

IN THE CORONERS COURT
OF VICTORIA
AT MELBOURNE

Court Reference: COR 2013 4295

FINDING INTO DEATH WITHOUT INQUEST

Form 38 Rule 60(2)

Section 67 of the Coroners Act 2008

I, AUDREY JAMIESON, Coroner having investigated the death of KHODR EL MUSTAPHA

without holding an inquest:

find that the identity of the deceased was KHODR EL MUSTAPHA

born 10 September 1936

and the death occurred on 24 September 2013

at the Royal Melbourne Hospital, 300 Grattan Street, Parkville 3052

from:

- 1 (a) COMPLICATIONS OF REACTION TO AN IRON INFUSION IN A MAN WITH ISCHAEMIC HEART DISEASE
- 2 BONE MARROW HYPOPLASIA (IDIOPATHIC)

Pursuant to section 67(1) of the **Coroners Act 2008**, I make findings with respect to **the following circumstances:**

1. Mr Khodr El Mustapha was 77 years of age at the time of his death. He lived in Glenroy East.
2. Mr El Mustapha's medical history included iron deficiency anaemia of unknown cause, hypertension¹ and diabetes mellitus type 2.² Mr El Mustapha was from Lebanon and had

¹ Hypertension is a consistent blood pressure greater than 140/90mmHg.

² Diabetes mellitus type 2 is a metabolic disorder that is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency.

previously undergone gastroscopies³ overseas to investigate his anaemia.⁴ According to documentation in his medical record, Mr El Mustapha reported the gastroscopies were unable to find a cause of the anaemia. Mr El Mustapha was allergic to aspirin and the antibiotics sulfamethoxazole and trimethoprim (Bactrim).

3. Mr El-Mustapha attended the Royal Melbourne Hospital (RMH) Emergency Department (ED) on Friday 20 September 2013 with tiredness and lethargy. Mr El Mustapha had blood tests revealing low haemoglobin at 69grams/decilitre.⁵ The doctors suggested a packed red cell blood transfusion, but Mr El-Mustapha declined treatment on that day, wishing to wait for the issue of a Medicare card.⁶
4. Mr El-Mustapha re-presented to the RMH on Monday 23 September 2013, after having received a Medicare card, and was admitted to the ED short stay unit for a blood transfusion. The management plan included consideration of iron transfusion if blood tests indicated iron deficiency.
5. Mr El Mustapha had blood tests revealing:
 - a. lower haemoglobin from 69 to 66g/dLitre;
 - b. low mean cell volume;
 - c. low serum ferritin and iron; and
 - d. low transferrin, or total iron binding capacity.
6. The blood tests performed diagnosed iron deficiency anaemia (IDA).⁷ The RMH ED short stay pathway for blood transfusion was commenced. The consent for blood component transfusion was signed by Mr El Mustapha, for which his family provided interpreting assistance.
7. The two units of packed red blood cell (PRBC) transfusion occurred overnight, and was completed by 9.45am. An iron infusion (iron polymaltose, Ferrum H)⁸ was commenced according to the RMH renal protocol on 24 September 2013 at 3.35pm. At 5.40pm, Mr El

³ Examination of the upper digestive tract (the stomach and duodenum) using a long, thin, flexible tube with a camera.

⁴ Anaemia is a decrease in number of red blood cells (RBCs) or less than the normal quantity of haemoglobin in the blood.

⁵ The normal range is 130-170g/dLitre.

⁶ Mr El-Mustapha was a recent arrival to Australia and was awaiting a Medicare card.

⁷ Iron deficiency results when iron losses or requirements exceed absorption, and the causes are often multifactorial.

⁸ E Newnham, I Ahmad, A Thornton, et al., 'Safety of iron polymaltose given as a total dose iron infusion' (2006) *Internal Medicine Journal*, 36: 672-674.

Mustapha developed swelling of his lip and was reviewed by a doctor. Upon review, Mr El Mustapha's lips and cheeks were swollen, but his tongue and internal mouth appeared normal. There was diffuse wheeze audible in the lungs. At this time, Mr El Mustapha's heart rate and blood pressure were normal. The staff ceased the iron polymaltose infusion. After consultation with the ED Physician, 100mg hydrocortisone⁹ and 50mg intramuscular (IM) promethazine¹⁰ were administered at 5.50pm, followed by 300ug IM adrenaline and inhaled salbutamol¹¹ at 6.10pm.

