Heroin withdrawal as a possible cause of acute concomitant esotropia in adults.

Alison Y Firth, Department of Ophthalmology and Orthoptics, University of Sheffield.

Correspondence to:

Alison Y Firth MSc DBO(T)

University Department of Ophthalmology and Orthoptics

O Floor

Royal Hallamshire Hospital

Glossop Road

Sheffield

S10 2JF

Tel: 0114 2712064

Fax: 0114 2766381

Email: a.firth@sheffield.ac.uk

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Abstract

Aim: To report the possible effects of heroin withdrawal on binocular vision.

Methods: To present a case series of patients in whom esotropia developed on cessation of heroin use.

Results: In each case the esotropia was concomitant and prismatic correction restored binocular single vision. Intermittent spontaneous control occurred in one patient, the deviation resolved in one and one patient was lost to follow-up.

Conclusions: Heroin withdrawal should be considered as a cause of acute concomitant esotropia. However, accurate history of other medication is needed to ensure that this is not the cause of decompensation.

Key words

Heroin, diamorphine, substance withdrawal syndrome, diplopia, esotropia.

Introduction

Heroin is an opiate, a morphine derivative also known as diamorphine. It is produced from raw opium obtained from the opium poppy (Papaver Somniferum). Some ocular

problems are associated with heroin use. On the street buyers will often taste the heroin, which is bitter, to test quality. Quinine is sometimes used as a cutting agent, because of its bitter taste, to disguise dilute heroin and also as its hypotensive effect intensifies the 'rush'. Toxic amblyopia, or toxic maculopathy due to quinine has been reported in heroin addicts [1-3]. Metastatic endophthalmitis (due to candida albicans) may occur where lemon juice has been used to dissolve the heroin and injected; or some cutting agents may embolize to the eye. Tolerance to heroin rapidly increases with use, so that increasing doses are needed for the same effect. The mechanism of desensitisation is not fully understood.

A higher number of strabismic children are born to drug dependent women than in the normal population [4], although low birth weight and other drug use during pregnancy may be significant. Diplopia has been reported, amongst other symptoms, in wound botulism in heroin users [5,6]. However, it rarely appears amongst possible symptoms of withdrawal.

Untreated heroin withdrawal starts within a few hours and reaches its peak 36-72 hours after the last dose. Symptoms will have mainly subsided after 5 days. The genearally accepted signs and symptoms of withdrawal are shown in table 1. Himmelsbach[7] in 1941 when describing the signs and symptoms of abrupt withdrawal states: 'Occasionally a patient will complain of double vision. Nearly all patients, if they try to read, complain of some impairment of vision'. The incidence of 'diplopia / blurred vision' during both previous attempts of withdrawal and current attempts at withdrawal have been reported in US soldiers who had served in Viet Nam [8] and are shown in table 2. However, no detail is given as to the reasons for diplopia and no

distinction made between diplopia and blurred vision. In a series of 100 consecutive patients admitted to a drug treatment centre, none complained of a recent change in vision [9], but visual acuity measurements were not performed.

Acute concomitant esotropia without disruption of fusion (e.g by occlusion) was first described by Burian[10]. Several reports have appeared in recent literature in children[11 – 16] and in children or adults[9,17,18]. In some instances this type of strabismus has been related to a disease or general condition[19-23].

Three cases are presented in which acute concomitant esotropia developed in the early period of detoxification (planned withdrawal from heroin).

Case Series

Case 1.

A 27 year male presented to the accident and emergency department in February 1995 complaining of diplopia and headache for 8 to 9 days. The patient reported no problems with general health and no medication being taken, but commented that his left lid used to droop as a child. On examination by an orthoptist visual acuity was 6/5 either eye and a moderate left to alternating esotropia (Near 30Δ ET; Distance 25Δ ET) was present with diplopia. Ocular movements appeared full and fusion was demonstrated on the synoptophore. The patient was fitted with a 25Δ base out Fresnel

prism left eye on planos and told that he would be referred to an ophthalmologist and follow-up would be in clinic.

