Tranexamic acid and Iron in Haematology

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Why consider an alternative?
Can’t we just give blood?

NO!
Why consider an alternative?
Can’t we just give blood?

Blood transfusion not without its risks- SHOT report 2015 shows deaths as a result of transfusion

Entirely reliant on donors-donor pool ageing

Risk of TTI
What is Tranexamic acid

• Anti Fibrinolytic
• Developed in 1960’s in Japan, used for menorrhagia
• More recently used for major Haemorrhage
• Cheap! (60-80p for a 500mg vial for IV)
• Effective (see NICE NG24)
• Available as oral tablets, IV and mouthwash and is available OTC for menorrhagia
• On the WHO list of essential medicines (minimum medicine needs for a basic health care system)
How does it work?

- Anti Fibrinolytic-prevents clot breakdown by inhibiting the activation of plasminogen to plasmin, preventing plasmin degrading fibrin.
Indications for Tranexamic acid

• Well used in major haemorrhage
• all expected bleeds >500mls in surgery (Nice NG24)
• Management of haemorrhage due to the administration of a fibrinolytic agent.
• Prevention and treatment of haemorrhages due to general or local fibrinolysis
# Contraindications and cautions

## Contraindications

- Acute venous or arterial thrombosis
- Fibrinolytic conditions following consumption coagulopathy except in those with predominant activation of the fibrinolytic system with acute severe bleeding
- Severe renal impairment (risk of accumulation)
- History of convulsions
- Intrathecal and intraventricular injection, intracerebral application (risk of cerebral oedema and convulsions)

## Cautions

- Irregular menstrual bleeding (investigate cause first)
- Massive Haematuria (risk of obstruction)
- Patient on oral contraceptive (increased risk of Thrombosis)
Case Study 1

- 76 year old man with Myelofibrosis
- Needs regular transfusions
- Hb could drop to 45-55 g/l, Plts ran 1-6
- Developed oozy GI Bleed
- Commenced on Tranexamic acid PO 1g TDS
- Difficult to judge effect as Myelofibrosis progressing
Case study 2

- 73 year old lady
- Myeloma
- Plts 12 Hb 54
- Sores and localised bleeding to mouth
- Commenced on Tranexamic acid mouthwash to good effect (reported by Patient)
Case Study 3

- 63 year old lady
- ITP
  - Difficult to control
  - Poor Response to steroids
  - And steroids not well tolerated by Patient
- Hb 143 Plts 29
  - As ITP would not respond to Plt Transfusion
- Tranexamic acid started whilst waiting to start rituximab
Conclusion

• Cheap
• Quick
• Effective
• But be aware of contraindications (few absolute)
• Be aware of bleeding- may need additional treatments (Blood, Platelets, Iron etc)
What is Iron?

- Element - atomic number 26
- Fundamental in structure of Haemoglobin
- Haemoglobin accounts for 65% of iron in body (between 2g and 4g total)
Main Causes of iron deficiency

**Inadequate Dietary Intake**
- Poor nutrition
- Chronic alcoholism
- Decreased consumption of animal protein and ascorbic acid

**Iron Loss**
- Menstruation
- Gastrointestinal bleeding
- Haemodialysis
- Puerperium
- Surgery
- Blood donation

**Increased Iron Demands**
- Pregnancy
- Infancy/adolescence

**Inadequate Gastrointestinal Iron Absorption**
- Malabsorption syndromes
- Systemic inflammation
- Interference with certain foods/drugs
What's the fuss? - small numbers?

- The most common and widespread nutritional disorder in the world
- Most Common cause of Anaemia
- 2 billion people – over 30% of the world’s population – are anaemic, many due to iron deficiency
- Iron deficiency affects more people than any other condition
- Modern “epidemic”
- Iron deficiency exacts its heaviest overall toll in terms of ill-health, premature death and lost earnings.

- WHO 2016
What does that mean in Haematology?

- Often multifactorial – patients with multiple conditions
- Linked with cause- Bleeding means increased risk of iron deficiency
Iron Turnover in the body

**Dietary iron**
- 5-10 mg/day

**Duodenum**
- Absorption of iron (~1-2 mg/day)

**RES of liver, spleen**
- (~1,000 mg)
- Storage of iron

**Transferrin**
- (~3 mg iron)
- Transport of iron

**Other cells and tissues**
- (~400 mg)
  - e.g., myoglobin

**Iron losses**
- (~1-2 mg iron/day)
  - Sloughed senescent enterocytes and skin cells, blood loss

**Macrophages of the RES**
- (~600 mg iron)
  - Recycling of RBCs

**BM**
- (~300 mg iron)
  - Erythropoiesis

**RBC**
- (~1,800 mg iron)

RES – reticuloendothelial system; BM – bone marrow; RBC – red blood cell
Progression of Iron deficiency

- Iron deficiency anaemia is the result of a process that starts with iron store depletion.

