Major Haemorrhage in the Remote and Retrieval Environment

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RFDS

Aims

- Audit approach to major haemorrhage within RFDS (WO)
- Ascertain current major haemorrhage strategies within aeromedical retrieval organisations worldwide
- Evaluate potential solutions to shortfalls in care

A bloody revolution

- Greater understanding of pathophysiology of major haemorrhage and its associated coagulopathy (Brohi *et al* 2008)
- Development of the concept of damage control resuscitation - it's not just surgeons who stop bleeding (Beekley 2008)
- The earlier and more aggressive use of fresh frozen plasma (Hess *et al* 2008)
- Introduction of novel therapeutic agents (Berkhof & Eikenboom 2009), new roles for old agents (CRASH-2 2010) and changes to blood product preparations (Bruce & Nokes 2008; Rahe-Meyer *et al* 2009)
- Evolution of Major Haemorrhage Protocols (O'Keeffe *et al 2008;* Dente *et al* 2009)

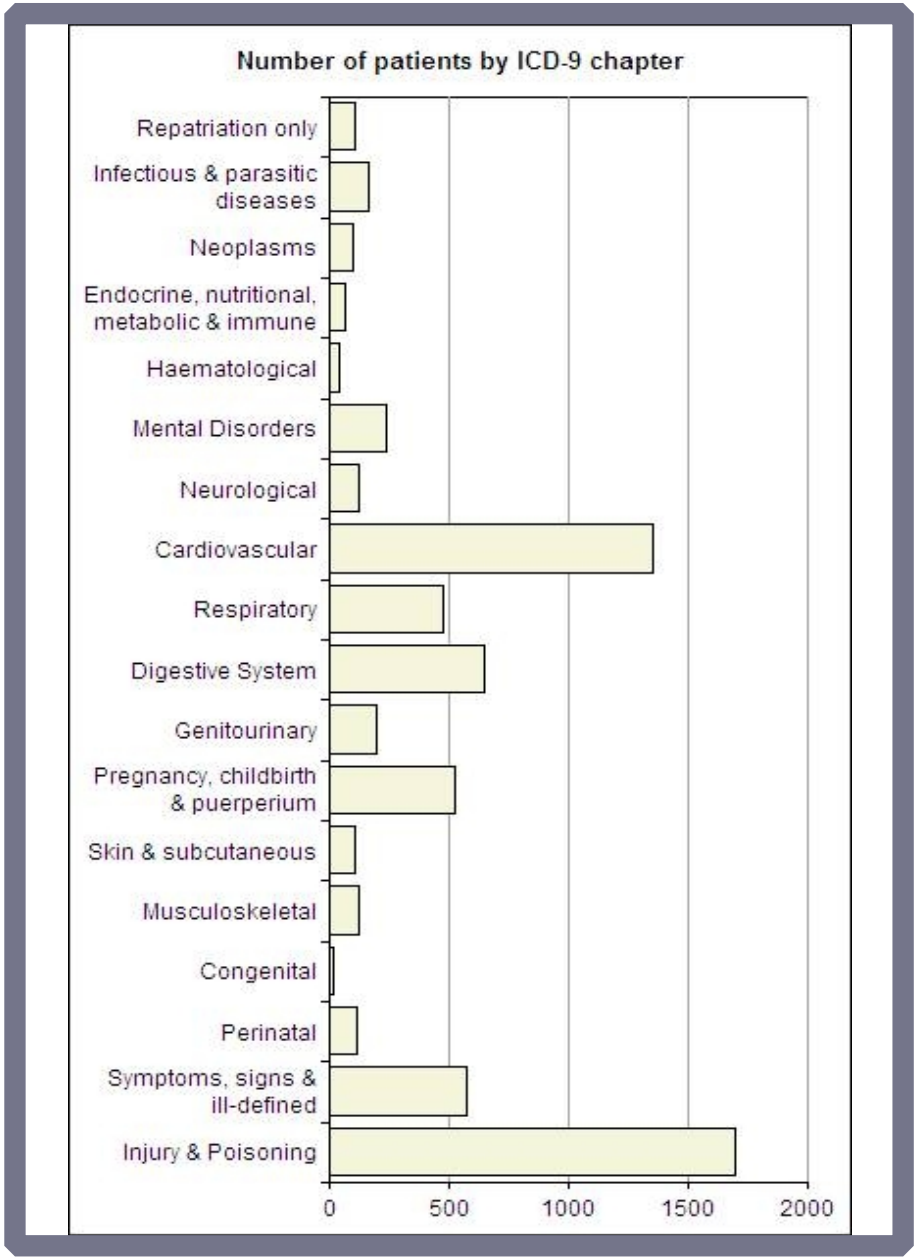
The Western Australian Situation

Methods

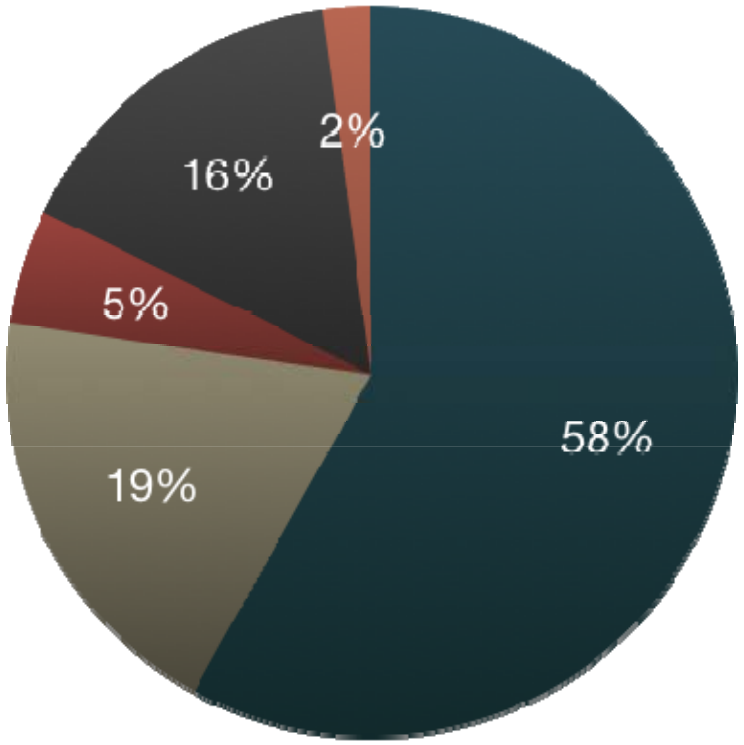
- RFDS database search: financial year 2009-10
- ICD-9 codes manually searched for diagnoses deemed at risk of major blood loss
- Identified patients then searched for blood product administration
- Clinical notes of those *at risk* of bleeding who received blood products in flight pulled for further analysis
- Operational information, physiological parameters and blood product usage collected
- Follow up haemotological data collected from tertiary centre laboratory reporting system

Royal Flying Doctor Service (Western Ops)

- 7585 patients transported
- 1193 primary evacuations



ICD-9 diagnoses compatible with major haemorrhage

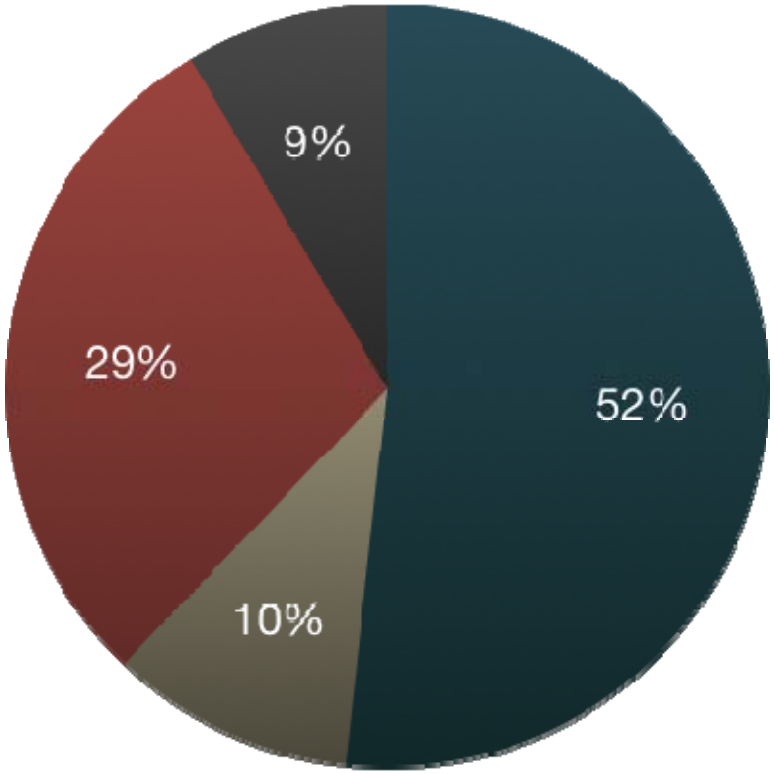


610 patients (8% of total patient population)

