Intravenous Abuse of Propylhexedrine (Benzedrex®) and the Risk of Brainstem Dysfunction in Young Adults

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ABSTRACT: In 1949, amphetamine sulfate was replaced by propylhexedrine in the nasal decongestant agent Benzedrex® because of psychosis, sudden death, and widespread abuse. Propylhexedrine is not without risks, and reported cases of psychosis, myocardial infarction, pulmonary vascular disease and pulmonary hypertension, and sudden death are well documented in the medical literature. We are reporting 2 cases of definite brainstem dysfunction and 5 cases of transient diplopia secondary to IV abuse of Benzedrex®. This widely abused drug is prepared by heating Benzedrex® and hydrochloric acid, and the resulting crystals are dissolved in water for injection. This agent is called "stove-top speed". All 7 patients had transient diplopia, within seconds after injection. One patient had evidence of a right-internuclear opthalmoplegia, and another had a depressed right gag reflex and paralysis of the right half of the tongue. The deficits in these two patients, persisted for many months. In young adults with history of drug abuse, the IV use of Benzedrex® should be considered in the differential diagnosis of transient or permanent focal brainstem deficits.

RÉSUMÉ: Le risque de dysfonction du tronc cérébral chez le jeune adulte faisant l'abus de la propylhexédrine (Benzedrex®) par voie intra-veineuse En 1949, le sulfate d'amphétamine a été remplacé par la propylhexédrine dans les décongestifs nasaux à la suite de psychoses, de morts subites et d'abus largement répandus. L'usage de la propylhexédrine n'est pas sans risque, comme en témoigne la littérature médicale: cas de psychose, d'infarctus du myocarde, d'atteinte vasculaire pulmonaire, d'hypertension pulmonaire et de mort subite. Nous rapportons 2 cas de dysfonction nette du tronc cérébral et 5 cas de diplopie transitoire secondaire à l'abus du Benzedrex® par voie intra-veineuse. Cette substance dont l'abus est répandu, est préparée en chauffant le Benzedrex avec de l'acide chloridrique; les cristaux ainsi obtenus sont dissouts dans l'eau pour être ensuite injectés. Cette préparation est appelée "stove-top speed". Les 7 patients ont présenté une diplopie transitoire quelque secondes après l'injection. Un patient a présenté des manifestations d'ophtalmoplégie internucléaire droite et un autre, un réflexe pharyngé diminué et une paralysie de la moitié droite de la langue. Chez ces deux patients, le déficit a persisté pendant plusieurs mois. Dans le diagnostic différentiel des déficits, transitoires ou permanents, en foyer au niveau du tronc cérébral, on doit penser à la possibilité de l'utilisation intra-veineuse du Benzedrex® chez l'adulte jeune qui a une histoire d'abus de drogues.

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In 1949 amphetamine sulfate was replaced by propylhexedrine in the nasal decongestant agent Benzedrex® because of psychosis,[1,2] sudden death[3] and widespread abuse.[4] Propylhexedrine is not without risks and reported cases of psychosis,[5,6,7] myocardial infarction,[8] pulmonary vascular changes and pulmonary hypertension,[9] and sudden death[10,11,12] are well documented in the medical literature. This is the first report, to our knowledge, of neurological dysfunction secondary to intravenous Benzedrex® abuse.

Case Reports

Cases with Persistent Neurological Dysfunction

Case 1. A 31 year old homosexual caucasian, was admitted because of generalized skin ulcers and sepsis, both secondary to intravenous injections of Benzedrex®. He had been a polydrug addict for 15 years. During the last 4 years he restricted himself exclusively to 2 to 3 daily injections of Benzedrex®. When he used neck veins, he experienced a severe generalized headache and horizontal diplopia, both lasting approximately two hours. He reported similar symptoms when using limb veins with higher concentrations of propylhexedrine. Physical examina-

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tion revealed purulent skin ulcers in the 4 extremities up to 5 cm in diameter, surrounded by cellulitis. He had evidence of a right internuclear opthalmoplegia with partial inability to adduct the left eye, and horizontal nystagmus of the right eye when looking to the right. Metabolic and electrolyte parameters were normal except for elevated SGOT and SGPT and a positive Hbs-Ag. EEG and CT scan were normal.