8. At 7.00pm, Mr El Mustapha felt nauseated, vomited, and then lost consciousness. Advanced life support was commenced and a Code Blue called. During the resuscitation there was some return of spontaneous circulation and an electrocardiograph (ECG)¹² showed possible myocardial ischaemia, however further deterioration occurred and despite appropriate resuscitation attempts, including temporary pacing, Mr El Mustapha died.
9. It appears that Mr El Mustapha remained in the ED Short Stay Unit following the onset of his symptoms, the diagnosis of anaphylaxis and the administration of adrenaline without continuous ECG monitoring. The last set of nursing observations were at 6.15pm, five minutes after the administration of adrenaline.¹³

INVESTIGATIONS

10. Dr Linda Iles, Forensic Pathologist at the Victorian Institute of Forensic Medicine (VIFM), performed a post mortem examination on the body of Mr El Mustapha, reviewed a post mortem CT scan and reviewed the Victorian Police Report of Death, Form 83 and e-Medical Deposition. Anatomical findings included mild residual upper airway oedema, oedema of large and medium sized bronchi, pulmonary oedema, moderate double vessel coronary artery atherosclerosis associated with patchy myocardial scarring, pituitary adenoma, hypoplastic bone marrow, and mild chronic small vessel cerebral ischaemic changes. No evidence of upper gastrointestinal tract haemorrhage was identified.

⁹ Steroid to decrease allergy and inflammation.

¹⁰ Antihistamine to decrease allergy.

¹¹ Medication to treat wheezing/asthma.

¹² A transthoracic interpretation of the electrical activity of the heart over a period of time, as detected by electrodes attached to the outer surface of the skin and recorded by a device external to the body. An ECG will show any silent myocardial ischaemia or infarction and demonstrate cardiac arrhythmias.

¹³ Melbourne Health Executive Director Clinical Governance and Medical Services Dr Peter Bradford later confirmed vital sign observations were performed at 6.15pm and later at 7.00pm.

11. Dr Iles commented that while at post mortem examination there was no evidence of gross upper airway oedema or swelling of the tongue, the oedema seen in the large and medium calibre airways within the lung is in keeping with an anaphylactoid reaction. Dr Iles stated that these symptoms as described in Mr El Mustapha's RMH record are in keeping with an anaphylactoid reaction to the iron infusion. Dr Iles noted this is a well-recognised complication of such treatment.
12. Dr Iles highlighted that Mr El Mustapha also had underlying ischaemic heart disease with severe double vessel coronary artery atherosclerosis and evidence of previous ischaemic changes to his heart. Dr Iles stated that in this context, it is likely the physiological stress of anaphylactoid reaction has precipitated Mr El Mustapha's death.
13. Dr Iles noted post mortem serum tryptase is only mildly elevated, but stated this does not preclude the possibility of an anaphylactoid reaction during life. No ante mortem specimens were available for analysis.
14. Dr Iles ascribed the cause of Mr El Mustapha's death to complications of reaction to an iron infusion in a man with ischaemic heart disease. Contributing to his death but not directly related to the cause was his underlying condition of bone marrow hypoplasia¹⁴ (idiopathic).
15. The Coroner's Prevention Unit (CPU)¹⁵ reviewed the indications and consent for iron infusions and the management of Mr El Mustapha's apparent anaphylactoid reaction on my behalf.

Iron Infusion

16. According to the international clinical database Up to Date, the following management of iron deficiency anaemia and iron infusion is suggested.¹⁶

'Because of ease of treatment, we recommend that patients with uncomplicated iron deficiency anaemia be treated with oral iron rather than an intravenous (IV) iron formulation (Grade1B). For patients who have a history of intolerance to oral iron therapy, published evidence supports a larger and earlier role for intravenous iron.'

¹⁴ The bone marrow contains very few blood cells.

¹⁵ The Coroners Prevention Unit (CPU) was established in 2008 to strengthen the prevention role of the coroner. The unit assists the coroner with research in matters related to public health and safety and in relation to the formulation of prevention recommendations, as well as assisting in monitoring and evaluating the effectiveness of the recommendations. The CPU comprises a team with training in medicine, nursing, law, public health and the social sciences.

¹⁶ Up to Date clinical database accessed 21 May 2014 at www.uptodate.com.