When the patient attended 6 months later for the clinic appointment, he volunteered that diplopia had occurred during rehabilitation for heroin abuse, and that the diplopia initially had been intermittent, but had quickly become constant. No medication was recorded as being taken at this visit. On examination, esotropia was still present without the prism, but the patient was able to control the deviation fixing a light. Intermittent left suppression was present when manifest, and the deviation had reduced very slightly (Near 18Δ ET; Distance 20Δ ET; Distance R gaze 16Δ ET; Distance L gaze 18Δ ET). The Fresnel prism was reduced to 15Δ base out.

One month later the prism was reduced further to 10Δ and over the following 21 months the patient wore the prism (achieving 55 secs of arc on Frisby), and was able to achieve some control without the prism. By June 1997 the prism was no longer being worn but intermittent diplopia was troublesome when tired. The angle of deviation was 20Δ ET near and distance. A slight ‘A’ pattern was present, 120 secs of arc was obtained on the TNO test and whilst good convergence was shown with prisms on fusion range testing, only 1Δ of divergence was present for near and distance. The patient was listed for surgery at the next visit, but has failed to attend since.

Case 2

A 31 year old male presented to eye casualty in December 1995 complaining of sudden onset of intermittent horizontal diplopia 10 days previously. The diplopia had now become constant. He had stopped using heroin 18 days prior to the hospital visit. There was no history of eye problems. Visual acuities were 6/5 either eye. On examination by the orthoptist a moderate left to alternating esotropia was present for near and distance (Near 12Δ ET; Distance 20Δ ET 2Δ RHoT; Distance R gaze 20Δ ET; Distance L gaze 20Δ ET). Ocular movements revealed a minimal underaction of the right eye on laevoelevation and a minimal underation of the left eye in abduction – although there was no increase in the deviation when measured in this position and the Hess did not show any underaction of the left eye on laevoversion. Binocular single vision was present with Bagolini glasses when the angle was corrected.

The patient was fitted with a 20Δ base out Fresnel prism on planos and failed to attend follow-up.

Case 3

A 22 year old female presented to eye casualty in August 1999 complaining of the sudden onset of horizontal diplopia 3 days after stopping heroin. Three days prior to the withdrawal of heroin, naltrexone hydrochloride (Nalorex), chlordiazepoxide (Librium) and clonidine hydrochloride (Catapres; Dixarit) had been started. Ten days after onset, she was seen by an orthoptist. Visual acuities were 6/4 right and left. A moderate alternating esotropia was present for near and distance (Near and distance:

30Δ ET). Fresnel prisms of 10Δ either eye were given on planos. One week later the prism was reduced by 6Δ and one week later the patient was able to gain binocular single vision unaided and demonstrated a slight esophoria with good recovery (10Δ E) and 340 secs of arc on Frisby. The angle of deviation at distance was 35Δ on dextroversion and 15Δ on laevoversion, but no limitations of movement were recorded. One month later a very slight esophoria was present (Near 6Δ E; Distance 4Δ E, Distance R gaze 8Δ E; Distance L gaze 4Δ E). 110 seconds of arc was achieved on Frisby and a good fusion range present (Near: 40Δ BO to 8Δ BI; Distance 20Δ BO to 3Δ BI). The patient failed to attend further follow-up.

Discussion

All of these cases presented with acute concomitant esotropia. In each case withdrawal from heroin had been without a substitute opiate such as methadone hydrochloride; dihydrocodeine phosphate; or buprenorphine. However, details regarding other medication in cases 1 and 2 are not known. In case 3 naltrexone hydrochloride (Nalorex; an opioid antagonist) was used at the start of the detoxification programme. This is usually started following the main withdrawal period otherwise patients go into acute withdrawal, however, it is sometimes used to precipitate withdrawal in combination with sedation. Also prescribed for this patient was Clonidine hydrochloride (Catapres; Dixarit; used to help reduce anxiety, muscle cramps, and is hypotensive). This reduces sympathetic tone but blurred vision is not listed as a side effect in Martindale[24], although it has been reported in one patient with no reason given[25], and diplopia has been queried as a possible side effect[26].

