



## Case report

## Adrenaline toxicity following accidental administration of the 1:1000 solution during dental procedures: Four case reports

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## ARTICLE INFO

**Article history:**  
Received 30 April 2011  
Received in revised form  
7 November 2011  
Accepted 13 February 2012  
Available online xxx

**Keywords:**  
Myocardial damage  
Dental  
Local anesthesia  
Muscle weakness  
Tremor

## ABSTRACT

Four patients aged between 35 and 50 years attended the out patients department of a dental hospital for tooth extraction. Following administration of, what was thought to be the local anesthetic, Lignocaine, to the gum and sub mucosa, they all collapsed. What had, in fact, been injected was 1:1000 adrenaline. We would like to report the symptoms, signs and investigation findings that followed. Significantly elevated Troponin T, CPK (total), CPK (MB) and ECG changes were seen. Electromyography and Nerve Conduction Studies showed a myopathic pattern and reduction in motor and sensory conduction respectively. These patients were followed up for a period of five years. Long term effects such as tremor, muscle weakness, easy fatigability and shortness of breath on exertion, which is not reported in the literature, were reported by all patients.

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## 1. Introduction

Adrenaline is a naturally occurring catecholamine synthesized from tyrosine in the adrenal medulla. It acts on the cardiovascular system, central nervous system and smooth muscles to bring about the physiological responses in the "fight or flight" reaction.

The 1:1000 solution of Adrenaline is used in emergencies such as acute severe asthma, anaphylaxis and cardiac arrest. The 1:80,000, 1:100,000 and weaker solutions are routinely used combined with local anesthetics to prolong the anesthetic effect. There are several studies and reports on the systemic effects of local anesthetics containing adrenaline used in dental practice. However, we were unable to find reports of the effect of gingival infiltration of the 1:1000 solution of adrenaline. Table 1.

## 2. Case reports

## 2.1. Case 1

A 50 year old female batik clothes maker with a past history of hypercholesterolemia attended the dental clinic for removal of her third mandibular molar tooth. Following injection of the 'local

anesthetic' she experienced severe pain at the site of injection. She also complained of a severe headache, dizziness and chest pain associated with palpitations. She had collapsed and was unconscious for 3 h. Her blood pressure (BP) was 89/43 mmHg and pulse rate was 60/minute with a low volume. ECG revealed T inversions in I, I, AVL, V2–V6 leads. Cardiac markers were elevated. 2D Echocardiogram showed an otherwise structurally normal heart with a sclerosed aortic valve. Nerve Conduction Studies (NCS) and Electromyography (EMG) showed a slight reduction in motor conduction. She was reviewed three weeks later and complained of vertigo, tremor, muscle weakness, easy fatigability and shortness of breath (SOB) on exertion. On examination she was found to have a fine tremor. We were unable to review her in five years as she had moved from the area.

## 2.2. Case 2

A 47 year old female seamstress attended the dental clinic for extraction of an upper pre molar tooth. Following injection of the 'local anesthetic', she experienced severe pain at the site of injection, severe headache and chest pain associated with palpitations and dizziness. She had collapsed and was unconscious for a few minutes. On examination her heart rate was 100/minute and blood pressure was 90/50 mmHg. ECG revealed T inversion in V1 and Troponin T was positive while CPK levels were normal. 2D Echocardiogram showed a structurally normal heart. She also

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**Table 1**

Clinical features and investigation findings.

Case number	1	2	3	4
Age and Sex	50 yrs, female	47 yrs, female	42 yrs, male	37 yrs, female
Severe pain at site	+	+	–	+
Severe headache	+	+	–	+
Chest pain	+	+	+	+
Loss of consciousness	+ (~3 h)	+ (minutes)	+ (tightening type) + (~1 h)	+ (tightening type)
Troponin T	+	+	+	+
CPK (Total) (N-24–190u/l)	232	81	288	103
CPK (MB) (N-1.8–24u/l)	26	15	26	12
ECG	T inversion (I, AVL, V2–V6)	T inversion (V1)	T inversion (AVL)	Normal
NCS and EMG done 2 days later	Reduction in motor conduction	Myopathic pattern	Reduction in sensory & motor conduction in lower limbs	Normal
Days in hospital	10	04	09	04

+ = present.

