All Wales Clinical Biochemistry Audit Group

Standards for Screening for Cushing's Syndrome

INTRODUCTION

A survey of urine free cortisol measurements in use in Wales, presented at an audit meeting in May 1995, showed wide variations in practice and the need to review methods used for screening for Cushing's syndrome. A further survey on this latter topic was presented at another audit meeting in May 1996. The following standards are recommended in the light of the presentations and discussions at these meetings and consultation with the Welsh Endocrine and Diabetes Society.

STANDARDS

1. **Patient Assessment**

   The diagnosis or exclusion of Cushing's syndrome can be difficult and it is recommended that non-expert clinicians should seek the advice of a consultant physician or paediatrician with specialist endocrinology experience. Laboratory tests should not be used in isolation; results should be interpreted together with a full clinical assessment of the patient.

2. **Choice of Test**

   First-line screening tests must have high sensitivity to minimise the incidence of false negative results and reference (cut-off) values chosen to achieve these aims. The overnight dexamethasone suppression test is particularly recommended, but 24 hour urine free cortisol determination is also suitable. Measurement of 9 am serum cortisol alone is not adequate. In many cases it is desirable to perform more than 1 test. If cyclical Cushing's syndrome is suspected, repeat testing may be required on several occasions.

3. **Overnight Dexamethasone Suppression Test**

a) The dose of dexamethasone used should be 1 mg, except for small children who may require a relatively smaller dose. The dexamethasone should be given at 11 pm (± 1 hour).

b) Serum cortisol should be measured at 9 am (± 1 hour) on the following morning.

c) The 9 am serum cortisol concentration used as a cut-off level to exclude Cushing's syndrome should not exceed 50 nmol/l [1].

4. **24 hour Urine Free Cortisol**

a) This should be determined using an assay which incorporates an extraction step.

b) Results should be interpreted with caution in young children and in patients with significant renal dysfunction.

c) The reference range should be quoted on reports; the upper limit should not exceed 300 nmol/24 hours [2, 3].

5. **Further Investigation**

If a positive result is found on screening, it is recommended that the patient is referred to a consultant physician or paediatrician with specialist endocrinology experience.

6. **Precision and Bias**

Each laboratory should ensure that appropriate internal quality control and external quality assessment (EQA) procedures are in place. Any laboratory consistently unable to meet the following criteria and which cannot change to a superior assay should refer samples elsewhere.

a) For serum cortisol, the precision should be less than 15% and bias should be less than 15% [5].

b) For urine free cortisol, the precision should be less than 20% and the bias should be less than 25% [5]. Laboratories offering this assay should use a urine internal quality control material and should subscribe to an appropriate EQA scheme specifically for urine free cortisol.

ACKNOWLEDGEMENTS

Dr.D.Oleesky, Mrs.A.Owen and Dr.G.F.Read.

REFERENCES

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Version: 1

DATE: 3rd April 1998. [Reviewed Spring 2001 and re-confirmed, without changes]