Human case and an experimental study of postmortem distribution of lidocaine by intravenous drip

Wei Zhiwen 1, Zhang Heping 2, Yun Keming 3, Yujin Wang 4

Abstract: An unusual case is reported in which death was caused by intravenous drip lidocaine. Toxicological analysis by liquid–liquid extraction and gas chromatography–mass spectrometry (GC–MS) analysis was carried out to identify and quantify the individual substances present in the biological fluids and organs. The lidocaine concentration were blood (from heart) 18.95 μg/mL, gastric content 5.24 μg/g and urine 54.4 μg/mL. The animals experiment findings were discussed to provide useful information to the case with this particular murder. Lidocaine concentrations were as follows in dogs: blood (from heart) 25.2 μg/mL, blood (from femoral vein) 15 μg/mL, gastric wall 16.9 μg/g, gastric content 16.8 μg/mL, liver 21.8 μg/g, kidney 46.8 μg/g, brain 43.6 μg/g, spleen 57.9 μg/g, lung 19.7 μg/g, heart 34.5 μg/g, muscle (from left lower extremity) 18.3 μg/mL, urine 23.3 μg/mL, vitreous humor 2.4 μg/mL and bile 6 μg/mL. The distribution of lidocaine in biological fluids and organs after intravenous drip reveals gastric content were influenced by post-mortem redistribution. The lidocaine contained in the blood can diffuse towards the gastric content and other tissues very early after death. When blood lidocaine reached toxic or lethal levels, the chief cause of death and the way of lidocaine into body should be ascertained. The distribution after death was significant difference between oral and intravenous drip lidocaine. In this case, according to animal experimental, autopsy findings and toxicological analysis, the cause of death was most likely cardiac failure by intravenous drip overdose lidocaine.

Keywords: lidocaine; postmortem distribution; intravenous drip

Lidocaine (lignocaine, xilocaine), the first amino amide-type local anesthesia, was a common local anesthetic and antiarrhythmic drug, and used topically to relieve itching, burning and pain from skin inflammations, injected as a dental anesthetic, and in minor surgery[1]. It was also administered as a subcutaneous injection, epidural anesthesia, subarachnoid anesthesia and acute myocardial infarction as prophylaxis against ventricular fibrillation. The formulation of lidocaine is parenteral solution. The formulation for oral is rare except for gels designed to treat irritated or inflamed mucous membranes of the mouth or pharynx, and spray used as local anaesthetics in dentistry.

Various several accidental fatalities and suicides following intravenous injection of lidocaine, medical homicide and extreme negligence in epidural anesthesia, a rare side effect induced by lidocaine[2-8]
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and associated with cocaine in drug users have been reported[9]. While, rare are the homicide cases realized after intravenous drip of lidocaine.

In the case we report here, the concentration of lidocaine was detected in blood and urine, especially it was found in gastric content after death and autopsy was carried out.

Case history
The body of a 43-year-old male was found died at home by his wife, on the bed in his room. The wife claimed she had smelled gas leak and the son of the deceased suspected his father was murdered. The eternal examination revealed no external signs of injury, but the trace of injection was found in left antebrachium. A complete autopsy was performed 48 h after death. Autopsy was carried out, specimens were collected include (blood, urine, stomach contents). All samples were collected and stored at -20℃ until analysis.

Experimental

Chemicals and reagents
All chemicals were analytical grade with purity greater than 98% and were supplied by Sigma. Lidocaine and SKF 525A standards (1 mg/ml in ethanol) were obtained from Institute of Forensic Science Ministry of Public Security P.R.C.

Animal models
Seven domestic dogs, the weight of each being within a range of 15.0–17.4.5 kg were used, one was used as the negative control and remaining six were used for intravenous drip lidocaine. The dose was calculated considering the estimated fatal dose of 60 kg for humans and the body weight of the dogs used. The lidocaine-treated dogs were dissected after sacrifice, specimens of organs and biological fluids (the brain, heart, lung, liver, spleen, kidney, bile, urine, heart blood, peripheral blood, humor vitreous, and muscle in no injection location, gastric wall and gastrointestinal tract) collected during autopsy were frozen (-20℃). The control dog was sacrificed in a carbon dioxide chamber and necropsied.