– = not present.

complained of muscle weakness. Her EMG showed a myopathic pattern. Three weeks later she was found to have a fine tremor, muscle weakness, easy fatigability and SOB on exertion. Upon review five years later, she still complained of easy fatigability, SOB on exertion and had a fine tremor on examination. However, muscle weakness was not present.

### 2.3. Case 3

A male vegetable vender aged 42 years who attended the dental clinic for the removal of an upper incisor tooth was administered the 'local anesthetic'. He developed a severe tightening type of chest pain associated with palpitations, a severe headache and collapsed soon after and remained unconscious for about an hour. On examination his blood pressure was 122/64 mmHg and pulse rate was 92/minute. ECG revealed T inversion in the AVL lead. Cardiac markers were elevated. He was also found to have generalized muscle weakness with reduced power and tone in the lower limbs. EMG and NCS showed reduced sensory and motor conduction in the lower limbs. A review done three weeks later revealed that the patient had a coarse tremor, muscle weakness, easy fatigability and shortness of breath on exertion. He was unable to come for review as requested in five years as he still suffers from severe muscle weakness and is unable to walk without crutches and gets severe dyspnea on mild exertion.

### 2.4. Case 4

A 37 year old female, who makes food packets, attended the dental clinic for the extraction of a third lower molar tooth. Following administration of the 'local anesthetic' she experienced severe pain at the site of injection, severe tightening type chest pain associated with palpitations and a severe headache. There was no loss of consciousness. On examination her blood pressure was 90/50 mmHg and pulse rate was 64/min. No abnormalities were detected in her ECG. Troponin T was positive while CPK levels were normal. She was finding it difficult to perform fine movements of the hand following the incident. On reviewing the patient three weeks later she complained of shortness of breath on exertion, easy fatigability, and was found to have muscle weakness and fine tremor. On review five years later, she still had SOB on exertion and a fine tremor. However she did not have easy fatigability or muscle weakness.

All were admitted to a tertiary care hospital after resuscitation with cases 1 and 3 requiring treatment in the Intensive Care Unit. All of them had normal urine myoglobin levels, and Troponin T was back to normal on discharge. The stay in hospital ranged from 4 to 10 days. EMG repeated on all of them three weeks later was normal.

### 3. Discussion

Local anesthesia is without doubt the most frequently used drug in dentistry and in medicine.<sup>1</sup> Since the beginning of the last century, vasoconstrictors have been added to local anesthesia solutions to reduce toxicity and prolong the activity of local anesthetics. Adrenaline is one of the most common drugs used for this purpose. The 1:80,000 and 1:100,000 and weaker solutions are routinely used combined with local anesthetics to bring about the above effects.

Adrenaline increases both the force and rate of contraction of the heart resulting in an increase in the systolic blood pressure and the cardiac output.<sup>2,3</sup> The total peripheral resistance decreases due to the collective effect of vascular beds in muscle and heart being dilated, (increasing the blood supply to those areas) and the vascular beds in skin and viscera being constricted (reducing the blood supply to those areas). The O<sub>2</sub> consumption of the cells increases. Adrenaline also stimulates the central nervous system leading to tremors and feelings of fear and anxiety. It also results in relaxation of bronchi, intestine and bladder and constriction of sphincters. All these contribute in bringing about the physiological responses in the "fight or flight" reaction.<sup>2,3</sup>

When this drug is administered the above effects are brought about in varying degrees according to the concentration of the solution. Thus, it is known to cause an increase in myocardial excitability, causing extra systoles, and occasionally, more serious cardiac arrhythmias.<sup>2,4</sup> Adrenaline is also known to cause anxiety, headache, hypertension, dizziness and weakness. The use of vasoconstrictors combined with local anesthesia in patients with coronary heart disease is controversial and there is concern regarding the risk of cardiac decompensation.<sup>1</sup> Therefore they are generally contraindicated in patients with cardiac disease.<sup>5</sup>

