Understanding metabolism in severe malnutrition: from cellular mechanisms to improved child survival

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Disclosure slide

In the past 12 months, I have had no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity.

The role of malnutrition in childhood mortality

• About 45% of all child deaths are linked to malnutrition.
• Severe malnutrition contributes to 516,000 child deaths annually.
• Profound diarrhea or hypoglycemia common direct causes of death in SAM.

Black et al, Lancet 2013
Holkens et al, Lancet 2008
The two forms of severe malnutrition

Marasmus Kwashiorkor

Metabolic dysadaptation in severe malnutrition

- Electrolyte disturbances
- Hypoalbuminemia especially in kwashiorkor
- Abnormal glucose concentrations common:
  - Glucose absorption impaired *
  - Glucose clearance affected #
  - Impaired glucose production
- Fatty liver in kwashiorkor

Glucose production is reduced in children with severe acute malnutrition

* P<0.05
The regulation of hepatic glucose production

Glucose  Fatty acids  Amino acids  Mitochondrion  ATP  ADP  Alanine  Pyruvate  Lactate  glucose

Assessing mitochondrial function using isotope breath testing

Liver glucose production is correlated with hepatic mitochondrial function

Glucose production (mg/kg/min)

Mitochondrial function (%)

r 0.56, P<0.05

PedRes 2011
Aim

- To understand the hepatic metabolic dysfunction in severe malnutrition.

**P<0.001**

Severe fatty liver in an animal model of malnutrition

Control Malnourished
Malnutrition is associated with proliferation of abnormal hepatic mitochondria

![Control](image1)  ![Malnourished](image2)

Impaired mitochondrial function in malnutrition

![Bar chart showing oxygen consumption](chart)

Malnutrition is associated with a loss of hepatic peroxisomes

![Control](image3)  ![Malnourished](image4)
Malnutrition is associated with a loss of hepatic peroxisomes

Fibrate treatment improves steatosis and ATP content in malnutrition

Fibrates (FF) are PPAR-alpha agonists, stimulating peroxisome biogenesis and mitochondrial lipid oxidation.