17. In 2009, an Australian national meeting brought together a multi-professional group of experts with a common interest in improving the management of iron deficiency anaemia. This led to the publication of a clinical update to guide the diagnosis and management of iron deficiency anaemia. The article was published in the Medical Journal of Australia in November 2010, as a national educational strategy to improve practice in this area.¹⁷
18. The CPU informs me that while oral iron remains the cornerstone of IDA therapy, some patients will require intravenous (IV) iron therapy. There have been concerns about the risk of serious allergic reactions with the administration of IV iron. It was established that 0.6% of people administered the high molecular weight iron dextran, which is no longer available in Australia, had life-threatening allergic reactions.¹⁸
19. According to Up to Date, while the preponderance of published evidence indicates that low molecular iron preparations are associated with fewer adverse reactions than high molecular weight iron preparations, it is not otherwise possible at this time to conclude that any one intravenous iron preparation is safer than another.
20. According to results from an Australian audit of the in hospital safety and tolerability of iron polymaltose, which was the type of iron infusion Mr El Mustapha was administered, in 401 infusions there were no cases of anaphylaxis or other cardio respiratory compromise identified, however there were infrequent minor side effects during infusion.¹⁹ I note however that the product information for iron polymaltose states ‘Since parental use of complexes of iron and carbohydrates has resulted in fatal anaphylactoid reactions, iron polymaltose should be used only in patients in whom a clearly established indication for parenteral iron therapy exists, confirmed by appropriate laboratory tests.’
21. The 2014 Victorian Department of Health (as it then was) guideline ‘*Guiding principles for the development of intravenous (IV) iron infusion practice*’²⁰ suggests that when establishing or reviewing policies, consideration must be given to:
 - a. patient consent;
 - b. preparation and storage of infusion once reconstituted per product information;

¹⁷ S Pasricha, C Flecknow-Brown, K Allen et al., ‘Diagnosis and management of iron deficiency anaemia: a clinical update’ (2010) *Medical Journal of Australia*, 193 (9): 525-532.

¹⁸ R Hamstra, M Block, A Schocket, ‘Intravenous Iron dextran in Clinical Medicine’ (1980) *JAMA*, 243: 1726-1731.

¹⁹ Above no 17.

²⁰ www.health.vic.gov.au/bloodmatters/management; accessed 15 April 2015.

- c. anaphylaxis protocol;
 - d. approval from related committees within the facility; and
 - e. awareness and education to relevant staff.
22. The Victorian Department of Health have published several sample hospital policy templates to guide the development of hospital specific IV infusion protocols. For example, Ballarat Health Service's Iron Polymaltose Infusion Clinical Practice Guidelines²¹ state the indications for iron infusion are:
- a. oral therapy is contra-indicated;
 - b. enteric absorption of iron is defective;
 - c. patient non-compliance or intolerance;
 - d. inadequate response to oral iron; and
 - e. the intramuscular route is impractical or unacceptable.

Management of anaphylaxis

23. The CPU informs me that following the onset of symptoms of anaphylaxis and the administration of adrenaline,²² continuous ECG monitoring in an environment where resuscitation facilities are available is required. It appears Mr El Mustapha remained in the ED Short Stay Unit and appears to have not been monitored by ECG.
24. Given the cause of Mr El Mustapha's death was an anaphylactic reaction in a man with ischaemic heart disease associated with an iron infusion, the CPU requested further information from the RMH (Melbourne Health) treating doctors.
25. The statements from Melbourne Health were sought in respect of the indications for the infusion, whether specific consent had been obtained and whether an iron infusion was normally administered in the Short Stay Unit of the ED. In addition, the CPU requested information regarding the monitoring of Mr El Mustafa in the Short Stay Unit and following the administration of adrenaline.

²¹ www.health.vic.gov.au; accessed 15 April 2015.

²² Adrenaline is a drug administered to treat cardiac arrest and other cardiac dysrhythmias resulting in diminished or absent cardiac output.

26. RMH Medical Administrator Dr Malcom Mohr, and later Executive Director Clinical Governance and Medical Services Dr Peter Bradford, both provided statements outlining the RMH incident management and recommendations arising from an internal hospital review.
27. Mr El Mustapha's diagnosis of iron deficiency anaemia was confirmed and therefore an iron infusion was administered, however the RMH appears to have relied upon historical clinical information, with no investigations performed at the RMH to determine the cause of the iron deficiency.
28. According to the RMH statements, iron infusions are commonly carried out in the RMH ED Short Stay Unit. However, at the time of Mr El Mustapha's presentation, it was not standard practice to obtain specific consent for individual medications, nor was there any indication that any potential risks were discussed with the family.
29. Following a review of Mr El Mustapha's death, a change in practice was implemented where the RMH staff obtain consent prior to the administration of an iron infusion. The changes in the iron infusion consent were incorporated in a broader review undertaken by the RMH of current consenting practice.
30. Dr Mohr also stated that Mr El Mustapha's death was reviewed in the ED mortality meeting and a hospital root cause analysis had been conducted. The review and recommendations focussed on anaphylaxis recognition and management. The anaphylaxis was reported to the Therapeutic Goods Association (TGA) Adverse Drug Reactions Advisory Committee (ADRAC).²³ Education was developed on anaphylaxis and presented to clinicians at a hospital grand round, in addition to the general nursing and medical clinical education.