- Trauma 58% (n=354)
- Gastrointestinal 19% (n=117)
- Vascular 5% (n=31)
- Obstetric 16% (n=95)

Transfusion in Flight

- 9.5% (n=58) of patients with potential for major haemorrhage received blood products in flight.
- Demographics
  - Mean transport time 1 hour 55 min (range 0:34 -4:30)
  - 71% (n=41) male
  - Mean age 47.3
  - 24 P1; 32 P2; 3 P3



- Gastrointestinal 52% (n=30)
- Trauma 29% (n=17)
- Obstetric 10% (n=6)
- Vascular 9% (n=5)

In flight physiology

- Lowest recorded systolic blood pressure: mean 94.1 mmHg; median 96 mmHg; SD 21.5
- Highest recorded heart rate: mean 108.7; median 107; SD 19
- Lowest recorded haemoglobin: mean 84.5 g/l; median 83 g/l; SD 18.9
- Lowest recorded temperature: mean 36.5 degrees
- 3 patients warfarinised; 2 post thrombolysis, 7 with documented liver dysfunction prior to haemorrhage

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Physiology on arrival tertiary care

- Haemoglobin: mean 113g/l; median 110 g/l; SD 29
- Platelets: mean 151; median 135; SD 85
- International Normalised Ratio: mean 1.4; median 1.3; SD 0.4
- Activated Partial Thromboplastin Time: mean 36.8; median 34.0; SD 9.5
- Fibrinogen: mean 2.4; median 2.4; SD 0.9
- Bicarbonate: mean 20.0; median 20; SD 4.4
- Lactate - mean 3.0; median 1.5; SD 3.27

Management

- Packed Red Cells (mean number transfused)
    - Pre transfer - 2.6
    - During transfer - 1.5
    - Total - 4.1
- Fresh Frozen Plasma (mean number transfused)
    - Pre transfer - 1.2
    - During - 0.1
    - Total - 1.3

Management

- Platelets (mean number transfused)
    - Pre-transfer - 0.03
    - During transfer - 0.13
    - Total - 0.16
- Prothrombinex used 4 times (once in a non-warfarinised patient); calcium supplementation used once.
- In the trauma subgroup volume crystalloid and colloid infused: mean 4262ml; median 4925ml; IQR 2400.

Average blood product ratio of 4.1: 1.2: 0.2

Borgman *et al* (2007) describe mortality rates of 19, 34 and 65% with PRC:FFP ratios of 1.4:1, 2.5:1 and 8:1 respectively ($p<0.001$).

Regional hospital vs other

Comprehensive blood banks available in regional centres (Bunbury, Albany, Kalgoorlie, Geraldton, Carnarvon, Hedland, Karratha, Broome, Derby & Kununurra)

Regional hospital - 3.5:1
Non regional hospital - 13:1

The international approach to major haemorrhage in the pre-hospital and retrieval environment

International survey of the pre-hospital approach to major haemorrhage

- October 2010
- Pre-hospital and retrieval organisations identified via umbrella organisations
- Clinical contacts requested and invitations to participate issued
- 20 replies from 29 invitations (69%)

International survey of the pre-hospital approach to major haemorrhage

- Does your organisation carry blood products?
- Do you have immediate access to these blood products?
- Does your organisation regularly utilise pro-haemostatic agents in the context of major haemorrhage?
- Does your organisation operate a Massive Transfusion Protocol specific to your pre-hospital environment?