Case 2. An 18 year old native Indian woman was admitted for evaluation of two episodes of diplopia and lower cranial nerve involvement. She had been a polydrug abuser for six years including solvents. Six months prior to admission she abused mostly intravenous Benzedrex®, 2 to 4 injections every two days. Three months prior to admission and a few minutes after a right neck injection, the patient claimed that she was completely unable to move the right eye for approximately four hours. A month before admission, again after a right sided neck injection, she experienced horizontal diplopia, right hemiparalysis of the tongue, dysphagia and numbness in the right lower face. Examination disclosed several areas of indurated and partially healed ulcers over the four limbs. Extraocular movements were normal. The perception of pain and temperature was decreased in the inferior right half of the face and touch was impaired on the right side of the palate. The right sternocleidomastoid muscle was weak. The tongue was deviated to the right. Sequelae of a left ulnar palsy, secondary to a misplaced injection in the past, were noted. Raised alkaline phosphatase and GGTP, and a microcytic anemia were detected on admission, but normalized within 2 weeks. The EEG was normal, but the CT scan showed cortical atrophy and marked ventricular dilatation, likely due to solvent abuse,[13] but no focal brainstem abnormalities.

Cases with Transient Neurological Dysfunction

Case 1. A 24 year old caucasian male, toluene abuser for 11 years, was admitted because of memory impairment and cerebellar ataxia. Two years prior to admission, he had abused Benzedrex® intravenously. When neck veins were used, he experienced horizontal and vertical diplopia lasting from two to four hours each time. Physical examination revealed subcutaneous induration surrounding superficial veins. Neurological examination was normal. Other cranial nerves, the motor and sensory examination were normal. Alkaline phosphatase, SGOT, SGPT, and GGPT were raised. EEG was normal but the CT scan showed mild cortical atrophy and ventricular dilatation likely due to solvent abuse,[13] but no focal brainstem abnormalities.

Case 2. A 40 year old man was using 10 units of Benzedrex® i.v. per week for 6 months previous to admission. He had abused amphetamines and narcotics in the past. When neck veins were used he experienced an immediate severe generalized headache and horizontal diplopia. Examination disclosed that the right pupil was larger than the left, but both reacted equally to light and accommodation. No other abnormalities were noted. Skin ulcers and cellulitis were found in both upper limbs, likely due to misplaced injections.

Case 3. A 30 year old woman, poly drug user for almost 10 years had been using i.v. Benzedrex® for 2 years PTA. She injected Benzedrex® twice or three times a month. After each injection she experienced double vision lasting one to two hours. Neurological examination disclosed no abnormalities.

Case 4. A 28 year old caucasian was admitted because of alcohol withdrawal. He has been a chronic alcoholic and polydrug abuser for more than 14 years. Benzedrex® i.v. was injected once or twice weekly. After each injection (neck or arm veins), episodes of diplopia lasting one to two hours were experienced. No neurological abnormalities were detected on admission, but multiple scars were seen near neck and arm veins.

Case 5. A 24 year old native woman was seen in Emergency Room due to alcoholic intoxication. She was also using i.v. Benzedrex® daily, (2 to 4 units) for 1 year. When neck veins were used ("for a better high and rush") she experienced severe headache and diplopia lasting 3 to 5 minutes. No neurological abnormalities were observed. Healed skin ulcers over the arms and legs were present.

Discussion

The potent sympathomimetic, propylhexedrine, has similar pharmacological properties to methamphetamine and is abused because of its CNS stimulant properties. The pathological findings in cases of sudden death from this drug[14] include intimal and medial proliferation of pulmonary vessels, coronary occlusion and hypertrophy-fibrosis of the myocardium.[12] In amphetamine abusers, similar changes have been documented, as well as cerebral vessel damage in experimental animals[15,16] and humans.[17,18]

All our cases represent examples of transient or permanent neurological dysfunction after intravenous injections, particularly when using neck veins. The first case had evidence of damage to the right medial longitudinal fasciculus, the second case probably corresponds to right sided brainstem damage and the five other cases had transient neurological deficit affecting cranial nerves. These episodes may be due to biochemical or ischemic changes in the brainstem, peripheral nerves, or even at the neuro-muscular end plate. Further investigations couldn't be done in our cases. The pathogenesis of this condition is not known, but there are similarities with the cerebral vasculitis syndrome associated with amphetamine abuse.[15] The vasoconstrictor effects of propylhexedrine combined with the low pH of the solution (the abusers extracted the crystals of propylhexedrine with hydrochloric acid, obtaining a pH solution of less than 2), could be responsible for brainstem dysfunction, either biochemically or ischemic. Similar mechanisms are postulated in the neurotoxicity of hydantoins, carbamazepine and barbiturates.[19] The damage to the peripheral veins in all cases was presumably due to the acidity of the solutions injected. Intravenous Benzedrex® abuse should be considered in the differential diagnosis of transient or permanent neurological impairment affecting cranial nerves in young adults, particularly those with a history of drug abuse.

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