Instrumentation
The analyses were performed with a Thermo-Fisher gas chromatography/mass spectrometry system: GC/DSQ, column, DB-5 MS, 30 m length, i.d.0.25 mm (0.25 mm film thickness). Carrier was helium at the flow rate of 1 ml/min. Injector temperature, 280℃, injection mode was split, split ratio, 50:1. Transfer line temperature, 250℃. Ion source temperature, 250℃. The column temperature program used for lidocaine was: initial temperature 150℃ for 1 min, 10°C/min to 280℃, maintained for 3 min. The instrument was used in full scan EI (70 eV) mode, scanning in the range between 40–650 m/z.

Extraction
One gram of each organ and 1 ml of blood, urine and bile brought with distillate water to a volume of 3 ml, were homogenized in a 10 ml tube of centrifuge. Prior to vortex for mixed, internal standard solution (SKF 525A) was added for final concentration of 4μg/ml. The solution was brought to pH of 10 with the addition of NaOH 2 M. To each sample, 5ml of ethyl ether was added. After horizontal agitation during 10 min and centrifugation at 3000 rpm for 5 min, the organic extract was transferred into a glass tube then evaporated to dryness at 40℃ under a gentle stream of air. The residues were reconstituted by 50μL of ethanol and one microliters were injected into the GC/MS.

Results

Animals experimental results
Lidocaine concentrations were as follows: blood(from heart) 25.2μg/mL, blood (from femoral vein) 15μg/mL, gastric wall 16.9μg/g, gastric content 16.8μg/mL, liver 21.8μg/g, kidney 46.8μg/g, brain 43.6μg/g, spleen 57.9μg/g, lung 19.7μg/g, heart 34.5μg/g, muscle(from left lower extremity) 18.3μg/mL, urine 23.3μg/mL, vitreous humor 2.4μg/mL and bile 6μg/mL(Fig.1.)
Case results

Lidocaine concentrations in samples were as follows: blood (from heart) 18.95μg/mL, gastric content 5.24μg/g and urine 54.4μg/mL (Table 1).

No other drugs or alcohol were detected.

**Table 1** Tissue concentration for lidocaine in the matrixes

<table>
<thead>
<tr>
<th>Matrixes</th>
<th>Lidocaine</th>
</tr>
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<tbody>
<tr>
<td>Blood</td>
<td>18.95μg/mL</td>
</tr>
<tr>
<td>Gastric content</td>
<td>5.24μg/g</td>
</tr>
<tr>
<td>Urine</td>
<td>54.4μg/mL</td>
</tr>
</tbody>
</table>

Discussion

As reported in the present case, analysis results showed the presence of lidocaine in all samples collected. Lidocaine is a drug commonly used as a local anesthetic and as an antiarrhythmic [2-3], it also used as an epidural anesthesia and subarachnoid anesthesia in primary hospital of China [10-12]. It is generally administered intravenously or parenterally, but at blood concentration greater than 8μg/mL, it may appear toxic, greater than 10μg/mL, it may result in death.

According to the results of animal experimental, the concentration of lidocaine in urine and kidney were higher than other matrixes. Also lidocaine was found in vitreous humor and gastric contents. Lidocaine concentrations in blood, urine and gastric content were 18.95μg/mL, 54.4μg/mL and 5.24μg/g from the case. The concentrations found in the case were similar to animal experimental. Our results indicate that the victim had received lidocaine intravenous drip overdose, and the manner was ruled a homicide. The pathologist ruled the cause of death to be cardiac dysrhythmia due to lidocaine effects.

A phenomenon of post-mortem redistribution was naturally suggested. Lidocaine rapidly distributed into well-perfused tissue (lungs, liver, heart, kidney, etc.) after death. The hypotheses reported in the literature could explain the cause of lidocaine concentration in gastric content is redistribution in the early post-mortem period of the lidocaine in the blood. The lidocaine contained in the blood can diffuse towards the well-perfused tissue very early. The distribution of lidocaine in postmortem materials showed significant differences between different organs, the results revealed the manner of death.

It was difficult that interpretation the results by phenomena of post-mortem redistribution and the cause of death. Our report provides useful information from these experiments that autopsy findings should be compared with the results of toxicological analysis.

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