



Death due to imipramine

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ABSTRACT

An unique poisoning case leading to death by imipramine. Quantitative analysis of imipramine and was performed by liquid chromatography. The concentration of imipramine was 16.60 µg /ml in the collected blood sample during post mortem examination.

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Keywords

Imipramine,
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Introduction

Tricyclic antidepressants (TCAs), a group of structurally three-ringed drugs, are widely prescribed for major depression.¹ The major pharmacological action of TCAs are sedation, anticholinergic effects, and inhibition of norepinephrine or serotonin reuptake.² Imipramine, a promazine analogue and a prototype of the TCA drugs,³ is one of the most commonly prescribed drugs among TCAs. It is absorbed rapidly from the gastrointestinal tract and produces many metabolites by several cytochrome P450 isozymes in the liver.^{4,5} Here is a case of death by imipramine overdose.

Case Report

A 40 years male was found in a deep coma by his relatives and while admission process in the emergency department declared dead by the doctors. Subsequent history revealed that the deceased had been taking medications for depression from last 6 years, and a lot of empty strips of imipramine were found in his room. The autopsy was performed after 18 hours after his death.

Autopsy Findings

The deceased was a male, 165 cm in height, moderately built and nourished. No external injuries were found. The stomach contents, containing granules was noticed. There were no notable changes, other than congestion in the other organs. Postmortem samples such as blood, contents of the stomach, duodenum, and jejunum were collected for toxicological investigation.

Toxicological Examination

On a high-performance liquid chromatography was applied for drug screening and quantitation of imipramine. Using this system, quantitation of imipramine was carried out.⁶

Results and Discussion

The concentrations of imipramine in the postmortem blood sample was 16.60 µg / ml. We detected imipramine alone in the stomach contents and imipramine in blood, duodenal, and jejunal samples, but did not detect other drugs, including

alcohol. Since only imipramine was detected in the stomach contents, we concluded that the deceased ingested imipramine alone.

Therapeutic plasma levels of imipramine are 0.008 to 0.105 µg/ml, while toxic levels exceed 0.5 µg/ml, and the blood concentration in fatal cases ranges from 2.8 to 7.8 µg /ml.⁷ It has been reported that the combined blood concentration of the parent drug and major active metabolite of the TCAs is in excess of 1 µg/ml in overdose cases.⁸ In the present case, the concentration of imipramine itself in blood was within the fatal range. This evidence supports the diagnosis of imipramine poisoning as the cause of death.

Most fatalities due to TCA overdose are primarily due to its cardiovascular toxicity.¹ Clinically, severe cardiac symptoms such as cardiac arrest or death occurring in a patient with plasma TCA levels over 1 µg /ml have been reported. Furthermore, the measurement of plasma TCA concentration accurately predicts major adverse effects. This suggests the importance of monitoring for plasma drug concentration when managing a TCA overdose.

Here we used imipramine concentrations in the blood for the toxicological estimation. Postmortem imipramine concentration depends on the samplings site, which may be due to postmortem redistribution from the accumulation organ and incomplete distribution while still alive and the drug concentration in peripheral blood is closer to that the time of death. The present result also indicates that the blood sample collected should be suitable for post mortem toxicological analysis.

Based on the forensic pharmacological factors of imipramine such as distribution volume,¹ bioavailability, the body weight, and blood concentration, we estimate that he ingested at least 5.7 g of imipramine. In this case, however, the ingested amount of imipramine may have been larger than the estimated amount because his survival period was not clear and during this period, metabolism would have occurred and

decontamination by the emergency treatment was performed. There was approximately 1% of the estimated amount of drugs remaining in his stomach at autopsy. This may be due to the strong anticholinergic action of imipramine itself it inhibits stomach emptying and intestinal peristalsis, resulting in a delay in absorption of imipramine.⁹

From the autopsy findings and the results of the toxicological examination, we conclude that the death was due to an overdose of imipramine.

Conclusion

Even though such case reports of suicidal deaths due to overdose of drug appears to very frequent, the findings during post-mortem are very few and most of the time only toxicological report and circumstantial evidences will help in coming to conclusion. Here is such a case report where death was due to imipramine overdose.

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