Inferior Petrosal Sinus Sampling

A Metabolic Unit Registrar's Guide

Introduction

Bilateral inferior petrosal sinus sampling (BIPSS) is performed to assess the degree of pituitary ACTH production in the setting of confirmed Cushing's syndrome. It is performed in Edinburgh by neuroradiology in the DCN catheterisation lab (DCN x-ray, ground floor) and samples are processed by dedicated personnel in biochemistry.

Metabolic Unit (MU) registrars are asked to organise this from time to time. The investigation involves simultaneous sampling from three sites, the left and right petrosal sinus sites and a peripheral venous sample. This can be a challenging exercise but with adequate preparation it is straightforward.

Your task is to:

- provide relevant endocrinologists, biochemists, neuroradiologists and neurosurgeons with situational awareness beforehand;
- co-ordinate collection of samples and administration of CRH;
- organise the samples and their transport to biochemistry for processing; and
- present the results at a MU meeting,

in order to ensure this invasive, complex investigation runs efficiently.

ACTH and cortisol (to assess response to CRH) and prolactin (to assess adequate inferior petrosal sinus cannulation) are measured at six time intervals (2 baseline, 4 post-CRH administration).

Preparation

When notified about BIPSS

- Agree a date for the procedure with the patient, the MU Charge Nurse and Dr Peter Keston in neuroradiology (peter.keston@nhslothian.scot.nhs.uk). Dr Keston will arrange for the DCN team to write out to the patient with the confirmation of appointment and the arrangements for admission. Ask the MU Charge Nurse to put the procedure in the diary (this is for the benefit of Biochemistry; Metabolic Unit Nurses are not directly involved in the procedure).
- As soon as the procedure date is agreed notify the Duty Biochemist ext 31899 at the WGH. This should be done in advance of the theatre list being prepared. This will ensure that appropriate staff are available on the day to receive and process the samples

1 week beforehand

- Arrange with MU staff or pharmacy to procure 1 vial of CRH/CRF (100mcg). If ordering through pharmacy, it can take up to 1 week to arrive.
- Arrange with the Duty Biochemist to visit the Biochemistry Department (Clock Tower building, below ward 9) at least 1 week before the procedure in order to:
  1. Collect
     - paediatric blood tubes (18 EDTA (red) for ACTH prolactin and cortisol),
     - a large tray
     - 3 test tube racks (figure 1), i.e. one for each site
  2. Be familiarised with usage of ice machine to form an ice-water slurry (the departmental machine makes crushed ice rather than cubes)
     - ACTH is very unstable at room temperature and must be transported back to the lab immersed in ice as quickly as possible. However, it is also essential to avoid contaminating any of the samples with H_2O.
  3. Discuss pre-labelling of the samples
     - Agree nomenclature for time interval, e.g. R_x, L_x or P_x, i.e. right, left side petrosal sinus and peripheral, where 'x' corresponds to time interval – see appendix 1
     - Arrange the specimens in time order in labelled slots on the three test tube racks (one each for right, left and peripheral)
- Label and organise the blood tubes. This should be done by writing directly onto the tubes' manufacturing label in permanent pen ('sharpie fine tip' works best – there should be a couple in the MU registrars' room), with patient name, DOB, date, time interval, and PRL/COR/ACTH. N.B. you must not use printed Trak labels, as these fall off in water.
- Call DCN x-ray reception to speak to the duty theatre nurse for the list.
  - Confirm the time of the procedure
  - Request 2 extra nurses to help with handling of specimens

EDTA tube for prolactin and cortisol. Until recently, 2 tubes were required: Li-Hep for prolactin and cortisol and EDTA for ACTH (as with testing in other settings). As of Spring 2015, the Biochemistry Dept have offered to perform ACTH, prolactin and cortisol assays from **one 1.3 ml EDTA tube** for IPSS. This leads to a 5% reduction in cortisol over the standard sample (gel or Li-hep), however as only ratios are relevant (see *after the procedure*), rather than absolute cut-offs, this is not an issue.

The day of the procedure

- Visit the patient on ward 31 DOSA. Perform a cursory clerking, including BIPSS indication and a drug history. The radiologists will obtain consent.
- Soon after the time the patient is called to theatre, collect the ice or ice-water slurry from Biochemistry. It should not be allowed to melt too much, so leave this as late as possible.
- Fill out a biochemistry request form for each of the 3 sites, i.e. left , right and peripheral, to accompany the samples to the lab (figure 2). Ensure that there is space to enter the actual sample time for each of the 6 samples.

