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Fatal Combined Anileridine-Pethidine Poisoning. A Gas Chromatography, Thin Layer Chromatography and Mass Spectrometry Investigation

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Summary. Anileridine and pethidine were established by gas and thin layer chromatography and mass spectroscopy. In the mass spectrum the main peak of anileridine is found at m/e 246 and that of pethidine at m/e 71. The determination was made by gas chromatography from the blood, urine, liver, muscle and stomach contents.

Zusammenfassung. Anileridin und Pethidin wurden mittels Gas- und Dünnschichtchromatographie sowie massenspektroskopisch festgestellt. Im Massenspektrum liegen die Hauptspitze von Anileridin bei m/e 246 und diejenige von Pethidin bei m/e 71. Die Bestimmung erfolgte gaschromatographisch aus Blut, Harn, Leber, Muskel und Mageninhalt.

Key words: Anileridine, Gas chromatography-Mass spectrometry — Pethidine, Gas chromatography-Mass spectrometry — Poisoning, Anileridine, Pethidine.

Anileridine and pethidine are analgetics with effect and application similar to those of morphine [1]. Pethidine was the first totally synthetic analgetic by which morphine could be replaced in many situation. During the last three decades thousands of phenylpiperidines related to pethidine have been synthetized, some of which could be clinically applied, such as anileridine for instance. Pethidine and anileridine have appreciable addiction-inducing properties, which are in fact stronger in anileridine than in pethidine.

The estimated minimum lethal dose of anileridine is 0.5 g and of pethidine 1 g, but the daily dosage of abusers may be up to 3—4 g [2]. 5% of anileridine and pethidine are excreted unchanged into the urine.

Blomqvist *et al.* [3] have in their report described the mass spectrum of pethidine. The main peak in the spectrum is found at m/e 71, and it corresponds to cleavage of the methylpiperidyl component from the molecule. The peak at m/e 57 is produced when the methylene group departs from the methylpiperidyl component. The peak at m/e 174, again, is obtained at departure of the ester group; when the ethyl group is split off, the peak at m/e 218 appears. The molecule ion peak at m/e 247 is about 40% of the main peak.

A number of pethidine intoxications have been reported in the literature [3—7], but no report of anileridine poisoning could be discovered; at our department this was the first time that anileridine was encountered.

Case Report

A physician (32 years old) was travelling together with friends. In the morning he was absent from his sleeping compartment, and a search revealed him dead in the lavatory of the train. On the lavatory table a bottle, not full, of a liquid by name Leritine and a syringe were found. The man was known to be a pethidine abuser; use of alcohol was also known. On the strength of the results of analysis presented below, the Medical Examiner (R. Lehessaari, M.D.) entered the basic cause of death as combined intoxication from anileridine, pethidine and ethyl alcohol (intoxicatio combinata anileridini, petidini, alcoholi aethylici).

Methods

Qualitative Analysis. 200 g liver tissue were extracted by the acetone procedure, divided into acid, neutral and alkaline groups [8]. Each group was first examined by thin layer chromatography.

Thin Layer Chromatography System. The alkaline group was examined on Kieselgel G plates in a solution containing 5 ml NH_3 (25%), 10 ml ethanol, 40 ml dioxane and 50 ml benzene. The plate was sprayed with Dragendorff's reagent [9].

Gas Chromatography-Mass Spectrometry System. The substances of the alkaline group were analyzed in a Varian Mat 111 gas chromatograph-mass spectrometer with a 3% OV-17 glass column 1.8 m long. The column temperature was 150 and 280°C, helium flow 15 ml/min and ionization energy 80 eV.

Quantitative Analysis. Anileridine and pethidine were determined from 10 ml of blood and urine and from 10 g each of liver, muscle and stomach contents.

Pethidine. The homogenized samples were made alkaline with potassium hydroxide and extracted with 100 ml of ether. Washing of the ether followed by extraction with 1 ml approx. 9% H_2SO_4, addition of one KOH pellet to the acid layer in the microtube, and extraction of the solution with 1 ml of ether. 1 µl of the ether layer was injected into the gas chromatography apparatus.

100 µg pethidine were added to 10 ml water. After extraction a 70% recovery was obtained.

Anileridine. On shaking anileridine (100 µg) added to water, according to the preceding extraction procedure, the recovery was only 15%. The following procedure was therefore chosen. The homogenized samples were shaken in alkaline condition in 100 ml of ether. Upon cautios evaporation, in acid condition, of the ether the residue was dissolved in ethanol and injected into the gas chromatography apparatus.

