

RISKS FOR DRIVING UNDER THE INFLUENCE OF CLOMETHIAZOLE

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ABSTRACT: In a case history the risks of driving a motor vehicle under the influence of clomethiazole are demonstrated. A 53 year old male car driver caused an accident by deviating from the lane in a traffic circle, but he continued his trip without stopping. The police could follow the winding lines of the car for about 2000 m, ending in the garage of the car owner since the oil tank of the car and the entrance of the garage were damaged. Toxicological analysis (GC-ECD) of a blood sample of the car owner indicated the proof of 3300 ng clomethiazole/ml serum. Neither alcohol (headspace GC; ADH) nor any other drug (GC/MS, HPLC) could be detected in this blood sample. Policemen reported that one day after the event the car owner committed suicide by swallowing at least 60 capsules of Distraneurin® (clomethiazole). In this case no post-mortem blood sample was taken and no dissection of the corpse was made.

KEY WORDS: Chlormethiazole; Distraneurin; DUI.

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INTRODUCTION

According to the definition of WHO any substance which impairs one or more functions of the central nervous system in living organisms is a drug. In view of problems concerning traffic medicine the most important drugs considered are alcohol, addicted drugs and pharmaceuticals such as hypnotics, sedatives and psychoactive drugs. In general, the routine screening of blood and urine samples, which are analysed in cases of traffic medicine, comprises – besides alcohol analyses – an immunological screening procedure for addicted drugs, benzodiazepines, barbiturates and tricyclic antidepressants and the confirmation of positive immunological results with GC and/or HPLC methods. Specific analysis of clomethiazole in a medicament screening is performed according to Eisenmenger only in special cases, i.e. whenever the ingestion of this medicine has been reported or quite unusual traffic offenses have to be judged [4].

Clomethiazole (syn. chlormethiazole) is a hypnotic and sedative used particularly in elderly patients and also for symptomatic treatment of alcohol withdrawal (main indication), sometimes used as an anticonvulsant [1, 7, 8]. Dependence may occur after prolonged use, particularly of high doses [7].

In Germany clomethiazole is marked under the trade mark Distraneurin®, in other countries under the trade mark Heminevrin®. One capsule of Distraneurin® contains 192

mg of clomethiazole [1, 8]. According to Rote Liste [8] the therapeutic dose at acute withdrawal symptoms after chronic alcohol abuse is 2 to 4 capsules. In case the sedation is not finished within 30 to 60 min the dose can be enhanced by additional 2 capsules up to 8 capsules of Distraneurin® within 2 hours.

CASE HISTORY

In January 1999 a 53 year old male car driver (64 kg, 178 cm) caused an accident by deviating from the lane in a traffic circle, but he continued his trip without stopping. The police could follow the winding lines of the car for about 2000 m (at least three deviations of up to 6 meters along this route; damage of a traffic sign on a traffic refuge) ending in the garage of the car driver, since the oil tank of the car and the entrance of the garage were damaged. The oil trace indicated that the car driver made several attempts to reach the entrance of his garage with deviations up to three meters. At the time of the traffic accident the quality of the road and the weather conditions were good and dry. At the car no technical deficiencies could be detected, which could have caused this accident.

In the habitation of the car driver policemen found a packing of 100 Distraneurin® capsules (contents: more than 60 capsules). In the interrogation with the policemen and the physician the car driver declared that he had taken one capsule of Distraneurin® in the morning time and two capsules at noon. The car driver was described by policemen as follows: reaction: delay; articulation: characterless; state of mind: tranquil, partly dump; problems to keep in equal balance; tottering motion. The eyes of the car driver were unobtrusive, each pupil about 4 mm diameter measured at daylight.

Toxicological analysis of a blood sample of the car driver (taken at 5.40 p.m.) and quantification of clomethiazole [6, 9] was performed by extraction of the underivatized drug from the serum under alkaline conditions with toluene (1 ml serum, 1 ml 1N NaOH, 0,5 ml toluene, vortex 2 min, centrifuge) and gas chromatography of the organic layer (2 ml) with electron capture detection. The gas chromatographic system consisted of a Fisons Model 8000 series equipped with an nickel-63 ECD (370 Mbq i.e. 10 mCi). A capillary column: Restek Rtx®-5 (Crossbond® 5% diphenyl-95% dimethylpolysiloxane) 30 m, 0.32 mm i.d., 1.0 mm df was used; temp. program: 140°C 10 min., 15°C/min., 300°C 10 min; nitrogen carrier gas 55 kPa; retention time 6.0 min. The temp. of the injection port was maintained at 250°C, the temperature of the detector at 320°C. An external standard: clomethiazole-ethanedisulfonate (Astra Chemicals GmbH, Wedel/Germany) was used for quantitation. Neither alcohol (head space GC; ADH-method) nor any other drug (GC/MS; HPLC Remedy-System BioRad) could be detected in this blood sample.

In total the analyses indicated the proof of 3300 ng clomethiazole/ml serum.

Policemen reported that one day after this event the car driver was found dead lying on the back in the entrance hall of his habitation. The Distraneurin®-packing was found

empty. A testimonial on leaving was found. Policemen and the court of justice imputed suicide of the car driver by swallowing at least 60 capsules of Distraneurin® (clomethiazole). In this case no post mortem blood sample was taken and no dissection of the corpse was made.

DISCUSSION

Baselt et al. [2] reported that the ingestion of 2 capsules (384 mg) clomethiazole produced an average blood peak level of 280 ng clomethiazole/ml after 45 minutes. According to CLARKE [3] therapeutic concentrations of clomethiazole in plasma are usually in the range of 100 to 2800 ng/ml. Toxic effects are associated with plasma concentrations of 1600 to 13000 to 26000 ng/ml and fatalities with concentrations of 8000 to 50000 to 170000 ng/ml [3]. Plasma half-life of clomethiazole is about 3 to 7 hours, increased in elderly subjects and in patients with liver disease [3].

In the present case the drivers blood level of clomethiazol was within the range of intoxication. At the date of the accident he obviously had taken considerably more than three capsules – as asserted by him – of Distraneurin®. On the other hand it has to be taken in consideration that the range of therapeutic clomethiazol blood level is very broad [3].

It is well known [8] that alcoholics after Distraneurin®-intake can develop a secondary clometriazol-dependence analogous to other sedatives, hypnotics and psychoactive drugs. For that reason as a rule predeliria as well as fully developed deliria should be treated in a hospital. The out-patient treatment of alcoholics with Distraneurin® is only recommended in special cases when the daily dosis is supervised [8]. A recommendation of the physician to the patient: “to measure out the medicine according to the requirement” resp. “to repeat the ingestion in case of lacking or reduced effect” encourages to overdosing.

According to informations of the manufacturer Astra strong drowsiness, stupefaction, headache and palpitation can occur even at low doses of clomethiazole [1]. Even after recommended use of this medicine the capability of reaction can be changed to such extent that the active participation in traffic is affected.

Summing up it has to be stated that every blood sample taken in connection with traffic offences should be checked on chlomethiazole.

Further examples of traffic accidents, where drivers were affected with clomethiazole, have already been reported [5].

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