COMMENTS

Pursuant to Section 67(3) of the **Coroners Act 2008**, I make the following comments connected with the death:

1. The investigation identified a number of shortfalls in the management of Mr El Mustapha at the Royal Melbourne Hospital, including the failure to move Mr El Mustapha to a resuscitation cubicle when it was deemed that he was having an anaphylactic response to the iron polymaltose infusion and/or when he was administered adrenaline. The failure to move Mr El Mustapha appears to have impacted upon the level of monitoring he subsequently received, including an

²³ The Australian adverse drug reaction reporting system involves the reporting of adverse drug reactions from health professionals to ADRAC.

apparent absence of ECG monitoring, which I am informed is indicated following the onset of symptoms of anaphylaxis and the administration of adrenaline.

2. I however accept the Royal Melbourne Hospital's internal review, subsequent acknowledgements and restorative measures taken in areas of clinical education of anaphylaxis management and the requirement of patient consent for iron infusion, and commend these initiatives.

RECOMMENDATIONS

Pursuant to Section 72(2) of the **Coroners Act 2008**, I make the following recommendation connected with the death:

1. It appears that there were several contributing factors to the death of Mr El Mustapha from anaphylaxis. The first was the indication for the iron infusion. It appears Mr El Mustapha had had prior gastroscopies overseas to look for a cause of the anaemia but was awaiting a repeat gastroscopy organised by a General Practitioner to search for a current cause of anaemia.
2. There is no documentation of contraindications for Mr El Mustapha to commence oral iron supplements. Therefore, it appears that Mr El Mustapha had neither been completely investigated nor commenced on oral iron prior to the commencement of the iron transfusion.
3. Following the death of Mr El Mustapha, the Royal Melbourne Hospital have developed a more comprehensive consent procedure for iron infusions and a standard anaphylaxis procedure. The anaphylaxis procedure is supported by educational strategies to assist staff in the early identification of anaphylaxis and correct medical management.
4. Dr Bradford states that the Royal Melbourne Hospital have implemented changes to improve both the knowledge and understanding of anaphylaxis by the nursing and medical staff, and the need for close monitoring following the administration of adrenaline, which I commend.
5. Although there is an '*Iron Infusion*' document located in Mr El Mustapha's Royal Melbourne Hospital medical record, which lists indications and contra-indications, the document does not cover the pre-treatment investigation of anaemia, indications for an iron infusion, consent and the most appropriate locations within the hospital to deliver an iron infusion.
6. I therefore **recommend** that Melbourne Health reviews their clinical practice guideline with an aim of developing a clinical practice guideline for iron infusion that includes pre-treatment investigation of anaemia, indications for an iron infusion, consent requirements and indicates the

most appropriate locations within the hospital to deliver an iron infusion taking into account the need for close monitoring of patients in these circumstances.

FINDINGS

I accept and adopt the medical cause of death as identified by Dr Linda Iles and find that Mr Khodr El Mustapha died from complications of reaction to an iron infusion in a man with ischaemic heart disease. Contributing to his death but not directly related to the cause was his underlying condition of bone marrow hypoplasia²⁴ (idiopathic).

I direct that this finding be published on the internet.

I direct that a copy of this finding be provided to the following:

Mrs Wafaa El BeyRoutie

Mr Mahmoud El Moustapha

Dr Malcolm Mohr, Medical Administrator, Melbourne Health

Australasian College for Emergency Medicine

The Society of Hospital Pharmacists of Australia

Royal Australasian College of Physicians

Adverse Drug Reaction Advisory Committee, Therapeutic Goods Administration

Ms Jennifer Williams on behalf of the Australian Red Cross Blood Service

Signature:


AUDREY JAMIESON

CORONER

Date: **2 December 2015**



²⁴ The bone marrow contains very few blood cells.