Higher Serum Ferritin Levels up to 1,200 ng/ml Enhance Erythropoietin Responsiveness in Maintenance Hemodialysis Patients

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Background

- Identification of factors that enhance erythropoiesis stimulation agent (ESA) [such as erythropoietin (EPO)] responsiveness in maintenance hemodialysis (MHD) patients can optimize anemia management.
- Adequate iron stores may significantly enhance the responsiveness to ESA in anemia management of MHD patients.
- However the optimal range of iron stores for the greatest ESA responsiveness is not known.

Hypothesis

- **Hypothesis # 1: Higher serum ISAT ratio levels are associated with more effective ESA response**
- **Hypothesis # 2: Serum ferritin levels higher than KDOQI-recommended 500 ng/mL is associated with more effective ESA response**

Methods

- We examined Hb response to ESA treatment in a 12-month (July 2001-June 2002) cohort of 10,455 MHD patients across the USA.
- All patients had received ESA for at least 3 consecutive calendar quarters.
- Using repeated measure models, the ESA response coefficient at individual level was separated from the population responsiveness.
- Cross-sectional (conventional) model:

$$Hemoglobin_i = \beta * rHuEPO_i + \varepsilon_i$$

- Longitudinal (repeated measure) model:

$$Hemoglobin_{ij} = \beta_C . rHuEPO_{i1} + \beta_L . (rHuEPO_{ij} - rHuEPO_{i1}) + \varepsilon_{ij}$$

Results

- The OR (and 95% CI) of upper vs. lower quartile of ESA response coefficient at patient level was calculated.

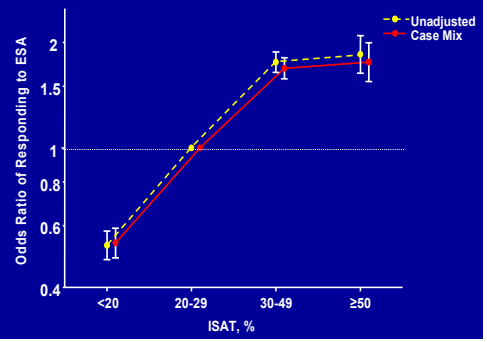
Ferritin & EPO Responsiveness

- After dividing serum ferritin range into 5 a priori selected groups
- The greatest ESA responsiveness was observed with serum ferritin in 500-1200 ng/mL range
- Case-mix adjusted OR of ESA responsiveness for serum ferritin in 800-1200 ng/mL range was **1.39** (95% CI, 1.27-1.52), indicating 39% greater responsiveness
- Serum ferritin <200 ng/mL was associated with 23% lower responsiveness: adjusted OR **0.77** (95% CI, 0.70-0.86), *P*<0.0001

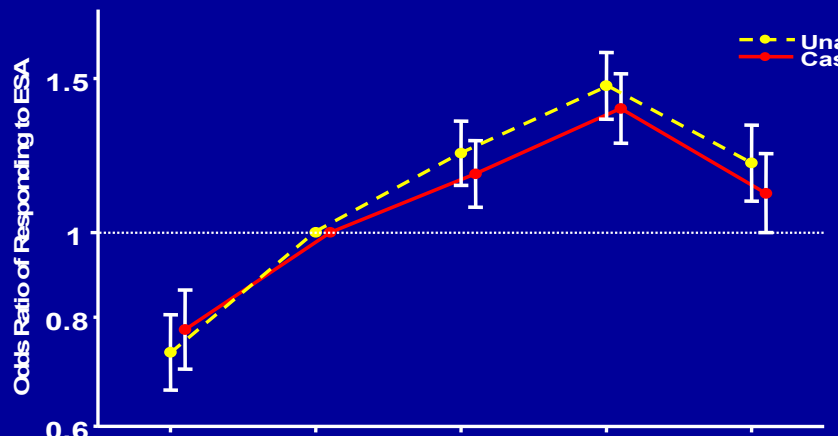
TSAT & EPO Responsiveness

- In both unadjusted and case-mix adjusted logistic regression models, each 10% increase in serum ISAT was associated with at least 30% higher ESA responsiveness (*P*<0.0001)
- Unadjusted OR: **1.39** (1.36-1.43)
- Case-mix OR: **1.32** (1.32-1.40)
- After dividing the entire serum ISAT range into 4 a priori selected groups (<20%, 20%-30% [ref], 30%-50%, and ≥50%) the greatest ESA responsiveness was observed with ISAT >30%, i.e., almost 50% higher ESA responsiveness compared to ISAT 20%-30%
- ISAT <20% was associated with almost 50% lower responsiveness (*P*<0.0001)
- Unadjusted OR: **0.53** (0.48-0.58)
- Case-mix OR: **0.54** (0.49-0.59)

Odds Ratio of Greatest Response to ESA based on Serum TSAT in 10,455 MHD Patients



Odds Ratio of Greatest Response to ESA Based on Serum Ferritin in 10,455 MHD Patients



Conclusions

- **In MHD patients, hemoglobin response to EPO treatment may be significantly enhanced by maintaining higher serum ferritin levels in 500 to 1,200 ng/ml range, but not higher than 1,200 ng/ml.**

Acknowledgements

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