CLINICAL CASES FOR PORPHYRIN

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Porphyrin Scheme

The Weqas Porphyrin EQA scheme includes performance assessment of both quantitative and qualitative analysis of Total Urine Porphyrin (TUP), Porphobilinogen (PBG) and plasma porphyrin. 120 laboratories in the UK currently participate in the Scheme. 3 fresh, filtered human urine samples are spiked with PBG and coproporphyrin and are distributed every three months. The analytes are available in separate samples to ensure individual stability. The pools are produced to ensure that an adequate pathological range is covered in all distributions.

Both analytical and interpretative elements are examined in the Scheme. Laboratories are asked to analyse the sample and provide interpretive comments suggesting further investigation if appropriate. The correct interpretation is given by an expert advisor and is made available to all participants along with a summary of the responses. Key phrases used by the expert are used to evaluate the responses. These are highlighted in the examples. 24 cases have been distributed to date. The provision of appropriate operating protocols; repeat and positive samples are provided to participants to aid performance improvement. Please find below example cases.

Case 1 **Raised PBG 86µmol/L**

Clinical information
18 year old girl presenting to A & E with a 5 day history of abdominal pain and vomiting. Clinically dehydrated (Urine creatinine = 48.5 mmol/L)

Expert Report comment
Borderline increase in PBG. These results exclude a current attack of acute porphyria. During an attack PBG is grossly elevated. If symptoms were already resolving when this specimen was collected, and porphyria is still suspected clinically, then plasma/serum and faeces should be examined. These results do not exclude a neurological porphyria in remission or the latent phase.
The urine is very concentrated due to the patient's dehydration. The upper limit usually quoted for random urine PBG:creatinine ratio is usually 1.5 µmol/mmol. Therefore the upper reference limit for this urine (creatinine = 48.5 mmol/L) is 1.5 x 48.5 = 73 µmol/L. Therefore a current attack of acute poprhyria is very unlikely on the grounds that the PBG:creatinine ratio is only minimally raised. It is important to take urine "concentration" into account – difficult to do with qualitative screening tests. Again both VP and HCP can be excluded by examination of faeces and plasma/serum if symptoms are already starting to resolve.

Result comments summary - 78 sets of comments were received
Out of the 78 comments only 11 commented that this was a borderline increase in PBG, 7 commented that the result exclude a current attack of acute porphyria and 9 would have examined plasma and faeces. Only 2 commented that the result did not exclude neurological porphyria in remission or in latent phase, however 55 (71%) participants stated that they would have referred the sample to a specialist laboratory.

Case 2 **Porphyrin Concentration 1400 - 1500 nmol/L**

Clinical information
46-year-old gentleman complaining of skin fragility and blistering lesions on the backs of his hands.

Expert Report Comment
Raised urinary porphyrin requires further investigation. Please send faeces (approx. 5 g) and EDTA blood.
The raised urinary porphyrin is very suggestive that one of the cutaneous porphyrias is responsible for the patient's skin lesions (which are typical). Confirmation of this and identification of the type of porphyria requires fractionation of the individual porphyrins in urine and stool and examination of plasma by fluorescence emission spectroscopy. This will probably entail referral to a specialist laboratory. All three specimens should be sent.
It is particularly important to differentiate between cutaneous porphyrias in which potentially fatal acute attacks may occur (variegate porphyria and hereditary coproporphyria) and those in which they do not (porphyria cutanea tarda and congenital erythropoietic porphyria). Furthermore effective treatments exist for porphyria cutanea tarda but not the other types.

Summary of results– 73 sets of comments

45 out of the 73 laboratories, (62 %) would have carried out the appropriate further investigation on all three samples, whilst 27 % would have carried out selective analysis of either blood urine or feces, eight would have also carried out Urine PBG on the sample. Three would have referred the sample, two laboratories would have investigated for family history and two for alcohol abuse.

The same clinical details with a porphyrin of 1500 nmol/l was distributed as Case 9, a year later. On this occasion, 45 out of 56 (80%) would have asked for EDTA and faeces and 14 (25%) would have referred the sample to a specialist laboratory.

Conclusion

The Scheme has highlighted the variability of expertise in reporting Porphyrin results within the UK.
The results in Case 9 compared with Case 3 suggests that the educational exercise has led to some improvement in reporting. It was also noted that a higher percentage of laboratories would have referred samples to a specialist laboratory in the more recent distributions compared with the earlier exercises.
The Scheme fulfills the criteria of the International Federation of Clinical Chemistry (IFCC), Guidelines for the Requirement for the Competence of EQAP organizers, providing: Participant performance evaluation, Interpretation, Method performance evaluation, Post marketing vigilance of in vitro diagnostic devices and Continuous education, training and help. These additional pre- and post analytical components of Scheme design introduce elements of quality assurance rather than assessment and are pivotal in facilitating quality improvement of the services provided by the participating laboratories.