However, work done by Blinder and co-workers showed that when the local anesthetic contained a vasopressor, there was a greater incidence of tachycardia but less arrhythmia or ST depression.<sup>6</sup> Conrado et al. have shown that dental extraction performed under anesthesia with 1:100,000 adrenaline does not imply additional ischemic risks, as long as performed with good anesthetic technique and maintenance of the pharmacological treatment prescribed by the cardiologist.<sup>7</sup>

A study was conducted to evaluate the electrocardiographic and blood pressure parameters during restorative dental procedure under local anesthesia, with and without a vasoconstrictor, in patients with coronary artery disease. No difference was observed in blood pressure, heart rate, or evidence of ischemia and arrhythmias in either group.<sup>4</sup> Another study concluded that lidocaine-epinephrine (1:80,000) was safe, and had few, if any, hemodynamic consequences in patients with cardiovascular

disease.<sup>8</sup> It was also recommended to limit the amount of epinephrine containing local anesthetics to a maximum of 4.4 ml of a 1:18,000 solution or to use epinephrine free solutions such as prilocaine with felypressin as the first choice for dental treatment under local anesthesia in cardiac transplant patients.<sup>9</sup>

However the literature search failed to find adrenaline toxicity following injection of the 1:1000 solutions. Therefore, this case series may be the first to report the immediate/delayed clinical features, together with investigation findings.

In all our cases they had experienced severe pain at the site of injection. This could be the result of severe vasoconstriction of the blood vessels in the adjacent tissue. Severe headache, dizziness and loss of consciousness can also be explained by the fact that vascular beds in the brain, skin and viscera being constricted by adrenaline in order to increase the blood supply to the heart and muscle. Furthermore, the low blood pressure that three of them had, leads to lack of O<sub>2</sub> to the brain, which might have contributed to the severe headache and transient loss of consciousness.

Blood pressure one hour after the incident was low in three of them, while in case 3 it was relatively normal. Although the systolic blood pressure should increase due to the effects of adrenaline, a drop in blood pressure may have occurred due to compromised cardiac muscle resulting from ischemia. A significant myocardial ischemic event results in low blood pressure due to low cardiac output.<sup>10</sup> As a result, a refractory tachycardia can occur as seen in case number 2, or, due to cardiac compromise, a normal pulse rate or bradycardia can occur. (Cases 1 & 4).

All the patients had experienced palpitations and chest pain with two of them experiencing a chest pain of a tightening nature. This could be explained by the fact that increased heart rate followed by arrhythmia leads to a lack of blood supply to the cardiac muscle causing ischemia. Furthermore, adrenalin may have caused spasm of the coronary arteries by a direct effect. Severe central chest pain has been reported in a 23 year old after local gingival injection of a local anesthetic containing 0.36 µg of adrenaline and noradrenaline.<sup>5</sup> The ECG taken while in pain had showed ST depression of 3 mm in all limbs and precordial leads with ST elevation of 2 mm in aVR. Following sub lingual nitroglycerine the pain had decreased and ECG at two hours had been normal.<sup>5</sup> Likewise, in our cases, ischemic changes were seen on ECG in three cases. In all four cases Troponin T, which is considered to be the most sensitive and specific indicator of myocardial damage, was elevated. In addition, in two of the cases Total CPK, and the cardio specific MB levels, was elevated. Case 4 was the last to be injected and the doctor had stopped giving the drug and checked it, while the other three were having signs and symptoms. Therefore, she was the least affected. We conclude that most probably all four suffered cardiac damage due to adrenaline induced coronary artery spasm and arrhythmia.

Stimulation of the central nervous system by adrenaline is known to cause tremors. But a literature search failed to reveal muscular weakness, conduction defects and delayed effects of adrenaline toxicity. In three of the cases changes in NCS and EMG were seen; this, we are unable to explain.

