



## Review Article

## Fatal anaphylactic reactions to lignocaine

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## ABSTRACT

Fatal anaphylactic reactions to lignocaine are very rare. In this review of published reports, the main objective is to determine the characteristics of fatal allergic reactions to lignocaine and describe the forensic investigations of anaphylaxis related deaths. From 1957 to 2012, there were seven reports of single case and one report of 8 cases with sufficient information for review. Fatal anaphylactic reactions to lignocaine were generally characterised by fast onset of symptoms (within seconds to <30 min of drug exposure) and rapid progression to cardiopulmonary arrest and death (23 min to ~1 h). Features of cardiovascular, respiratory and neurological system involvements were often seen. Autopsy might reveal laryngeal oedema, pulmonary oedema, cerebral oedema, eosinophil infiltrates in many organs and other changes. Elevated blood tryptase level caused by mast cell degranulation was also used to diagnose acute anaphylaxis.

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## Contents

1. Introduction .....	449
2. Methods .....	449
3. Results .....	450
4. Discussion .....	451
5. Conclusions .....	451
References .....	451

## 1. Introduction

Lignocaine is a commonly used local anaesthetic agent in medical, surgical, ophthalmic, obstetric and dental practice. When used properly [1,2], serious adverse events such as local anaesthetic systemic toxicity (LAST) are extremely uncommon. This should be differentiated from the even rarer anaphylactic reactions since their pathogenesis and specific treatments are very different [1,3].

In this review of published reports, the main objective is to determine the characteristics of fatal allergic reactions to

lignocaine and describe the forensic investigations of anaphylaxis related deaths.

## 2. Methods

To identify relevant reports in indexed journals, a search of Medline (1946–23 June 2016) was conducted, using lignocaine, lidocaine, xylocaine, anaphylaxis and anaphylactic shock as the key words. Google Scholar was also searched to identify additional papers in non-indexed journals and relevant papers missed in the Medline search. Only fatal cases were included in the present review. Non-fatal cases and overdoses of lignocaine were excluded.

The diagnosis of lignocaine induced anaphylaxis was generally based on the acute onset of illness (minutes to hours), the presenting clinical features [4] and exclusion of other sudden-onset multi-system diseases. Overdoses (as indicated by larger

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than recommended doses used for local injections or topical applications and toxic blood lignocaine levels) were excluded.

### 3. Results

The Medline and Google Scholar search had identified 60 original reports of non-fatal and fatal lignocaine induced anaphylaxis. Between 1957 and 2012, 13 reports of fatal cases were published in English [5–9], Russian [10–13], Chinese [14,15], Korean [16] and Japanese [17] languages from indexed [5–13,17] and non-indexed [14–16] journals.

Three papers in Russian language without an abstract [10–12] could not be analysed. One report of sudden death in a 53-year-old man during gingival injection of a therapeutic dose of lignocaine was excluded in view of the marked coronary artery atherosclerosis, large areas of myocardial ischaemic changes and a normal tryptase level [9]. One report in Korean language [16] involving a 67-year-old man with multiple comorbidities was also excluded because the clinical features were atypical, with bronchospasm recurring on day 2 and day 3 and cardiac arrest, ventricular tachycardia and death occurring on day 4 after topical lignocaine spray for bronchoscopy. Therefore, seven reports of single case [5–8,13,15,17] (summarised in Table 1) and one report of 8 cases [14] formed the basis of this review. The case series [14] with forensic investigation data only was described separately.

A healthy 20-year-old man had an anaphylactic reaction to Xylocaine (brand of lignocaine) used as a local anaesthetic for dental procedure [5]. Around 45 s after the injection, he was noted to be pale, soon followed by unconsciousness, irregular breathing and convulsions. Resuscitation failed even with the help of a medical officer. Based on the average duration of unsuccessful on-site resuscitation, the time from symptom onset to death was estimated to be around 30 min.

