Int J Leg Med (1991) 104:289–291

International Journal of
Legal Medicine

Two deaths from intravenous nifedipine abuse

B. N. Purdue, G. C. A. Fernando, and A. Busuttil

Forensic Medicine Unit, Department of Pathology, University Medical School, Teviot Place, Edinburgh EH8 9AG, Scotland

Received July 4, 1991

Summary. An incident is reported in which 2 intravenous drug abusers died as the result of uncontrolled experimentation with intravenous injection of the common anti-hypertensive and anti-anginal drug Nifedipine (Adalat *t.m.Bayer*), probably in mistake for the commonly abused short-acting benzodiazepine drug Temazepam. Large quantities of Nifedipine were identified in the blood of both deceased men by gas chromatography. Apart from intense gastric mucosal congestion, pulmonary oedema and general visceral congestion, the autopsy findings were entirely nonspecific. The similarity in colour, shape and texture between capsules of Nifedipine and those of Temazepam is likely to have prompted the mistake.

Key words: Nifedipine – Temazepam – Intravenous drug abuse

Zusammenfassung. Es wird über ein Ereignis berichtet, bei welchem 2 Fixer wegen unkontrollierten Experimentierens mit einer intravenösen Injektion des verbreiteten anti-hypertensiven und anti-pektanginösen Medikaments Nifedepin (Adalat, Bayer) verstarben. Wahrscheinlich wurde das Medikament mit dem normalerweise bei Mißbrauch benutzten, kurz wirkenden Benzodiazepin „Temazepam" verwechselt. Im Blut beider Verstorbener wurden mit Hilfe der Gaschromatographie große Mengen von Nifedepin identifiert. Neben ausgeprägter Hyperämie der Magenschleimhaut, einem Lungenödem und einer allgemeinen Kongestion der Bauchorgane waren die Autopsiebefunde insgesamt unspezifisch. Ähnlichkeiten in der Farbe, der Form und dem Aussehen der Kapseln für Nifedepin und jener für Temazepam ist wahrscheinlich die Ursache für die Entstehung des Fehlers gewesen.

Schlüsselwörter: Nifedepin – Temazepam – Intravenöser Drogenmißbrauch

Case report

The incident reported here took place in October 1990 when 2 young men, JS aged 19 and FW aged 21, visited the home of a companion late one night. JS was a drug abuser of some 2 years standing who was known to have injected drugs intravenously on previous occasions. FW was a more experienced drug abuser, having experimented with most illicitly available drugs, including opioids, both orally and intravenously for at least 5 years. Earlier in the evening, FW had consumed seven or eight 10 mg capsules of the common sedative drug Temazepam. This is a drug frequently taken by drug abusers in order to maintain them between doses of opioids. It is also abused intravenously as described below.

A quantity of orange coloured soft gelatin ovoid capsules, subsequently identified as Nifedipine 5 mg but new and unidentified to the 3 men, had been illicitly obtained and JS proceeded to inject himself with the liquid contents of 12 of them. Within 3 or 4 min he developed breathing difficulty, then collapsed unconscious and apparently lifeless. His companions attempted to revive him by mouth-to-mouth resuscitation and by placing him in a bath of cold water. This had the effect of restoring spontaneous respiration but not consciousness, and he was placed face down in the recovery position on the floor. The initial improvement in breathing was not maintained and signs of life once more disappeared.

Impressed by this evidence of the potency of the drug but quite undeterred by its effect, FW then took a similar number of the capsules and injected himself with the contents. He, too, collapsed apparently lifeless, this time within seconds of the injection. The occupant of the premises prudently refrained from imitating his companions and summoned an ambulance, shortly afterwards joined by a full resuscitation team, but the 2 experimenters were beyond help and were both pronounced dead despite prolonged and vigorous attempt to save them.

Autopsy findings

Full autopsy examinations were performed on the deceased men, each by 2 pathologists (GCAF and BNP) in accordance with Scottish legal practice in cases involving the possibility of criminal proceedings. The examinations took place approximately 36 h after death.

