The challenges of long term transfusion

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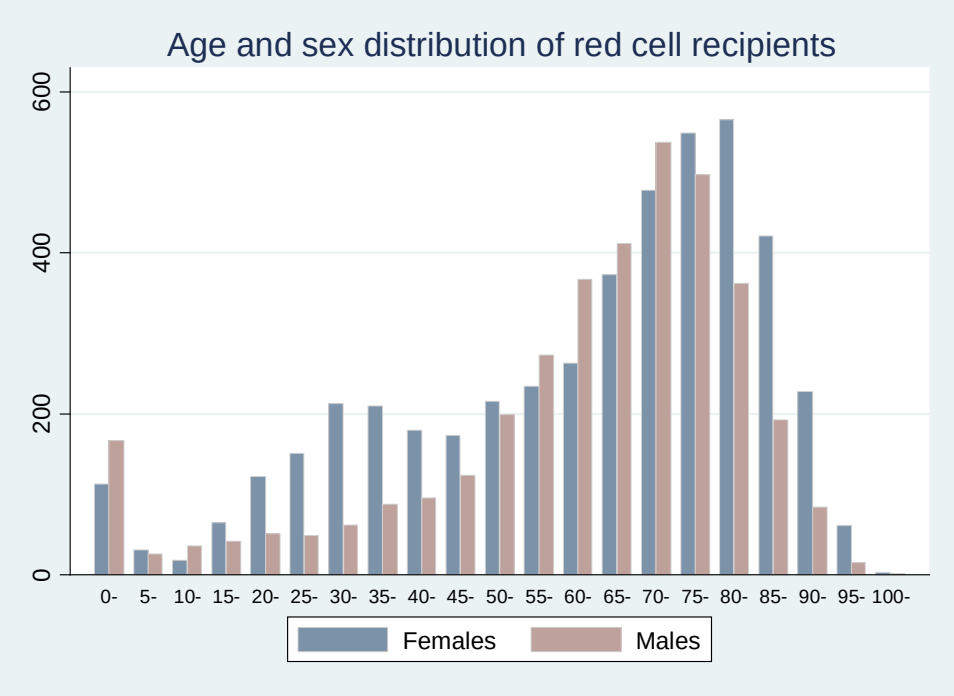
Who gets long-term transfusion?

Numbers are increasing and many are elderly

- **SAA & PNH**
- **Sickle cell disease**
  >12,500 patients in UK rising numbers on LT transfusion after abnormal transcranial doppler screening
- **Thalassaemia**
  >1,000 transfusion-dependent patients
- **Myelodysplasia**
  ~ 3000 new cases a year (30/100,000 age >70) transfusion main therapy for “low risk” subtypes



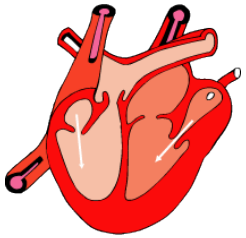
EASTR Study 2002

2009 *Where does blood go?* Audit in NE:
Medical patients got 64% of RC
MDS used 30% of all Haem/Onc RC
(nearly 10% of medical total)
But – not much haemoglobinopathy in NE!

Main complications of LT transfusion

- **Impaired quality of life** ←
- **Venous access**
- **Iron overload**
- **Red cell alloimmunisation**
- **Transfusion reactions/hazards**
- **Transfusion-transmitted infection**
  – now a very remote risk

Transfusional iron overload and chelation



- Each pack contains 160-250mg iron (>100 days of normal GI absorption)
- Organ damage (especially cardiac) was major cause of death in thal major patients
- Prophylactic iron chelation standard since 1970s – compliance a big problem with s/c desferal
- Major improvement in care (and QoL) with introduction of oral chelators (eg Exjade) and T2* cardiac MRI monitoring
- Principles extrapolated to LT transfused sickle cell patients – **BCSH guideline on transfusion in haemoglobinopathies in preparation**
- Chelation increasingly used in *stable* MDS, but many uncertainties over benefit:risk:QoL ratios – limited evidence

