Endocrinology Handbook

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BILATERAL SIMULTANEOUS INFERIOR PETROSAL SINUS SAMPLING (IPSS) WITH CRF

INDICATION

Patients with Cushing's syndrome and high ACTH levels in whom there is not a clinically definite pituitary source. The aim of this test is to differentiate pituitary from a non-pituitary source of ACTH and to lateralise a corticotroph adenoma.

CONTRAINDICATIONS

(Discuss with interventional radiology x34943)

- Allergy to contrast dye.
- Ischaemic Heart Disease.
- Orthopnoea.
- Bleeding tendencies (severe).

PREPARATION

If patient on aspirin/clopidogrel, discuss with radiology.

Metyrapone and ketoconazole need to be stopped 1 week before IPSS.

Order synthetic **human CRF** in advance from Pharmacy (allow 5 days). DDAVP (10 micrograms IV) is a poor but possible alternative if CRH is not available. Document (in the notes) what type of CRH is being used.

Warn endocrinology lab (34681) 48 hours in advance and on the day of the procedure. If no answer, contact the Duty Biochemistry via Switchboard.

Consent patient (risks of bleeding from cannula sites, CVA, dye allergy, pulmonary embolus). This should be performed by the radiologists.

The day before the procedure, check FBC, U + E, INR, G + S.

Fast for at least 4 hours.

2 people to attend to assist sample processing.

18 red Vacutainers.

18 EDTA Vacutainers, labelled before the study.

Syringes for sampling and flushing cannulae.

Ice.

Arrangements to transfer for immediate centrifugation.

SIDE EFFECTS

CRF can cause flushing and hypotension but this is rare with 100 mcg.

No complications of IPS sampling have been reported in over 50 patients reported in the literature, but we have had one patient who had a pulmonary embolus following the procedure and one who became asystolic during the procedure, but recovered when the procedure was abandoned.

METHOD

1. One catheter is placed in each inferior petrosal sinus (IPS) and their position confirmed on screening. A third catheter is placed peripherally (P) in the arm.
2. Two baseline samples are taken at approximately -5 and 0 minutes. Ask the radiologist for 10 ml from each site: one purple for ACTH and one red Vacutainer at each site. At T = 0 the CRF is injected intravenously as a bolus over 1 minute peripherally. For adults the dose is 100 mcg or 60mcg per square meter body surface in children.
3. Simultaneous samples from the 3 sampling sites are taken at T = 2, 5, and 10 minutes. At the same time as one of the sets of basal samples an arterial sample may be taken from the femoral artery if a pulmonary source of ACTH is possible, and peripheral samples may be taken at T = 60 and 90 minutes (see below). Only samples taken for ACTH should be stored in ice and spun within 15 minutes.
4. ACTH is measured in all samples. Cortisol is measured in the basal samples from all sites and in all the peripheral samples. Prolactin is measured in both IPS series.

INTERPRETATION

- A basal IPS:P ratio $\geq$ 2.0 indicates a pituitary source with 95% sensitivity and 100% specificity. A CRH stimulated ratio $\geq$ 3.0 increases the sensitivity to 100%, the 2 and 5 minute samples usually

being sufficient. Pituitary ACTHomas are usually paramedian or lateral and there is suppression of the normal corticotrophs on the contralateral side (Crooke cell changes).

- If in addition the basal or stimulated ACTH level for one IPS sample is 1.5 times as high as the simultaneous contralateral side, this localises the pituitary tumour to the ipsilateral side with a sensitivity of 99% and a specificity of 82%. It has also been reported that prolactin and GH are often raised on the side of the tumour and that this is augmented by CRF.
- In IPS sampling the principal difficulty arises from the positioning of the sampling catheter. Jugular venous samples do not consistently show lateralisation. The measurement of prolactin can be used as a marker of proximity to the pituitary.
- Using the peripheral samples it is possible to look at the response to CRF of venous levels of Cortisol. The interpretation of this response is difficult but in general patients with Cushing's disease tend to have an exaggerated response (>850 nmol/l) and ectopic ACTH sources have a reduced response. The interpretation of the CRF test at present is uncertain as the reported series use different end points, varying doses of CRF and small numbers of patients. Until there is more local experience (see above) of this test it should not be used to differentiate sources of ACTH.
- It appears that in ectopic ACTH production a cortisol response greater than normal has not been described. It is not a sensitive test as approximately 25% of Cushing's disease do not respond to CRF with cortisol responses greater than normals.

REFERENCES

IPS sampling: Clinical Endocrinology 25, 687-96 (1986).
CRF test: A. Grossman et al., Clinical Endocrinology 29, 167-178 (1988).
Petrosal sinus sampling: NEJM 325, 897-905 (1991).