



Gut permeability profile using PEG 400 July 2009

Changes in the permeability of the small intestine can result in *under-absorption* of nutrients or the converse, *over-absorption* of the intestinal contents. Either condition can be described as *malabsorption*, although this term is more commonly used in the case of under-absorption of nutrients. A number of investigators have suggested that over-absorption syndromes (increased gut permeability) are significantly underdiagnosed. This may be important, for example, in cases of food intolerance, where derivatives of maldigested food may be absorbed through the gut wall and into the circulation, resulting in characteristic hypersensitivity symptoms [1,2].

Indications

The use of PEG 400 as a probe for the investigation of intestinal permeability was first proposed by Chadwick, Philips and Hoffman in 1977 [3]. The rationale was that PEG (polyethylene glycol) contains a mixture of inert, water-soluble molecules of different sizes, whose absorption is independent of dosage, displaying decreasing mucosal transport with increasing molecular size. PEG 400 is also nontoxic, not degraded by intestinal bacteria, not metabolised by tissues, and rapidly excreted in the urine. PEG is polymerised ethylene oxide and is not the substance - ethylene glycol – which is found in anti-freeze.

The decreasing absorption of increasing molecular weights of PEG can be explained on the basis of the notional hydrogen bonding capacity of each molecule. Evaluation of this theoretical measure of the oil-water partitioning character of a molecule shows that PEGs, and other low molecular weight molecules used as intestinal probes, may pass through the intestinal cell membranes by a mechanism involving passive diffusion alone. However, a three-mechanism model of intestinal penetration has also been proposed [4].

Other factors that may influence the urinary excretion of PEG include its space of distribution in the body, the permeability profile of the kidney [5] and the luminal flow rate in the intestine [4].

Synonyms:

PEG test, leaky gut test

Patient preparation

The patient should fast for 3 hours before starting the test. Water intake during the first 2 hours of the 6 hour urine collection should be limited to 250 mL. Water consumption during the remainder of the test should be moderate.

The PEG test, which is a measure of mucosal permeability, should not be performed if the patient has gastroenteritis or is suffering from any other cause of intestinal hurry, as this will invalidate the urinary reference interval for the recovery of PEG.

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Interfering substances

The patient should not take medicine containing Movicol (Macrogol), which is a type of PEG given to relieve constipation. This could invalidate the test results and show apparent increased excretion of certain molecular weights of PEG.

Mannitol, or hexan-1,2,3,4,5,6-hexol ($C_6H_8(OH)_6$), is a polyol that is used as an osmotic diuretic agent and a weak renal vasodilator. It is also found in "Seven Seas zinc plus vitamin C". Mannitol co-elutes with the lowest molecular weight of PEG, so such supplements should be avoided prior to the test. Sorbitol (Mw 182.17), a non-stimulant laxative often used as a sugar substitute and xylitol (Mw 152.15) can cause similar interference. Both sorbitol and xylitol are found in stone fruits and xylitol occurs naturally in the fibres of many other fruits and vegetables, such as berries, corn husks, oats and mushrooms. Beer and various soft drinks may also contain similar interfering substances.

Specimen requirements

The sample required for the gut permeability profile is a 6 hour urine collection after a 3 gram oral dose of PEG. A 20 mL aliquot of urine may be sent for analysis if the volume of the total collection can be accurately measured.

Postal samples must reach Biolab within 3 days of collection.

Methodology

PEG fractions are converted to their acetyl derivatives [3,5,6] which are stable on storage and give good chromatographic separation. Extraction of PEG from urine is by ion exchange chromatography, using the procedure described by Sivakumaran et al [6]. PEG is then acetylated with acetic anhydride in the presence of a pyridine catalyst and the acetyl PEGs are separated by capillary GLC.

This method replaces the one previously used at Biolab.

Turn around time: 4-5 working days.

Interpretation

The Biolab reference interval for recovery of the different molecular weights of PEG in a 6 hour urine collection is displayed graphically. Results above the upper limit of the reference interval are suggestive of hyperpermeability. Results below the lower limit of the reference interval are suggestive of malabsorption.

References

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