Procedure

- It takes about 10-15 minutes for the radiologist to cannulate both sides of the inferior petrosal sinus so the following is best agreed before they start
- You also need a collection point for peripheral blood; this could be an extra port on the femoral vein catheterisation point or a separate peripheral venous cannula.
- Prepare 100mcg CRH in a labelled syringe and a saline flush
- Calmly brief the team:
    - Nominate 2 sample handlers (could be you and one other, or better, 2 other staff) and explain the process (blood to go into correct tubes)
    - You need the radiographer to set the screen stopwatch to zero and start the clock when three people are ready to simultaneously withdraw blood.
    - Three scrubbed staff (i.e. the consultant radiologist, their registrar/assistant and the scrub nurse) need to simultaneously flush then withdraw blood at the following time intervals **(1.0-1.3ml per site is required)**
        - 0mins - 5 minutes before CRH (t_{-5})
        - 2mins - 2 minutes before CRH (t_{-2})
        - 4mins - *Immediately after* you administer CRH (t_0)
        - 6mins - CRH plus 2 minutes (t_2)
        - 9mins – CRH plus 5 minutes (t_5)
        - 14mins – CRH plus 10 minutes (t_{10})
    - It is important that they withdraw 5ml to be discarded (the dead space) before withdrawing the specimen, then flushing again.
    - **100mcg CRH is to be administered at t_0**
    - Your role is to manage time keeping, document the precise times of blood withdrawal on the biochemistry form, and supervise the filling of the appropriate tube, ensuring they are kept on ice
- After the stopwatch has started, scrubbed staff should pass filled syringes to sample handlers, stating clearly which site it was taken from. You should also remind the team of the time interval so the right tubes are filled. They should be arranged in the rack in time order.
- Supervise the sample handlers promptly transferring blood into the 1.3 ml EDTA (red) tubes before being put on ice.
- Take the tray of filled tubes immediately to biochemistry, where the nominated Biochemist and cooled centrifuge should be waiting.

After the procedure

- The biochemist will be in touch with you directly when the tabulated results are available. It can take up to a week, as ACTH samples are processed at RIE.
- The results will be available in Trak once all analyses are complete. In addition the Laboratory will issue a hard copy report on a 3 sheets listing the results from the 3 sites.
- Prepare the results in the attached spreadsheet format (Appendix 1), before transferring them to a PowerPoint slide (Appendix 2).
- Present the results for discussion at a MU meeting: [1,2]
    - Describe how Cushing's syndrome was confirmed in the patient.
    - Sampling from both sides of the inferior petrosal sinus reduces the procedural failure rate (i.e. incorrectly placed catheter) and allows a degree of lateralisation of the adenoma.
    - ACTH is secreted in a pulsatile manner. CRH administration stimulates ACTH release from a corticotroph adenoma, accentuating the pituitary-to-peripheral ratio, thereby discriminating between pituitary and ectopic ACTH.
    - If the pituitary to peripheral ratio of is >3 after CRH, the patient has pituitary Cushing's. If it is <3, the patient probably has ectopic ACTH.[1]
    - Concurrent measurement of prolactin reduces the number of false negative results by identifying adequate IPS cannulation, and increases our ability to correctly lateralise the corticotroph adenoma by comparing the R to L prolactin adjusted ACTH ratios.
        - An IPS to peripheral prolactin ratio of 1.8 or greater indicates proper IPS sampling on that side
        - The prolactin-adjusted ACTH ratio is calculated by dividing the IPS ACTH level by a concomitantly drawn ipsilateral IPS prolactin level. Comparison of R and L ratios before and after CRH administration can improve ability of IPSS to lateralise the adenoma.
- Inform the patient's consultant of the result

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[1] See *http://pituitary.mgh.harvard.edu/E-F-942.HTM*

[2] For in-depth examples explaining the interpretation of IPS and peripheral prolactin, see *Mulligan GB, Faiman C et al; Prolactin measurement during inferior petrosal sinus sampling improves the localization of pituitary adenomas in Cushing's disease; Clin Endocrinol (Oxf). 2012 Aug;77(2):268-74*