International survey of the pre-hospital approach to major haemorrhage

- Responses from Europe, North America, Asia, Australia, New Zealand, Africa
    - 3/20 urban, 8/20 remote, 9/20 mixture;
    - 7/20 primary, 13/20 secondary
    - 19/20 carried doctor for patients with major haemorrhage
- Blood products
    - None of urban organisations have access to blood
    - 8/17 of those serving remote environments have immediate access to blood (<5min); all have arrangement for delayed access (45min)
    - 1 organisation has immediate access to FFP (South Africa), 2 immediate access to platelets (SA & NZ)

International survey of the pre-hospital approach to major haemorrhage

- Major Haemorrhage Protocol
    - 10/20 organisations utilise a protocol
    - 5/10 are specific to the retrieval environment
- Prohaemostatic drugs and freeze dried agents
    - Tranexamic acid 1/20
    - Calcium preparations 3/20
    - Recombinant fVIIa 1/20
    - Prothrombin Complex Concentrate 1/20

Potential solutions?

Logistics

- Greater awareness of modern transfusion practices
- Early recognition of potential major haemorrhage
- Improved communication between hospitals, retrieval service and blood bank
- Major haemorrhage protocol

Tranexamic Acid

- Cochrane advocates use in elective surgery (OR Mortality 0.61 (CI 0.32-1.12))
- CRASH II (2010)
    - >20000 patients; 274 hospitals; 46 countries
    - No laboratory investigations
    - Improved mortality (if given within three hours)
- Ongoing trial in obstetric haemorrhage
- Does it apply to our environment?
    - PATCH (Prehospital treatment of Acute Traumatic Coagulopathy and Haemorrhage)

An easily stored, easily transported alternative to Fresh Frozen Plasma?

Fibrinogen concentrate

- Just introduced into Australia
- Licensed for congenital deficiency alone
- Potential alternative to cryoprecipitate/FFP (Nienaber *et al* 2011)
- Arguably even greater benefit in the retrieval environment

Prothrombin Complex Concentrate

- Available, freeze dried preparation of II, VII, IX, X.
- Accepted, licensed role in patients on vitamin k antagonists
- Expensive
- Limited experience in non-warfarinised patients

ADIS DRUG PROFILE

Drugs 2009; 69 (14): 1977-1984
0012-6667/09/0014-1977/$55.55/0

Prothrombin Complex Concentrate (Beriplex® P/N)

Lesley J. Scott

Adis, a Wolters Kluwer Business, Auckland, New Zealand

Contents

Abstract

▲ Beriplex® P/N, a prothrombin complex concentrate derived from pooled human plasma, contains the vitamin K-dependent coagulation factors II, VII, IX and X, and the vitamin K-dependent coagulation inhibition proteins C and S.

▲ Intravenous Beriplex® P/N provided rapid and sustained normalization of elevated international normalized ratios and controlled bleeding in adult patients participating in several prospective, noncomparative clinical studies (n = 8–43), with these data supported by clinical experience during its use over more than a decade.

▲ Based on extensive clinical experience, Beriplex® P/N is also effective in the treatment of congenital deficiency of any of the vitamin K-dependent coagulation factors when purified specific coagulation factor products are not available.

▲ Over a decade of clinical experience and more limited data from clinical studies have shown that intravenous infusions of Beriplex® P/N were generally well tolerated in adult patients with acquired or congenital deficiencies of the vitamin K-dependent coagulation factors. To date, there have been no proven cases of viral transmission reported in any published studies.

Features and properties of prothrombin complex concentrate (Beriplex® P/N)

Indication	
Treatment and perioperative prophylaxis of bleeding in acquired deficiency of the prothrombin complex coagulation factors, such as deficiency caused by treatment with vitamin K antagonists, or in cases of overdose with vitamin K antagonists, when rapid correction of the deficiency is required, and in congenital deficiency of any of the vitamin K-dependent coagulation factors when purified specific coagulation factor products are not available	
Mechanism of action	
A prothrombin complex concentrate from pooled human plasma that inhibits bleeding through replacement of coagulation factors II, VII, IX and X, and of coagulation inhibition protein C and protein S	
Dosage and administration	
Dose	Depends on the severity of the disorder, on the location and extent of bleeding, and on the patient's clinical condition
Route of administration	Intravenous
Maximum infusion rate	3 IU/kg/min (maximum 210 IU/min)
Adverse events in prospective clinical studies	
Thromboembolic events occurred at an incidence of ≤4.7%	

Summary

- Major Haemorrhage is a common problem in rural western Australia
- Retrieval services do not currently have the facility to deliver 21st century gold standard care in these patients
- New products hold promise for all practitioners managing the bleeding patient
- Retrieval practitioners perhaps stand the benefit the most and therefore should actively research

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