the case.

In addition to the LC-MS/MS analysis; blood, bile fluid, liver, kidney and stomach content were also analyzed by gas chromatography mass spectrometry (GC/MS) for screening of basic, acidic, and neutral drugs and pesticides. No other drugs or pesticides were found in the case.

Quantitative and qualitative results obtained from LC-MS/MS and GC/MS are presented in Table 1.

## DISCUSSION

Overall, misused methadone is the most commonly reported opioid other than heroin, followed by buprenorphine. Heroin or its metabolites are present in the majority of fatal overdoses reported in Europe, often in combination with other substances. In addition to heroin, other opioids including methadone, buprenorphine, fentanyl and tramadol are regularly found in toxicological reports, and these substances are now associated with a substantial share of overdose deaths in some countries (17). The use of opiates was reported as 70.1% (n= 164) of the direct drug-related death cases in Turkey and 13.8% (n= 32) of these cases were foreign nationals (18). Methadone is not used for opioid dependence treatment in Turkey, therefore, deaths related to methadone are not often in Turkish citizens. Two deaths associated with methadone only and one death with methadone and heroin combination were reported in 2013 (18). None of the reported cases were Turkish citizens (unpublished data).

Children of addicted parents are in a drug intoxication risk. Several childhood drug intoxication cases have been reported (1-16). There are also

many cases in the literature related to methadone or heroin intoxication in children with high mortality and morbidity (1-13). Pediatric exposures to methadone have occurred both accidentally and non-accidentally (due to administration by a caregiver to sedate a child). Milroy and Forrest reported five children deaths involving methadone in one hundred and eleven cases with a methadone concentration range (200-489 ng/ml) in blood (3). Couper et al. presented a case of fatal intoxication in an infant who was administered by her mother. The subclavian blood methadone concentration was (670 ng/ml) in that case (4). Kintz et al. studied methadone in hair of children to distinguish chronic exposure. They recommended segmental hair analysis to discriminate between long-term exposure to a drug and an acute exposure close to the time of sampling (7). Bonsignore et al. reported a non-accidental methadone intoxication in an infant (methadone concentration; 633 ng/ml). They also analyzed hair segmentally and nail to reveal continuous methadone exposure (12). In our case, we determined methadone (317 ng/ml), morphine (34 ng/ml) and codeine (41 ng/ml) in blood. In addition to methadone, morphine and codeine, and 6-MAM (5ng/ml) was found in the

stomach content. Liver, kidney and bile were also studied. Toxicological results are summarized in Table 1. It seems to be an acute intoxication due to the (317 ng/mL) blood methadone concentration (toxic (from) dose: 200 ng/mL) (19), however due to the lack of hair or nail samples, the case is not assessed as acute or chronic exposure.

In this case, methadone, heroin metabolites and impurities were detected together. To the best of our knowledge, this is the first case reported in the literature describing intoxication in a child exposed to heroin and methadone, presumably due to the combined effect of acute exposure. According to the results of the stomach content, the route of administration can be considered as oral in this case.

## CONCLUSION

In this case, the cause of death was determined to be methadone and heroin intoxication and reported as multiple drug intoxication. The deceased child presumably took both heroin and methadone orally.

**Table 1:** Toxicological findings in the case.

	(Blood: µg/l; Stomach Content, Liver, Kidney: µg/g)							
Specimen	Methadone	EDDP	Morphine	Codeine	6-MAM	Meconin	Papaverine	Noscapine
Blood	317.0	n.d.	34.0	41.0	n.d.	n.d.	n.d.	n.d.
Bile Fluid	+	+	n.d.	n.d.	n.d.	+	n.d.	n.d.
Stomach Content	1160.0	+	17.0	112.0	5.0	+	+	+
Liver	197.0	+	0.3	15.0	n.d.	n.d.	n.d.	n.d.
Kidney	180.0	+	0.9	21.0	n.d.	n.d.	n.d.	n.d.

+ : detected by Shimadzu GC/MS-QP2010 qualitatively.

n.d.: Not detected

EDDP:2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (Methadone metabolite)

6-MAM = 6-monoacetylmorphine

Quantitative analyses of methadone, morphine, codeine and 6-MAM were performed by Agilent 6460 LC-MS/MS.

The lives of children of drug-dependent parents are in danger. Their hair samples can be taken periodically to control if they are exposed to the drug

or not. This precaution can decrease fatal drug intoxications in children.

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