Red cell alloimmunisation

- Up to 30% of LT transfused patients develop alloantibodies (but 70% don't, surprisingly)
- More common if racial difference between donors and patients (common in sickle and thal – eg cDe/cde in SCD)
- Rh and Kell antibodies most common – other alloAbs uncommon in absence of anti-Rh and/or anti-K
- Once anti-Rh/K develop – more likely to develop multiple alloantibodies and can become v difficult to transfuse
- In some patients with multiple Abs it is impossible to identify them all from panels – only option is to select units that are matched to the most clinically important groups (only possible if patient's extended groups are known)

Current recommendations

- Perform extended blood group phenotyping before starting transfusion (if possible)
- In patients already transfused who have multiple alloAbs or strong autoAbs – do molecular typing
- Routinely select ABO, Rh (D,C,E,c,e) and K matched units
- If clinically significant alloAbs are present, select Ag negative and crossmatch by IAT
- Minimise donor exposure by selecting units with the highest volume and, ideally, <14 days old (“double dose” red cells taken by apheresis would be ideal)

Acute transfusion reactions

(see new 2012 BCSH guideline on ATR)

- **Non-haemolytic febrile transfusion reactions** (NHFTR)
  – incidence uncertain, but much less since leucodepletion
  – SHOT only collects data on more serious reactions (<10/100,000 units for red cells)
  – routine *prophylaxis* with paracetamol is ineffective
  – for *recurrent* moderate or severe reactions, try paracetamol 1 h pretransfusion (evidence low) then trial of washed RC
- **Allergic reactions**
  – moderate or severe occur in <1/10,000 RC units transfused
  – no evidence for *routine prophylaxis* with antihistamines (or steroids) or their use in recurrent mild allergic reactions
  – patients who have recurrent moderate or severe allergic reactions or an anaphylactic reaction should be investigated and managed according to the BCSH guideline

Reducing the risk of TACO

- Increasingly recognised as a major transfusion hazard
- Elderly patients, rapid Tx, over-transfusion and poor monitoring are important risk factors
- Myth that 1 unit = rise of 1g/dl (only true for 70-80kg patients)
- ***New BCSH Addendum***
  – clinical preassessment
  – careful monitoring of *at risk* patients
  – use 4ml/kg for 1g/dl Hb rise as guide to prescription

71 cases in SHOT 2011 with 2 deaths

Use single unit transfusions where appropriate in small frail adults

Transfusion strategies in MDS and Quality of Life

Systematic Review by Pinchon et al, Am J Hematol 2009;84:671-677

- Most patients with MDS are transfused according to a Hb target, often based on those derived for post-surgery or critical care, or other arbitrary figures (8, 10 ….)
- Feel OK a couple of days after Tx, symptomatic by week 3, clinic in week 4, cycle starts again
- Key patient-centred outcomes (Focus Groups):
  – fatigue and other symptoms of anaemia
  – impact on daily life (for patient and family) of regular attendance for transfusion
  – impact of need for chelation therapy

Transfusion strategies in MDS and Quality of Life

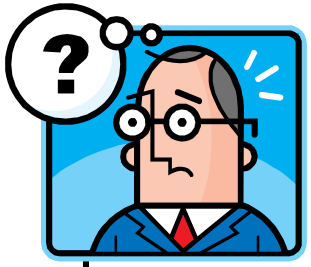
Systematic Review by Pinchon et al, Am J Hematol 2009;84:671-677

- Only found 17 studies, total 1724 patients, that used 14 different HRQoL instruments (mainly designed for cancer trials)
- Nearly all small, underpowered, selected patients, incomplete follow-up and poorly reported
- Most were “trials” of ESAs, growth factors or immunosuppressives
- Poorly standardised transfusion regimens

Could *anything* be learned from the review?