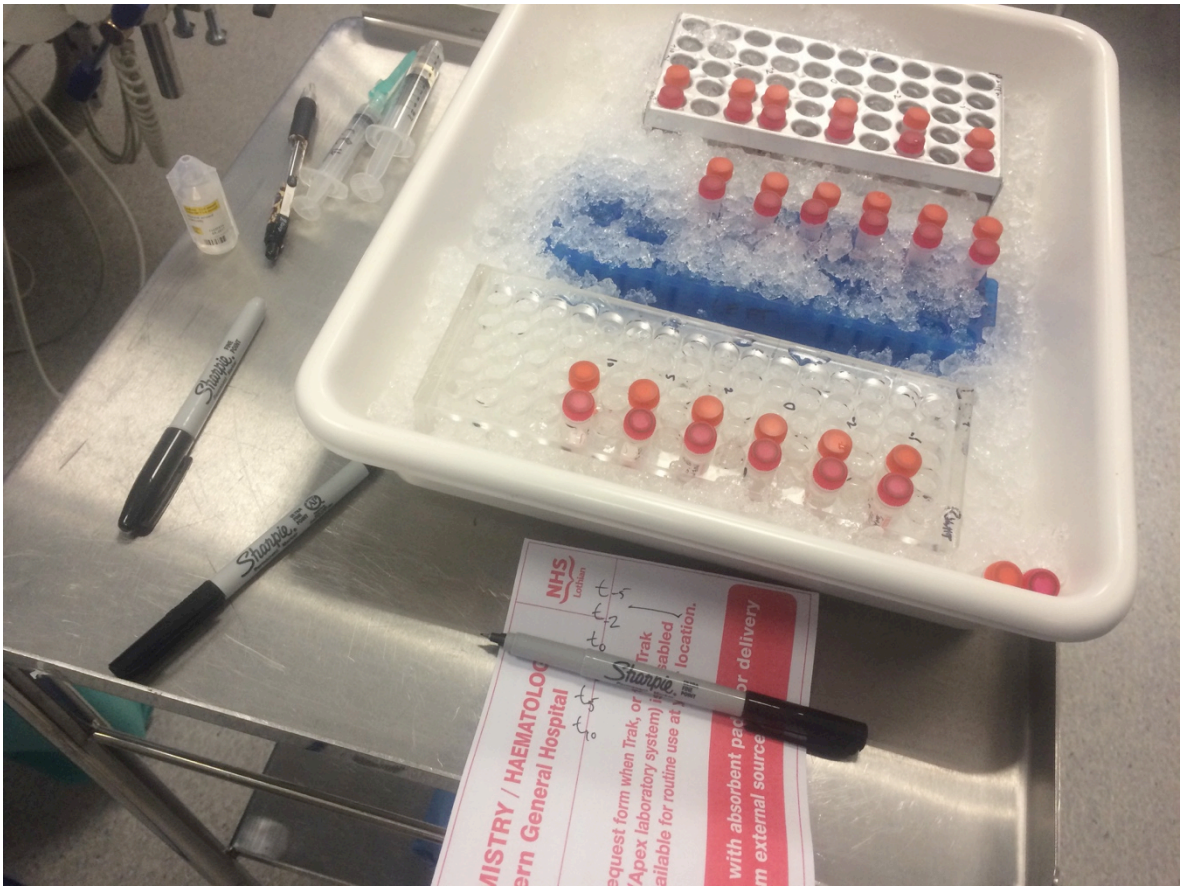

Figure 1 – NB, now only 1 EDTA (red) top tube is required per time interval/ site; Li-Hep (orange) is no longer necessary

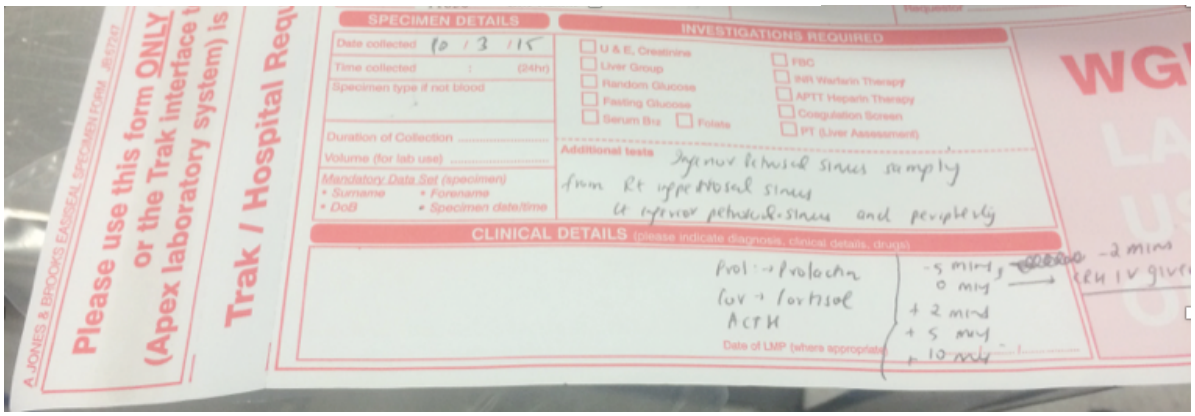

Figure 2

Appendix 1 – spreadsheet of BIPSS results

Appendix 2 – PowerPoint slide of results for unit discussion

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Last updated 3 Apr 15