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Post-analytical Proficiency testing - Experience with Interpretative Clinical Cases

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Introduction

Proficiency testing is an essential part of assuring the quality of laboratory diagnostic services, and should where possible include assessment of both pre and post analytical phases of the diagnostic cycle. Weqas programmes include pre and post analytical assessments as part of our educational role, either as case study exercises or with the distribution of challenging samples.

The following describes a typical analytical and post analytical assessment capturing both elements through distribution of samples and incorporating case studies.

Method

As part of the Weqas Porphyrin programme, laboratories were issued with 3 urine samples containing porphobilinogen (PBG) along with relevant clinical information for each sample. Laboratories were asked to analyse the sample and provide interpretive comments suggesting further investigation if appropriate. Participant responses were assessed for both analytical and post-analytical performance. The correct interpretation was provided by an expert advisor and made available to all participants along with a summary of the responses. Key phrases used by the expert are used to evaluate the responses. Participants were given a point if they identified one of the agreed 'key points' of the case.

Case 1

Clinical Details: A 35 year old known Variegate Porphyria (VP) patient, diagnosed on family screening, is admitted with acute abdominal pain, nausea and vomiting. A random urine sample is sent for PBG measurement.

Results:	Overall Mean	SD	n
PBG (µmol/L)	112.5	15.45	19
PBG / Creatinine Ratio (µmol/mmol)	23.4	3.21	14
Creatinine (mmol/L)	4.65	0.17	14

Case Results (Expert Opinion):

"In variegate porphyria (VP) urine PBG excretion is invariably normal during latency and increases only during an acute attack. In this case urine PBG excretion is increased 15-20 fold (PBG Reference range <1.5umol/mmol Creatinine) and therefore confirms an acute attack of porphyria as a cause of the symptoms. The patient is known to have VP so no other investigations are required. The result should be telephoned. Clinical advice (if sought) should be to provide symptomatic relief (opiates, IV fluids etc), to start haem-arginate therapy, establish possible precipitating factor (unsafe drugs, infection). Do not advocate monitoring of urine porphyrin and PBG following diagnosis and initiation of treatment for an acute attack."

Participant Comments - Quantitative PBG Users:

The 2 key points from the case were 'Results Confirms Acute Attack' and 'Seek Clinical / Specialist Advice'. Of the 16 users who provided comments 13 were awarded a point for 'Results Confirms Acute Attack', while 7 got a point for 'Seek Clinical / Specialist Advice'.

11 sites stated results are consistent with acute attack, 5 provided details of specialist porphyria services/referral labs for advice, while other comments included: result to be phoned, ensure exclude other causes, look for precipitating factors.

Case 2

Clinical Details: A 25 year old female known to have Acute Intermittent Porphyria (AIP) presenting to A & E with abdominal pain.

Results:	Overall Mean	SD	n
PBG (µmol/L)	33.4	4.45	19
PBG / Creatinine Ratio (µmol/mmol)	5.5	0.84	14
Creatinine (mmol/L)	6.2	0.28	14

Case Results (Expert Opinion):

"The elevation in PBG is minimal (PBG Reference range <1.5umol/mmol Creatinine) and typical of values seen during remission or the latent phase of AIP. Unfortunately there is no clear threshold value above which symptoms appear but a current attack of acute porphyria is very unlikely and an alternative cause for her abdominal pain should be sought. Attacks of AIP are usually associated with gross elevations in PBG (typically 10 to 100 fold). There is a danger of an attack of porphyria developing if she is not managed appropriately so there is justification for repeating the test at intervals should her symptoms fail to resolve."

Participant Comments - Quantitative PBG Users:

The 3 key points from the case were 'Results typical of latent phase / remission', 'Acute attack unlikely', 'Seek alternative cause of abdominal pain'. Of the 14 users who provided comments 9 were awarded a point for 'Results typical of latent phase / remission' 2 were awarded a point for 'Acute attack unlikely' and 9 were awarded a point for 'Seek alternative cause of abdominal pain'. 2 users reported that the results were typical of an acute attack and had a point deducted.

10 sites stated that PBG results can be elevated to this degree in between acute attacks, 4 stated PBG results do not exclude or confirm an acute attack and 5 provided details of specialist porphyria services/referral labs for advice.

Case 3

Clinical Details: A GP sends a random urine sample from the 55 year old mother of a patient recently diagnosed with Acute Intermittent Porphyria (AIP).

Results:	Overall Mean	SD	n
PBG (µmol/L)	11.4	1.42	19
PBG / Creatinine Ratio (µmol/mmol)	0.8	0.09	14
Creatinine (mmol/L)	13.9	0.46	15

Case Results (Expert Opinion):

"The normal PBG (PBG Reference range <1.5umol/mmol Creatinine) does not exclude latent porphyria in a family member of an affected patient. Urine PBG excretion can be increased in about 40% of pre-symptomatic AIP patients, although not before puberty. Further investigation is required using enzyme measurement or genetic testing. The gold standard test is genetics - Good practice would be to suggest referral of the patient to a clinical genetics service for counselling and to arrange genetic testing for this patient as well as testing for other family members."

Participant Comments - Quantitative PBG Users:

The 2 key points from the case were 'Does not exclude latent porphyria' and 'Further investigation required (Genetic testing)'. Of the 14 users who provided comments 10 were awarded a point for 'Does not exclude latent porphyria', while 12 were awarded a point for 'Further investigation required (Genetic testing)'.

5 sites stated that the results exclude current acute attack, 10 stated that latent AIP could not be excluded and 12 suggested further studies and / or discussion with the National Acute Porphyria Service.

Conclusion

The "additional value" of interpretation is a major contributor in the delivery of improved clinical effectiveness and laboratorians have a professional responsibility to provide this service [1]. However, the Weqas programme has highlighted the variability of expertise in reporting results and demonstrates the importance of assessing the post-analytical phase. Laboratories should consider whether post analytical assessment is considered when selected their PT provider.

[1] Beastall GH, Adding value to laboratory medicine: a professional responsibility. Clin Chem Lab Med. 2013 Jan;51(1):221-7.