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Death Involving Chloroquine: Analytical Aspects†

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An unusual death is described where the deceased, a foreigner in a closed rooom ingested a large quantity of chloroquine. The circumstances, autopsy findings and laboratory identification of chloroquine are described and the levels ot chloroquine in the viscera are interpreted as the cause of death.

Key Words: Chloroquine, Analytical.

INTRODUCTION

The deaths from ingesting tranquillizers, hypnotic drugs, etc. are common, but deaths from ingesting a chloroquine drug has hitherto been unrecorded to the knowledge of authors. Such a case is described in which this bizarre method was used to accomplish the suicide. In the present report, toxicological investigation by chemical and instrumental methods has been carried out in relation to the cause of death.

Case Report/Autopsy Findings

A 67 years old foreign resident was found lying dead in a closed room of his rented house. No injection marks at wrist or anywhere were noted indicating non-indulgence of any kind of injectable drug or psychotropic substance. The death of the deceased appeared to be suicidal by consuming either excess of some medicinal drug or other substance. He was found dead with a pool of yellow vomit material with some multiple superficial antimorten sharp cut injuries over accessible part of forearm, which were looking self-inflicted in nature. Both lungs, spleen, liver and kidneys were severely congested and pulmonary edema appeared. Body was found in a state that the yellowish content was coming out of the mouth. Stomach contained about 15 cc of yellow powdery, non-translucent material. The wall of stomach was found severely congested. The liver showed pale yellowish brown surface. The gall bladder contained about 30 cc of bile. Cyanosis was present in the nail beds. Some self-inflicted sharp cut injuries by means of blade were noticed on the left forearm, which indicated that the deceased

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died out of frustration by consuming either an excessive dose of medicinal drug or some other substance.

EXPERIMENTAL

Toxicological examination of viscera, blood and bile was performed. Analysis of alcohol and other volatile poisons were undertaken. But these volatile poisons and alcohol were found to be negative. Blood, bile, viscera and stomach content were tested for ammonium sulphate digestion and screened using alkaline, acidic and neutral ether extraction by chromatographic and spectrophotometric methods[1-8] for all important drugs, hallucinogens and psychotropic substances. While screening the viscera, blood, bile and stomach content by TLC and spectrophotometric method for identification of various drugs, the basic ether fraction showed absorption spectra identical to that of chloroquine showing peaks at 257, 329 and 343 nm wavelengths. The concentrated basic ether extract was identified as chloroquine with TLC method[9] using activated silica gel-G (0.25 mm thickness) on aluminium plate as stationary phase and methanol : amnumia (100 : 1.5) as a mobile phase and visualized under UV light sprayed with acidified potassium iodoplatinate as a chromogenic reagent. The violet spots for basic ether extract of viscera, blood and stomach content tallied with control chloroquine sample at R_f 35.

Further confirmation of chloroquine relied on the HPLC data. The HPLC procedure described by Brown[10] was attempted. The identification and quantitation of chloroquine was performed based on the peaks of chromatogram using the detecting wavelength 343 nm at a retention time of 2.14 min. The resolution of interfering peaks close to chloroquine peak was not found satisfactory by this method. Therefore, a new method for the analysis of chloroquine was developed to analyse the visceral extracts, which gave better separation and resolution of peaks. In this method, Water's HPLC system equipped with 510 pump, U6K injector and 481 Lambda-Max UV detector was used. The chromatography was performed on Water's μ Bonda pack (NH_2) column (3.9 mm × 30 cm) using mobile phase of ethyl acetate and acetonitrile (80 : 20) at the flow rate of 1.5 mL/min. Under these conditions chloroquine eluted at 4.5 min in all experiments of standard and visceral extracts (Figs. 1 and 2). The positive identification of chloroquine in the visceral extracts was further ascertained by observing the increase in area of the peak corresponding to standard chloroquine, on adding the standard in the visceral extract. The calibration curve was constructed by plotting three replicate measurements of six concentrations of standard, *i.e.*, 10, 20, 30, 40, 50 and 100 μg/mL against their peak area ratios. The concentration of chloroquine in the visceral extracts was determined from calibration curve. The

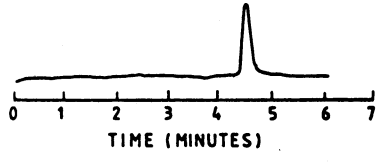

Fig. 1. Chromatogram of ether extract of standard chloroquine.

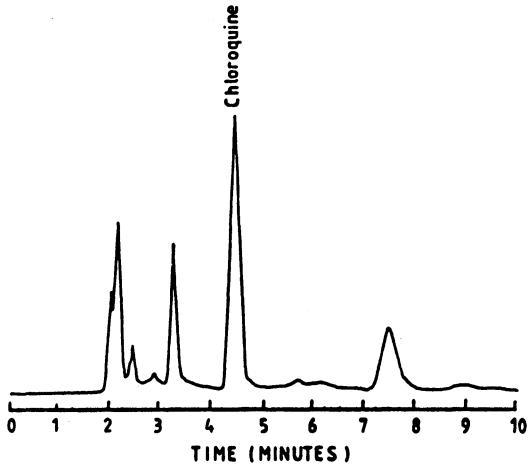

Fig. 2. Chromatogram of ether extract of viscera (Liver).

quantitative distribution of chloroquine in the visceral extracts was determined from calibration curve. The quantitative distribution of chloroquine in the visceral extracts is presented in Table 1.

TABLE-1
DISTRIBUTION OF CHLOROQUINE IN DIFFERENT SPECIMENS OF VISCERA

Specimen	Chloroquine concentration (mg/kg)
Liver	425
Kidney	442
Stomach content	9420
Blood	39.5
Lungs	206
Bile	45.6
Spleen	395

RESULTS AND DISCUSSION

The present case cannot be interpreted as intoxication because no alcohol or other psychotropic drug was found to be present in blood or viscera. Autopsy did not reveal any pathogenic change consistent with another cause of death. There is an autopsy evidence that the deceased might have ingested a large dose of any therapeutic drug, which was found in the stomach along with its content. On toxicological examination of blood, viscera and stomach content show a concentration considerably above the normal therapeutical level. Therapeutical blood concentration of chloroquine[11] following the oral or intravenous administration ranges from 0.05–0.25 mg/kg. Actual concentration of chloroquine found in the

viscera specimens was found to vary from 206 to 456 mg/kg. The content of stomach showed extremely high concentration, *i.e.*, 9420 mg/kg. However, 16-410 mg/kg concentration of chloroquine in different parts of body has been shown to be fatal among various postmortem subjects in earlier studies[12, 13].

Thus, in the present case, the cause of death was found to be acute chloroquine ingestion. The circumstances and the autopsy findings like self-inflicted injuries and sign of cuts on forearm and palm etc. lead to conclude the manner of death to be classified as death, out of frustration.

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