In patients with CHF, repletion of iron stores with oral iron could take more than 6 months.
Treatment 1- increase Nutritional intake

- Simple
- Also need to increase vitamin C intake
- Not to drink Tea or coffee with meals (inhibits absorption)

But
- can take months to resolve anaemia
- Limited by patients diet
- Usually too late for the haematology Patient
Treatment 2 Oral Supplementation

- Tablets or Liquid
- But still absorbed via GI Tract
- Cheap
- Relatively safe

BUT

- Side effects common
- Patients often stop taking if side effects are intolerable
- Takes weeks to months to take effect
- Side effects can include abdo pain, constipation, diarrhoea with a relatively high frequency
- OTC preparations are low doses
- Cannot be used in children
- Usually too progressed if they make it to Haematology referral- often tried by GP
Treatment 3 IV Iron

Ferinject used at Hinchingbrooke
• Dose is dependent on weight and Hb
• Given direct into blood- bypasses Gut
• Peak response 3-4 weeks post dose
• Short infusion time (30 mins)
• Relatively fast acting
But
• High reaction risk
• Relatively expensive
• Used when fast response needed or intolerant of Oral iron
• Not licensed for children
Treatment 4- Transfusion

THE LAST RESORT!

- Only for patients with symptoms that need immediate resolution
- Acts straight away

BUT
- Reaction Risk
- Infection risk
- Immunosuppresses
- Risk of ARF
- Stops people donating in the future
- Relatively expensive
- Contains a small amount of Iron (about 250mg per bag)- does not replenish Iron Stores effectively
- Relatively long infusion time
- Potentially SHOT reportable (if not used as last resort)
Case Study 1

• 90 year old man
• Myelodysplasia
• Managed with regular transfusions (for years), but ferritin always <100 (unusual!!)
• Added periodic Iron infusions, in conjunction with blood Transfusions (shorter infusion time)
• Appears to have slightly reduced blood requirements.
Case Study 2

- 94 year old male
- Lives alone, independently
- Longstanding iron deficiency- investigated repeatedly- NAD
- Subsequent referral to Haematology
- Has had 22 units of red cells since 2008 for IDA- multiple admissions (had developed atypical antibodies)
- Patient initially reluctant, but after iron said “that was much quicker” and happy to swap to iron infusions.
- No Transfusions Feb. 2015- May 2017 (Subsequent Cancer found- bone marrow failure)
Case Study 3

- 58 year old lady
- Longstanding Carcinoid Tumour being regularly resected - referred to Haematology for anaemia.
- Hb 134
- Ferritin 20, CRP 4, TF Sats 8%, TF 3.62
- Iron deficient - unclear Mechanism – being re-investigated
- Given IV iron infusion (intolerant of oral tablets)
IV Iron Service

- Often run by Transfusion Practitioner as an adjunct
- Different models- Telephone clinics, outpatient clinics
- Referred into service (GP, or within hospital (count as part of treatment))
- Have initial consult (phone/ in person)
- Booked into infusion suite (Haematology OPD/ Ambulatory Care/ Infusion suite)
- Generally bloods checked 3-6 weeks post IV iron
- Follow up (ie if needs referral and for monitoring of bloods)
Sounds Great! What are the problems?

• Perception issue- Iron deficiency perceived as diagnosis, but it’s a symptom- must have follow-up!
• Iron deficiency often falls between camps- “not haematology”, “not Gastro” or “not Gynae”
  – Makes where to administer difficult- Haematology OPD? Gastro Outpatient OPD?
  – Also makes setting up service difficult, where do the patients go? Who takes responsibility?
• What happens to Patients when investigations have been exhausted? Follow up can be patchy
• Demand v Supply – balancing resources
What next?

Continue to increase Iron use across the hospital (blood use also dropping)

Optimise the pathways for Iron deficiency
  – ? One stop Clinics
  – Better tie in with PBM

Specific follow up clinic

Uses of Iron still being researched- research into exercise tolerance and iron deficiency, and Heart failure ongoing
Conclusion

• Iron supplementation +- Tranexamic acid can be very effective
• Iron Appropriate *alternative* to transfusion
• Consideration to route needs to be given
• Increased role for Iron in NICE, and BCSH guidance, in optimisation of patients prior to surgery

BUT we are treating *symptoms*, a cause for iron deficiency should be identified.
Sources/ Further reading

- Vifor Pharma
- WHO
- Electronic Medicines Compendium
- Nice NG24
- BNF