Title: Hypokalemic Periodic Paralysis *GeneReview* – Clinical Testing Available
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Clinical Testing Available if the Diagnosis is Less Apparent

Clinical testing is often useful in making the diagnosis of primary hypokalemic periodic paralysis. However, the diagnosis cannot be established by clinical findings alone in the absence of a known family history of the condition.

In individuals who have had one or more paralytic episodes, several tests can be used to differentiate between primary HypoPP and the other possible causes.

Serum concentration of potassium during paralytic attack. During an attack, the serum concentration of potassium ranges from 0.9 to 3.0 mmol/L (normal range: 3.5-5.0 mmol/L).

Note: Measurement of the serum concentration of potassium during an attack is needed to classify a paralytic episode as hypokalemic.

Transtubular potassium concentration gradient and potassium-creatinine ratio during paralytic attack. The following can be used to distinguish between hypokalemia caused by renal (urinary) losses and hypokalemia caused by intracellular muscular shift of potassium (as occurs in primary HOKPP caused by a genetic ion channel defect) [Lin et al 2004]:

- Urinary potassium concentration >20 mmol/L indicates urinary loss of potassium.

  Note: The threshold value of 20 mmol/L is not sufficient to distinguish between renal and non-renal hypokalemia.
- Urinary potassium/creatinine ratio of >2.5 indicates urinary loss of potassium.
- A transtubular potassium concentration gradient (TTKG)* >3.0 suggests hypokalemia of renal origin.

  * The ratio: [urine potassium/plasma potassium]/[urine osmolality/blood osmolality]

Note: If a patient is already taking supplemental potassium, the urinary excretion of potassium is difficult to interpret, as high levels could be attributable to the supplementation.

Serum concentration of thyroid-stimulating hormone and free thyroxine and triiodothyronine may distinguish between primary HypoPP and thyrotoxic periodic paralysis (TPP) (see Differential Diagnosis).

Electromyogram (EMG). Muscle electrophysiologic testing must be performed during an interictal period. Protocols for implementation [Fournier et al 2004] and interpretation [Tan et al 2011] have been published. EMG testing includes:

- Assessment for myotonic discharges

- Repeated short exercise tests
- A long exercise test (the principal discriminating test for primary periodic paralysis)

The diagnosis of primary hypokalemic periodic paralysis relies on:

- The absence of myotonic discharges

  Note: One family with combined heat-induced myotonia and cold-induced hypokalemic periodic paralysis has been described [Sugiura et al 2000].

- The presence of a progressive and marked decrease in the amplitude of compound motor action potentials (CMAP) during a long exercise test [McManis et al 1986].

During an attack, EMG findings are not specific; EMG demonstrates a reduced number of motor units and possibly myopathic abnormalities.

Between attacks, EMG may exhibit myopathic abnormalities in individuals with long lasting interictal weakness.

Specific exercise tests can assist with the diagnosis of periodic paralyses and nondystrophic myotonias [Fournier et al 2004]:

- **Short exercise test (SET).** SET consists of recording evoked compound muscle action potential (CMAP) every ten seconds over one minute after a short effort (5-12 seconds) [Streib 1987].
- **Long exercise test (LET).** LET consists of recording evoked CMAP over 30-45 minutes, every one to two minutes and then every five minutes, after a long effort (2-5 minutes, with brief 3- to 4-second rest periods every 15-45 seconds) [McManis et al 1986].

Five patterns (I-V) of abnormal responses to SET and/or LET in periodic paralyses and nondystrophic myotonias have been described [Fournier et al 2004]. Genetically defined periodic paralyses specifically result in:

- **Pattern IV** (no or rare myotonic discharges, increase of CMAP on SET, immediate increase and late marked decrease in LET), more commonly seen in the hyperkalemic type

  OR

- **Pattern V** (no myotonic discharges, normal response to SET, no immediate increase but late marked decrease in LET), more commonly seen in the hypokalemic type

A false negative normal pattern may be noted in some individuals who have a pathogenic variant, especially in asymptomatic individuals or those who have not recently had a paralytic attack [Tengan et al 2004].

A decrease of at least 30% in CMAP amplitude and surface on LET is diagnostic for HOKPP. A decrease of less than 30% and greater than 20% is less specific and may

indicate a different diagnosis. This decrease corresponds to pattern IV (with initial increment) and pattern V.

Muscle biopsy. Muscle biopsy is not necessary when the diagnosis is that of one or several recurrent paralytic episodes.

References

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