Hypokalemic periodic paralysis
About me

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- Co-investigator on a project about permanent weakness in patients with HypoPP at Copenhagen Neuromuscular Center, Rigshospitalet.
Outline

• What is hypokalemic periodic paralysis
• Symptoms
• What triggers attacks?
• Treatment
• Research project
What is Hypokalemic Periodic Paralysis?

- Rare disorder of muscle. One of 100,000 individuals.
- Channelopathy – disorder of ion channel.
- Ion channels are tiny pores (openings) that allow ions (molecules) like sodium and calcium to move through the cell membrane.
- Inhereted disorder
  - Usually a genetic defect in the calcium channel CACNA1S or in the sodium channel SCN4A.
  - 10-20 % of cases remain genetically undefined.
Symptoms

• Attacks of muscle weakness associated with transient reductions in serum potassium levels.
• First attack before the age of 20 years.
• Most commonly occurs on awakening.
• Attacks may last an hour or two or (sometimes) a day or two.
• Attacks vary from mild weakness to complete paralysis.
• Before an attack, there may be leg stiffness or leg heaviness.
• Good muscle strength between (The classical phenotype).
Muscle activation
Motor endplate and muscle activation

• Membrane potential: Difference in electric potential between the interior and the exterior of a cell
• Used for transmitting signals
• It is believed that a defect in the CACNS1 channel leads to leakage – alters the response to activation during hypokalemia
• Precise mechanism for attacks require further research
What triggers attacks?

• Rest after unusual or vigorous exercise
• Meal high in carbohydrate and/or sodium.
• Prolonged immobility.
• Getting too cold (or too hot)
• Intense stress
• Alcohol
Treatment

• Oral potassium during an acute attack
• IV potassium

• Prophylactic use of acetazolamide. (Inhibits the enzyme carbonic anhydrase)

  • Side effects
    • Paresthesia, drowsiness...

• Prophylactic use of potassium
How to avoid having attacks?

• Lifestyle modifications
  
  • Avoid carbohydrate loads
  
  • Remain active. Adjust exercise by individual threshold for inducing an attack.
  
  • Diary – to get to know specific trigger factors – and avoid them
Diagnosis

- History of episodes of paralysis with rapid onset and spontaneous recovery
- (Lov) serum potassium during attacks
- Typical precipitating factors
- A family history

- Genetic testing
Permanent weakness

• A number of patients develop permanent proximal muscle weakness.

• Often in the fourth and fifth decade of life

• Independently of the frequency and severity of attacks
Case

• Years with slowly progressive proximal weakness
• No attacks of weakness
• Family history:
  • Mother and grandmother with walking difficulties at old age.
• Slightly elevated creatine kinase (CK)- enzyme that leaks out of damaged muscle
• Limb-girdle muscular dystrophy (LGMD) was suspected
• Genetic testing for LGMD - negative
Normal muscle biopsy

• The muscle fibers appear to be almost in direct contact with each other
• The muscle fibers are of relatively uniform size and shape
• Nuclei are located at the periphery
Case: Permanent weakness without attacks.

• Family history with HypoPP

• Additional genetic testing:
  • Mutation in the CACNA1S gene
Unanswered questions

• What is the reason for this permanent weakness?
• What percent of patients will develop permanent muscle weakness?
• What is the relation between periodic and permanent weakness?
• Are there markers for this risk?
• Is permanent muscle weakness preventable?
• Is it possible to treat permanent weakness?
Study on HypoPP and permanent weakness

• Systematic evaluation of permanent muscle weakness in patients with HypoPP caused by mutation in the CACNA1S

• Retrospectively try to assess the effect of potassium supplements / acetazolamide treatment for the development of permanent weakness
Descriptive study of permanent weakness

- Clinical assessment, especially muscle strength
- MRI muscle
- Muscle biopsy (optional)
Descriptive study of permanent weakness

• Frequency
• Severity
• Specific changes on MRI
• Specific changes on muscle biopsy

• Relationship between attacks and permanent weakness
• The effect of prophylactic treatment and permanent weakness
The team

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Thank you very much.

• Questions?

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