100 µg anileridine were added to 10 ml water and extraction was carried out. The recovery now amounted to 69%.

Gas Chromatography System. Quantitative analysis was performed with a Varian 1400 with AFID detector and an OV-17 glass column of 1.8 m length. The column temperature was 150°C for pethidine and 250°C for anileridine, and carrier gas pressure 35 ml/min. The quantity was evaluated from the peak area.

Blood alcohol was determined by the Widmark and ADH methods.

Results

In the thin layer chromatography examination spots were obtained at the locations of pethidine and anileridine (Rf appr. 0.65 and 0.75, respectively). Figs. 1 and 2 show the gas chromatograms of the liver and urine extract and those of pure pethidine and anileridine. The retention time of pethidine at 150°C is 2 min and that of anileridine at 250°C is 10.8 min. With regard to both pethidine and aniler-

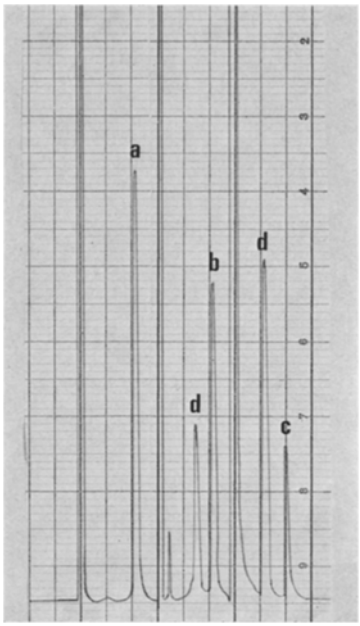


Fig. 1. Gas chromatograms of pure pethidine (*a*), pethidine isolated from urine (*b*) and pethidine isolated from liver tissue (*c*). The peak (*d*) has not been identified

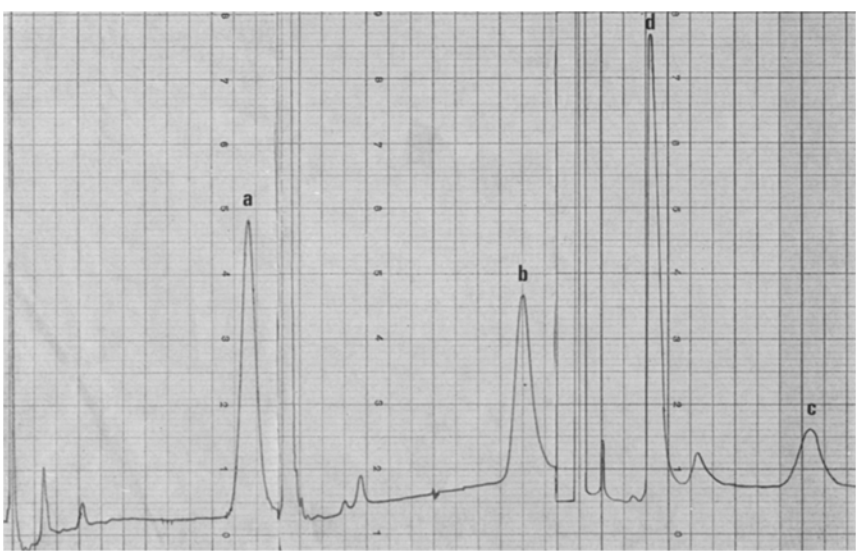


Fig. 2. Gas chromatograms of pure anileridine (*a*), anileridine isolated from urine (*b*) and anileridine isolated from liver tissue (*c*). The peak (*d*) has not been identified