On review, three weeks later all 4 patients were experiencing tremors. They also complained of muscle weakness, easy fatigability and shortness of breath on exertion. None of these delayed effects have been reported.

Five years later the patients were again reviewed but only case numbers 2 and 4 showed up (these two were the least affected of the four patients). Case number 3 was unable to come due to severe muscle weakness and being unable to walk without crutches. He also has severe dyspnea on mild exertion and course tremors. We were unable to contact case number 1, who was also severely affected initially, and had the longest stay of 10 days in hospital including ICU care.

Case number 2 complained of a significant increase in shortness of breath on exertion for which she had to undergo an exercise ECG test. This was found to be strongly positive while the 2D Echocardiogram and the coronary angiogram were found to be normal. She has experienced several syncopal attacks following exertion. These have significantly affected her day to day activities. On examination she was found to have fine tremors. Case number 4 also complained of increased shortness of breath over the years associated with a burning sensation in the back which radiates to the upper limbs on exertion. On examination she was found to have fine tremors.

We are reporting these cases, for the benefit of the scientific society, in order to enlighten them on these effects of adrenaline which have not been reported before.

#### 4. Medico-legal aspects

The 10 ml multi dose vials of 1:1000 adrenaline, and the 30 ml vial of lignocaine containing 2% adrenaline (1:80,000) used at that time were both brown and similar in shape and height with the lignocaine vial being wider.

The usual procedure followed had been that the nurse draws the local anesthetic into several syringes which are kept ready in trays by the side of the patient. The dental surgeon then administers the drug to the gum and sub mucosa of all the patients who require it, one after the other.

Doctors and nurses should be responsible for checking the drug being drawn and administered, respectively. If double checking had been done this accident may have been averted. Following this incident stringent measures including awareness programs, double checking, use of single dose ampoules, ampoule kept with the syringe and other safety measures have been instituted to prevent such episodes occurring in future.

**Conflict of interest**  
None declared.

**Funding**  
None declared.

**Ethical approval**  
None declared.

#### References

- Kaufman E, Garfunkel A, Findler M, Elad S, Zusman SP, Malamed SE, et al. Emergencies evolving from local anaesthesia. *Refuat Hapek Vehashitayim* 2002;19(1):13–8, 98.
- Guyton C, Hall JE. Text book of physiology. 11th ed. Reed Elsevier India Private Limited, India. p. 757–8.
- Ganong WF. Review of medical physiology. 22nd ed. A Lange Medical Book. p. 359–60.
- Neves RS, Neves IL, Giorgi DM, Grupi CJ, César LA, Hueb W, et al. Effects of epinephrine in local dental anesthesia in patients with coronary artery disease. *Arq Bras Cardiol* 2007;88(5):545–51.
- González Enriquez S, de la Torre Hernández JM, Sainz Laso F. Clinical episode suggestive of left main coronary artery spasm after gingival anesthetic infiltration. *Rev Esp Cardiol* 2003;56(10):1033–5.
- Blinder D, Manor Y, Shemesh J, Taicher S. Electrocardiographic changes in cardiac patients having dental extractions under a local anesthetic containing a vasopressor. *J Oral Maxillofac Surg* 1998;56(12):1399–402.
- Conrado VC, de Andrade J, de Angelis GA, de Andrade AC, Timmerman L, Andrade MM, et al. Cardiovascular effects of local anesthesia with vasoconstrictor during dental extraction in coronary patients. *Arq Bras Cardiol* 2007;88(5):507–13.
- Niwa H, Sugimura M, Satoh Y, Tanimoto A. Cardiovascular response to epinephrine-containing local anesthesia in patients with cardiovascular disease. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001;92(6):610–6.
- Meechan JC, Parry G, Ratray DT, Thomason JM. Effects of dental local anesthetics in cardiac transplant recipients. *Br Dent J* 2002;192(3):161–3.

