Current dilution methods cause large variations and inaccuracies when making up 1mcg Synacthen dose

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Background

• The low-dose Short Synacthen Test (LDSST) is a popular diagnostic test for adrenal insufficiency in UK children
• Although various dosing strategies exist, 1mcg is most commonly employed, but not commercially available.
• A BSPED survey¹ in 2012 revealed 14 different methods for diluting the 250mcg/ml ampoules.
• We investigated whether differing dilution strategies; made up using ward equipment (reflecting current practice) rather than laboratory conditions, result in different Synacthen doses being administered.

Methods

• The 10 most popular dilution methods were tested, varying in:
  • Diluents: 0.9% saline N=9, 5% dextrose N=1
  • Number of dilutions: Single N=6, Double N=4
  • Initial quantity of Synacthen: 0.1-1ml
• Each was made up five times by the same investigator with samples taken from the top, middle and bottom of the bag.
• Samples were frozen then batch-analysed on a hACTH radioimmunoassay validated for Synacthen detection.
• Samples were diluted with 0.9% saline by 1000-20,000 (under laboratory condition, using accurate, calibrated equipment) to achieve a final concentration of 250 pg/ml (most sensitive part of the assay measuring range).
• Mean concentrations and coefficient of variation (CV) were calculated for each dilution method.
• The inter-method, intra-method and intra-bag variability were calculated.

Results

• If no significant variation between or within methods exists, applying typical laboratory medicine standards, all samples should be 250 pg/ml ±10% (see dotted black lines fig 1).
• Mean Synacthen levels of the 10 methods ranged from 9.1 pg/ml to >490.48 pg/ml.

Discussion

Considerable variation was observed within and between methods.

There are many variables which may affect the actual dose of Synacthen:

• The use of inaccurate ward equipment causing drawing up inaccuracies and volume inconsistencies,
• Adsorption to plastic tubing is a particular issue with Synacthen,
• Further dilution of the samples to the most sensitive part of the assay range

Recommendations

• A commercial preparation of 1mcg synacthen be made available.
• In the absence of a commercial preparation, low dose Synacthen should be made up under laboratory conditions to minimise inaccuracies.

References