A 19-year-old woman with histiocytosis X had bronchoscopy performed with lignocaine solution used for topical anaesthesia [6]. She tolerated the procedure well. About 20 min after returning to her room, the patient developed hypotension, tachycardia and obtundation, followed by respiratory arrest. She was intubated. Frothy pulmonary oedema fluid continued to be sucked out. Chest X-ray showed extensive bilateral alveolar infiltrates. Hypotension and refractory bradycardia occurred. She died 5 h after bronchoscopy. If bronchoscopy lasted 30 min and the recovery time in observation room was 1 h, the latent period and time from symptom onset to death were estimated to be around 2 h and 5.5 h.

A 67-year-old man with chronic obstructive pulmonary disease (forced expiratory volume in 1 s 0.5 L) and occasional ventricular ectopics was given Xylocaine puffs for topical anaesthesia before bronchoscopy [7]. Two minutes later, he developed wheeze, dyspnoea and cyanosis, not responding to inhaled salbutamol. One minute later, he had a cardiorespiratory arrest. Manual ventilation

**Table 1**  
Fatal anaphylactic reactions to lignocaine after local injection or topical application.

Subject	Comorbidities	Indication	Dose	Latent period	Onset to death	Clinical features before cardiorespiratory arrest	Main autopsy findings; post-mortem blood levels	Ref.
1. M/20	None	Dental surgery	16 mg <sup>a</sup>	~45 s	? ~30 min	Pallor, LOC, irregular breathing, convulsions	Subepicardial/myocardial petechial haemorrhages, mild cerebral oedema, marked congestion of meningeal/cerebral vessels	[5]
2. F/19	Histiocytosis X	Bronchoscopy	<300 mg <sup>b</sup>	? ~2 h	? ~5.5 h	ARDS, shock, refractory bradycardia	ARDS, histiocytosis X <sup>g</sup>	[6]
3. M/67	COPD	Bronchoscopy <sup>c</sup>	80 mg <sup>d</sup>	2 min	23 min	Severe bronchospasm, cyanosis	Left sided pneumothorax <sup>e</sup> , extensive centrilobular emphysema <sup>e</sup>	[7]
4. F/43	Neck/back pain	Muscle spasm and pain	50 mg <sup>e</sup>	? s	? ~1 h	Dizziness, anxiety, LOC, convulsions, VF	Marked alveolar haemorrhage/pulmonary oedema; lignocaine 1.1 mg/L, <sup>f</sup> tryptase 37.6 mg/L (ref 0.4–10.9 mg/L)	[8]
5. F/50	Multiple allergies	Lumbar pain	80 mg	<2 min	NI	"Anaphylactic shock"	"Diagnosis confirmed at autopsy, mast cell degranulation in soft tissues, characteristic changes in internal organs"	[13]
6. F/44	Laryngeal obstruction	Tracheostomy	1000 mg	? <5 min	~1 h	Agitation, cyanosis, dyspnoea	Severe laryngeal oedema, tracheal stenosis, <sup>g</sup> pulmonary oedema, cerebral oedema, eosinophilic infiltration in multiple organs; lignocaine 0.41 mg/L	[15]
7. F/4	None	Dental surgery	18 mg	<30 min	NI	NI	Severe laryngeal oedema, severe pulmonary oedema, alveolar haemorrhage, eosinophilic infiltration in alveoli and interstitial tissues; histamine 260 nmol/L (ref 0.74–1.54 nmol/L)	[17]

ARDS, adult respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; LOC, loss of consciousness; NI, no information; VF, ventricular fibrillation.

Other drugs given with lignocaine:

<sup>a</sup> Adrenaline 1:50,000.

<sup>b</sup> Hydromorphone 1 mg, atropine 0.5 mg.

<sup>c</sup> Fatal anaphylactic reactions before bronchoscopy performed.

<sup>d</sup> Atropine 0.5 mg, salbutamol 5 mg.

<sup>e</sup> Botox 100 units.

<sup>f</sup> Pre-mortem blood.

<sup>g</sup> Related to underlying medical conditions.

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