JS was a well nourished Caucasian youth of medium build. Both arms and knees bore decorative tattoos,

some of professional and some of amateur design. There was a single area of reddish-orange discolouration of the front (volar aspect) of the right forearm surrounding a faint needle puncture mark. Other, separately identifiable, needle puncture marks of attempted resuscitation were present elsewhere. Single isolated small abrasions were present on the left knee and the right foot. There were no other recent injuries. The lungs (right 525 g; left 400 g) were congested and oedematous, exuding copious frothy fluid on section. The stomach contained a little dark red fluid and its mucosa was intensely congested. There were no obvious tablet or capsule residues in the stomach. The remainder of the internal organs, and, in particular, the cardiovascular system, showed no significant pathological abnormality. The brain (1425g) was not oedematous. Radioimmunoassay screens for Hepatitis B surface antigen, anti-HBc and antibody to HIV were negative.

FW was a well nourished young Caucasian adult of powerful build. Both arms and knees bore decorative tattoos, in several cases identical with those of his companion JS. There was a single small but clearly defined needle puncture mark in the right ante-cubital fossa surrounded by a small purple haematoma. This was distinguishable from needle puncture marks inflicted in the course of attempted resuscitation, present in other parts of the body. Two small superficial lacerations were present on the back of the right hand and ring finger, but there were no other recent injuries. The lungs (right 560 g; left, 450 g) were moderately congested and oedematous, exuding frothy fluid on section. The stomach mucosa was strikingly congested and haemorrhagic, but the stomach was empty. The remainder of the internal organs, and, once again in particular, the cardiovascular system, showed no significant pathological abnormality. The brain (1510 g) was not oedematous. Radioimmunoassay screens for Hepatitis B surface antigen, IgM specific anti-HBc and antibody to HIV were negative. However, similar screens for anti-HBc and anti-HBs were positive, indicative of past infection with Hepatitis B virus.

Histological findings

A range of body tissues from both deceased men were examined microscopically. The only significant findings common to both were copious intra-alveolar pulmonary oedema, intense congestion of gastric mucosal vessels and more moderate generalised visceral congestion. Portal tracts in the liver of FW showed a little non-specific chronic inflammatory cell infiltration, but there was no evidence of active hepatitis or significant fibrosis. Otherwise, neither man showed any significant pathological abnormality on microscopical examination of the tissues.

Toxicological examination

Specimens of blood, urine and vitreous from both men were each examined for ethanol with negative results. Temazepam was found in the blood of FW in a concentration of 1.6 μg/g, an amount which lies above the range associated with ordinary therapeutic dosage. No Temazepam was found in the blood of JS. The empty capsules whose contents the deceased men had injected intravenously were identified as those of Nifedipine 5 mg (Adalat *t.m. Bayer*). Preliminary gas chromatography, using automated electron capture detection analysis (Schmid et al. 1988), yielded a concentration of Nifedipine in the blood of JS of 172.4 μg/l and in the blood of FW of 154.7 μg/l. From the chromatography results on FW, it seemed probable that another drug was present, doubtless the Temazepam identified previously. As the other drug eluted closely to Nifedipine, a less polar extraction technique was performed and the presence of Nifedipine was again confirmed by chromatography. This was quantitated in the blood of JS at 181.9 μg/l and in the blood of FW at 144.2 μg/l. The therapeutic dose of Nifedipine is 12–18 μg/l of blood (Walley et al. 1987b). The deceased men had therefore experienced a roughly tenfold overdosage of Nifedipine in a single bolus.

Blood and urine specimens from both deceased men were screened for other common drugs and poisons with negative results.

The cause of death in both men was given as:

Ia) Nifedipine Overdosage

Discussion

Nifedipine is a well known and widely prescribed calcium channel blocker used in the treatment of angina, hypertension and Raynaud's phenomenon. As a specific and potent calcium antagonist, the main action of Nifedipine is to relax arterial smooth muscle (Sorkin et al. 1985; Walley et al. 1987a). It reduces the load on the left ventricle by peripheral vasodilatation and improves myocardial perfusion by coronary arterial vasodilatation, though its precise mode of action in angina and hypertension has not been elucidated. Most of the known side effects of the drug reflect its potent vasodilator function and comprise headache, dizziness and flushing (Schiffl et al. 1984; Herrington et al. 1986; Whitebloom and Fitzharris 1988). The effects of overdosage represent an accentuation of these phenomena. Death in the 2 men whose case is presented here appears to have resulted from hypotensive syncope. Krstic (1985), using an animal model, demonstrated that the effective intravenous dose of Nifedipine is approximately 100 times smaller than the oral one. However, Walley et al. (1987b) have shown that controlled 24-hour intravenous Nifedipine infusion can be useful and safe in the treatment of acute myocardial infarction. Death from oral overdosage with Nifedipine has not been reported and this does not appear to be a notable hazard, since a large overdose would be required.