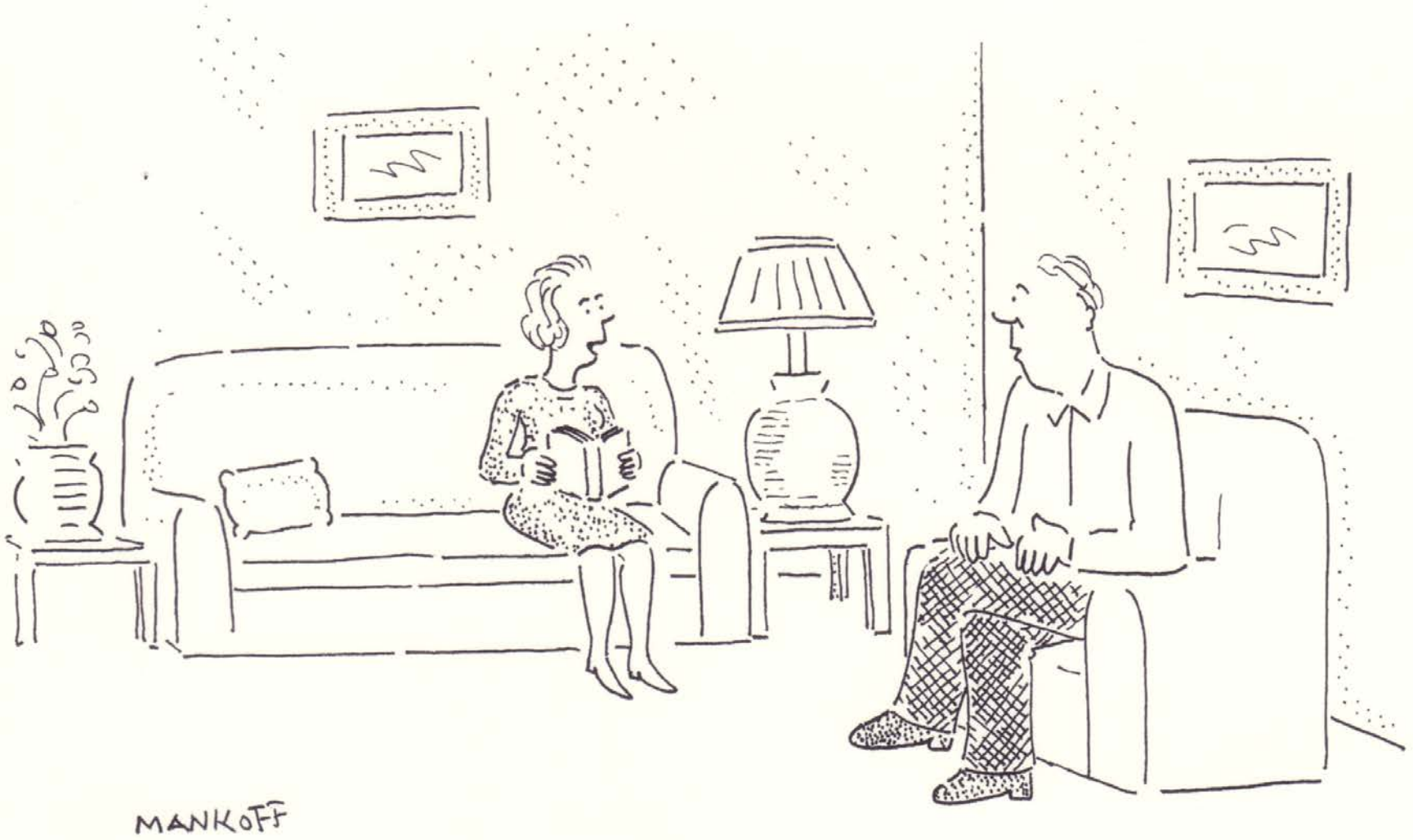
- It *is* feasible to measure HRQoL in MDS
- Patients generally had better HRQoL with higher mean Hb levels (similar to cancer anaemia studies where maximum gain was between Hb 10 and 12)
- One study looked at impact of fluctuations of Hb on HRQoL – showed that patients with least fluctuation felt best (one reason Epo responders feel well)

So, what next for transfusion in MDS?



- *One size fits all* transfusion triggers are clearly inappropriate
- The focus should be on Quality of life (patient and family), not a magic number (or red cell conservation)
- Many older patients will benefit from higher mean Hb levels (and might not need any more red cells for maintenance when get there)
- Avoiding big fluctuations in Hb is probably important – but balance against disruption of frequent transfusion
- A great area for patient-centred clinical research!

Thanks for your attention. Any questions?



"I'm sorry, dear. I wasn't listening. Could you repeat what you've said since we've been married?"