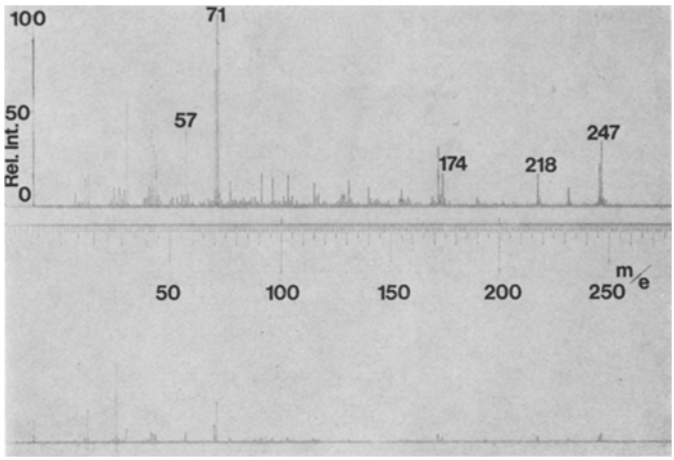


Fig. 3. Mass spectrum of pethidine isolated from liver tissue

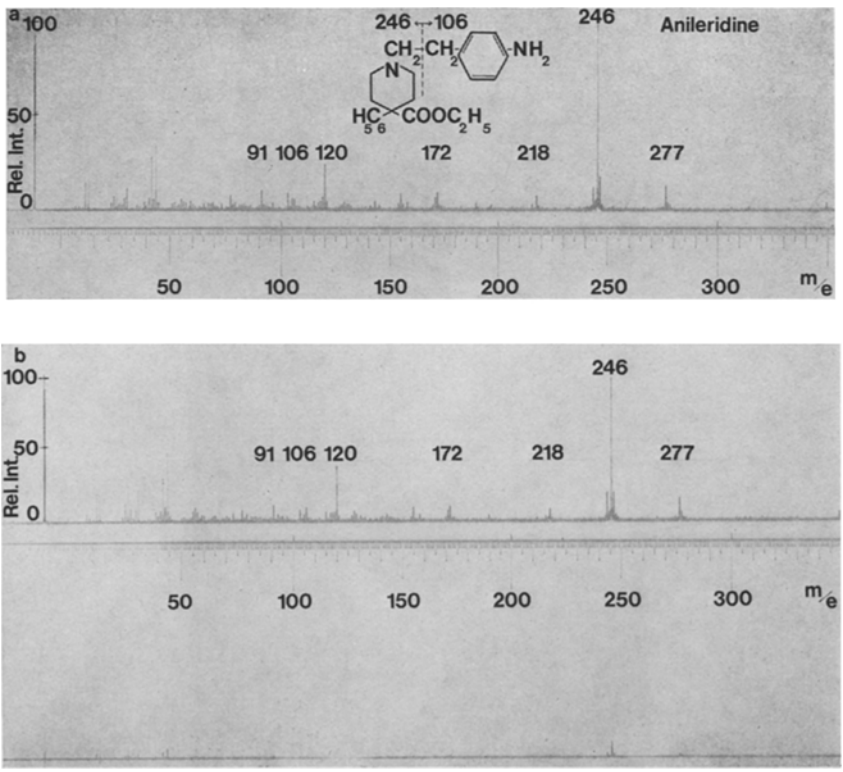


Fig. 4a and b. Mass spectrum of anileridine (a) and of anileridine from liver tissue (b)

Table 1. Quantitative results

Organ	Anileridine	Pethidine
Blood	0.5 mg/1000 ml	0.9 mg/1000 ml
Urine	49 mg/1000 ml	9.2 mg/1000 ml
Liver	1.3 mg/1000 g	0.4 mg/1000 g
Muscle	0.1 mg/1000 g	0.8 mg/1000 g
Stomach contents	0.1 mg/1000 g	—

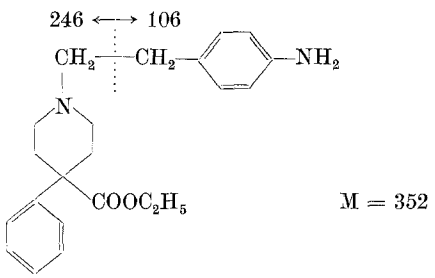
idine the gas chromatogram of liver and urine extract displays another peak, which could not be identified (cf. [3]). The pethidine mass spectrum obtained with the liver extract is almost identical with that by Blomqvist *et al.* (Fig. 3).

In Fig. 4 the mass spectra of pure anileridine and of the liver extract anileridine are seen, which also are nearly identical. The quantitative pethidine and anileridine contents appear from Table 1. The blood alcohol content was found to be 1.19 per mille.

Discussion

Anileridine proved to be a substance which is poorly extracted from ether into a small acid quantity, and it was therefore examined from the evaporation residue.

In the mass spectrum of anileridine the main peak is found at m/e 246, which probably corresponds to the following fragmentation:



It is thus observed that the main peak of anileridine has a structure nearly equal to that of the pethidine molecule, with only one hydrogen atom missing. The molecule ion peak of pethidine is 40% of the main peak. These facts are thought to demonstrate that the structure corresponding to that of the pethidine molecule is obviously stable. The peak at m/e 106 is also observable. No molecule ion peak is seen in the mass spectrum of anileridine. The peak at m/e 218 is thought to be due to cleavage of the ethylene group from the main peak at m/e 246.

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