Circulating 3-T1AM and 3,5-T2 in critically ill patients
a cross-sectional observational study

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Background

Critical illness hallmarks
• low circulating T₄ and T₃ concentrations
• elevated rT₃, normal 3,3' T₂, low-normal TSH
➢ referred to as non-thyroidal illness (NTI)
• Thyroid hormone (TH) metabolism substantially increased
  • enhanced deiodinase 3 (D3) / suppressed D1 activity
  • unaltered sulfotransferase activity (T₄- and T₃-sulfate formation)
• Thyroid hormone (TH) metabolism substantially increased
  • Decreased conversion of 3,5-T₂ to 3-T₁AM
  • Decreased availability of T₃ as precursor

Hypothesis

During critical illness T₄ is not only metabolized to rT₃. Increased deiodination of T₄ and/or T₃ to 3,5-T₂ and/or 3-T₁AM contributes to high TH turnover.

Methods

• TSH, TT₄, TT₃ (Beckman Coulter, Fullerton, CA),
• T₄, T₃ (RnDSystems, Minneapolis, MN)
• APACHE II score - mean ± SE
• APACHE II score - median [IQR]

Results

Multivariable analysis Estimated difference (95% CI) for 3-T₁AM (nmol/L) R² P-value

TT₄ (nmol/L) 0.05 (0.02 – 0.07) 0.129 <0.0001
TT₃ (nmol/L) 2.50 (1.73 – 3.27) 0.262 <0.0001
rT₃ (nmol/L) -0.45 (-0.73 – -0.17) 0.078 0.002
3,5-T₂ (nmol/L) -0.39 (-0.69 – -0.09) 0.055 0.01

TT₄ (nmol/L) -0.02 (-0.03 – -0.01) 0.062 0.006
TT₃ (nmol/L) -0.72 (-1.23 – -0.22) 0.064 0.005

TT₄ (nmol/L) -0.01 (-0.03 – -0.01) 0.2
TT₃ (nmol/L) -0.44 (-1.14 – 0.24) 0.2

Critical ill patients revealed:
• Median 44% lower serum 3-T₁AM
• Median 30% higher serum 3,5-T₂ compared to healthy volunteers

Non-survivors and sepsis-patients:
• Significantly higher 3,5-T₂
• Unchanged 3-T₁AM compared to other patients

Reduced serum 3-T₁AM positively correlates with low serum T₃ (p<0.001)

Conclusion

We observed in critically ill patients:
• Increased circulating 3,5-T₂, most so in patients with unfavorable outcome
• Possible explanations:
  ➢ Increased conversion from its precursors
  ➢ Decrease in 3,5-T₂, metabolism
  ➢ Decrease in tissue uptake
• Circulating 3-T₁AM was suppressed
• Independently correlated to lower T₁ concentrations
• Possible explanations:
  ➢ Decreased availability of T₃ as precursor
  ➢ Decreased conversion of 3,5-T₂ to 3-T₁AM

Further investigation on function of 3-T₁AM or 3,5-T₂ during critical illness is needed

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