Hargrave[27] reports the onset of a concomitant esotropia (angle not stated) in a patient (his wife!) who had previously undergone treatment for an exophoria of the convergence weakness type. The esotropia was initially attributed to pregnancy, and it resolved on taking diazepam (Valium). Diazepam had been stopped previously when the likelihood of pregnancy occurred and thus it was concluded that the cessation of this drug rather than the pregnancy was the cause of the strabismus. Diazepam is a tranquiliser (benzodiazepine based), not an opiate and thus acts differently. It is sometimes used to alleviate symptoms of withdrawal in opiate users who are either unable to obtain supply of heroin or during self withdrawal (i.e without medical help)[28]. There is no recorded evidence that diazepam was used in any of the cases reported in this series, although it is a possibility. It is possible that the strabismus in these patients was a side effect of medication used during detoxification.

One sign of opiate use is miosis. and whilst pupils are still found to be miosed in long term addicts, there is evidence that some level of tolerance develops[29]. Thus, during withdrawal, anisocoria may be observed[9] and mydriasis[30].

The mechanism for the miosis is unclear. Opiate receptors are located in various areas within the brain which include the pretectal area (medial and lateral optic nuclei), superior colliculus and ventral nucleus of the lateral geniculate body. However, whether it is stimulation in these areas; the lack of inhibition from the cortex to these areas or the Edinger-Westphal nucleus; direct action on the neurons subserving the parasympathetic light reflex in the Edinger-Westphal nucleus; or stimulation of opioid

receptors in the iris sphincter is not known (for review see Murray et al[31]). Effects on accommodation are not generally reported, although one reference to decreased accommodation both on use of heroin and withdrawal can be found[32]. Blur may occur as a result of the mydriasis alone.

Various hypotheses may be proposed for the development of the strabismus in these cases. Burian and Miller[33] state that in some cases with acute concomitant esotropia a 'physical or psychic shock may precede the onset'. The start of a detoxification programme certainly could be considered as this, particularly where acute withdrawal is precipitated (case 3). Hoyt and Good[34] consider that a rise in intracranial pressure could be relevant to the onset of esotropia in patients with brain tumours, and as hypertension is a sign of withdrawal this may be the mechanism here. Concomitant esotropia in the presence of raised intracranial pressure with resolution following therapy to lower the intracranial pressure has been reported previously[35]. Alternatively, the raised intracranial pressure may have an effect on the 6th nerve(s). There are elements in this series of patients which suggest subtle involvement of the sixth nerve, namely the A pattern recorded on one visit in case 1 and the increase in deviation on horizontal versions in case 3. If the sixth nerve was subtly involved, then a vasomotor disturbance could be responsible. The mode of detoxification is not known in cases 1 and 2, but in case 3 where acute withdrawal appears to have been precipitated the risk of complications would be higher.

Near response related neurons have been identified in the mid brain, in the pretectrum and possibly the anterior superior colliculus [36,37]. Other pre-motor vergence neurons have been identified in the brainstem (for review see Judge[38]). The equilibrium

between convergence and divergence may be altered as tolerance increases leading to an imbalance on withdrawal.

Where acute concomitant esotropia develops, detoxification should be suspected as a cause and specific questions posed relating to misuse of drugs and current medication. Until further study is undertaken, the precise mechanism of the cause remains unknown.

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Sweating

Lachrymation and runny nose / sneezing

Sore eyes

Mydriasis

Sore throat

Yawning

Feeling hot and cold

Anorexia and abdominal cramps

Nausea, vomiting and diarrhoea

Tremor

Insomnia and restlessness

Severe cramps and stiff joints

Tachycardia, hypertension

Gooseflesh

Irritability

Increased bowel sounds

Vasomotor disturbances

Increase in heart rate

Increase in respiratory rate

Increase in blood pressure

Increase in temperature

Table 1: Signs and symptoms of heroin withdrawal

Mode of use	Reported during previous withdrawal attempt	Observed during withdrawal in treatment centre
Smoking	32/178 18%	38/200 19%
Sniffing	15/50 30%	6/60 10%
Injection	17/51 33.3%	11/60 18.3%

Table 2: Mode of previous use of heroin in US soldiers who had served in Viet Nam and incidence of diplopia / blurred vision during withdrawal from Ream et al [8] (Number of subjects/total in group and % shown).