EPO and sTfR in altitude residents

Erythropoietin and soluble Transferrin Receptor concentrations in high altitude residents with excessive erythrocytosis

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Introduction.

• **Erythropoietin (EPO)** is a glycoprotein hormone.

• **EPO** is produced by specialized cells in
  * the kidneys (90 %)
  * the liver (10 %).
These cells are sensitive to the blood’s oxygen concentration.

They increase the release of EPO when the O₂-concentration is low.

Under conditions of hypoxia, the higher EPO-levels increase the production of red blood cells (hematopoiesis).
Transferrin Receptor.

- Transferrin Receptor (TfR) is a transmembrane protein, expressed mainly on the surface of erythroid cells.
Transferrin Receptor.

- **Transferrin** is a transport protein for iron (Fe).
- The diferric (2*Fe) transferrin is binding to TfR.
- During the phase of cellular proliferation iron is incorporated into erythroblast.
- This is important for the synthesis of hemoglobin.
Methods (I).

- We included 105 patients from La Paz and El Alto (Bolivia).

Inclusion criteria:

- whole life at high altitude: (3,600 - 4,100 m).
- Excessive erythrocytosis: \([\text{Hct} > 60\%]\)
**Excessive Erythrocytosis. (EE)**

- **Asmus** (Leadville CO, USA, 1993)
  
  EE → CMS:  
  - Hct ≥ 56% males  
  - Hct ≥ 51% females  

- **Vasquez** (Potosi-Bolivia, 2001)
  
  EE →  
  - Hct ≥ 61%  
  - Hb ≥ 21 g/dL males  
  
  - Hct ≥ 56%  
  - Hb ≥ 19 g/dL females  

- **Consensus Statement high altitude diseases** (Xining, China, 2004).
  
  CMS → EE:  
  - Hb ≥ 21 g/dL males  
  - Hb ≥ 19 g/dL females
La Paz – Bolivia (3600 m)
La Paz – Bolivia
El Alto – Bolivia (4100 m)
Altitude residents.
Methods (II).

- Blood samples were taken by venipuncture.

- Hemoglobin (Hb) and Hematocrit (Hct) were measured directly.

- Aliquots of serum were stored at -20°C and sent to Charité Universitätsmedizin Berlin for analysis.

- By ELISA we assessed concentrations of
  - Erythropoietin ([EPO], cut-off 36 U·l⁻¹),
  - soluble Transferrin Receptor ([sTfR], cut-off 28 nmol·l⁻¹).
**RESULTS (I).**

- **n = 105**
  - **34 Females**
    - Mean = 63.5 yrs
    - Std. Dev = 9.4 yrs
    - Min = 37 yrs
    - Max = 80 yrs
  - **71 Males**
    - Mean = 62.1 yrs
    - Std. Dev = 11.0 yrs
    - Min = 35 yrs
    - Max = 89 yrs
RESULTS (II).

Significant differences between females and males for Hct (p=0.011) and Hb (p=0.011).
RESULTS (III).

No differences between females and males for age (p=0.50), [EPO] (p=0.52) and [sTfR] (p=0.47).
RESULTS (IV).

No correlation between Hct and Hb with $\text{[EPO]}$.
RESULTS (V).

No correlation between Hct and Hb with \([sTfR]\).
RESULTS (VI).

No correlation between age with [EPO] and [sTfR].
CONCLUSION (I).

• The data of this study support the hypothesis that at least 2 groups of patients with excessive erythrocytosis (EE) exist:

  A) those with “normal” [EPO] ($\leq 38$ U·l$^{-1}$) and
  B) those with very high [EPO] ($\geq 78$ U·l$^{-1}$)

• No studies before evaluated “normal” reference levels for [EPO] and [sTfR] in altitude residents

→ can the published cut-off values be adopted?
EPO and sTfR in altitude residents

A) Group A) with “normal” [EPO] ($\leq 38$ U·l$^{-1}$)

B) Group B) with very high [EPO] ($\geq 78$ U·l$^{-1}$)

Intermediate group ($38 < [EPO] < 78$)

$n = 105$
**Group A** with “normal” [EPO] ($\leq 38$ U·l$^{-1}$)

**Group B** with very high [EPO] ($\geq 78$ U·l$^{-1}$)

what about the “intermediates” (38<$[^{\text{EPO}}]<$78)
No correlation between [EPO] and [sTfR] 

Majority of the subjects with high [sTfR]
EPO and sTfR in altitude residents

**HAPPOM**

**data distribution:**

No high correlations between two parameters

“every combination seems possible”

→ apparently no obvious clusters
CONCLUSION (II).

• Furthermore, it has to be clarified if patients with EE and low [EPO] had not performed **blood-letting** in contrast of patients with high [EPO].

• Finally, we found **high [sTfR]** in the majority of the subjects but no correlation to [EPO].

  ➔ In high altitude residents, the response of the sTfR in **hypoxia** ➔ **hematopoiesis** is increasing in relation to the response of EPO ???

  ➔ **differences in iron metabolism ??**
NEXT STEPS / OUTLOOK.

• clinical data
  - patients’ medical condition
  - anthropometry
  - cardio-vascular investigations (HR, BP, CVP(?)
  - questionnaire (previous history)
  - CMS ???
  - follow up
PROJECT ALFA HAPPM – 2006.

• Analysis of EPO and sTfR in high altitude residents with “normal” haematological values in the same age range.
  
  • * To determine normal values (cut-off) of EPO in high altitude residents.
  • * Evaluate the response of EPO before and after the blood-letting in these subjects.

*(depending on funding).*
Thank you for your attention.