At first sight, Nifedipine is an unlikely candidate for a drug of abuse. It is not hallucinogenic, stimulant nor sedative in effect and would thus appear to hold no attraction for addicts; indeed, it has not hitherto been described as a concomitant of drug abuse.

However, Nifedipine is available in a number of forms for therapeutic use, and these include the orange coloured soft gelatin ovoid capsules containing yellow viscous fluid found in connexion with the 2 deaths described. The capsules are marked with the trade name and manufacturer's mark (Adalat *Bayer*) but, to the unwary, somewhat resemble Temazepam capsules.

Temazepam is a much more familiar drug in abuse circles (Morrison 1989; Sakol et al. 1989; Hammersley et al. 1990). It is a short-acting benzodiazepine intended for the short-term treatment of sleep disturbances and as a premedication before minor surgery. Temazepam is marketed in the UK as opaque yellow oval soft capsules with liquid centres (*Normison t.m.* Wyeth Laboratories) or as green soft gelatin capsules with liquid centres (*Euhypnos t.m.* Farmitalia Carlo Erba Ltd.). Both manufacturers supply the capsules in 10 mg and 20 mg formulations, the normal therapeutic dosage being 20–40 mg 30–60 min before surgery when premedication is required. The capsules are widely popular in the Scottish drug abuse community, to whom they are known as "eggs" or "goosies" (Hammersley et al. 1990).

It is common practice amongst drug abusers to draw up the contents of a Temazepam capsule using a syringe and then to inject it intravenously. Clearly, this is completely contrary to the manufacturer's instructions for use, since Temazepam capsules are intended for oral ingestion. Nevertheless, so widespread is this form of abuse that liquid-centred capsules have become synonymous with Temazepam amongst intravenous drug abusers in the UK. This is by far the most probable explanation for the facts of the incident described and would explain why the capsules were obtained by the deceased men in the first place. The circumstances strongly suggest a mistake in drug recognition rather than a deliberate experiment. As such, the incident appears to be unique.

References

Hammersley R, Lavelle T, Forsyth A (1990) Buprenorphine and Temazepam – abuse. Br J Addict 85:301–303

Herrington DM, Insley B, Weinmann GG (1986) Nifedipine overdose. Am J Med 81:344–346

Krstic MK (1985) Cardiovascular response to intravenous administration of Nifedipine in rats. Periodicum Biol 87:243–246

Morrison VL (1989) Psychoactive substance use and related behaviours of 135 regular illicit drug users in Scotland. Drug Alcohol Depend 23:95–101

Sakol MS, Stark C, Sykes R (1989) Buprenorphine and Temazepam abuse by drug takers in Glasgow – An increase. Br J Addict 84:439–441

Schiffl H, Ziupa J, Schollmeyer P (1984) Clinical features and management of Nifedipine overdosage in a patient with renal insufficiency. Clin Toxicol 22:387–395

Schmid BJ, Perry HE, Idle JR (1988) Determination of Nifedipine and its three principal metabolites in plasma and urine by automated electron-capture capillary gas chromatography. J Chromatogr 425:107–119

Sorkin EM, Clissold SP, Brogden RN (1985) Nifedipine – A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy, in ischaemic heart disease, hypertension and related cardiovascular disorders. Drugs 30:182–274

Walley TJ, Heagerty AM, Woods KL, Bing RF, Pohl JEF, Barnett DB (1987a) Pharmacokinetics and pharmacodynamics of Nifedipine infusion in normal volunteers. Br J Clin Pharmacol 23:693–701

Walley TJ, Heagerty AM, Woods KL, Bing RF, Pohl JEF, Barnett DB (1987b) Nifedipine infusion in acute myocardial infactin: experience in twelve patients. Clin Cardiol 10:800–803

Whitebloom D, Fitzharris J (1988) Nifedipine overdose. Clin Cardiol 11:505–506