Audit on Macroprolactin

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Introduction

In most subjects the predominant circulating form of prolactin in serum is monomeric. However, in some individuals there is an additional circulating form, usually called macroprolactin, in which the prolactin is bound to immunoglobulins and has minimal bioactivity in vivo and is detected to varying degrees by different immunoassays. Unless detected by the laboratory, this can lead to diagnostic confusion, unnecessary further testing and possibly inappropriate treatment. Therefore, the investigation of an unexpected raised prolactin requires a logical and systematic approach in which a macroprolactin is excluded in every instance at the earliest opportunity.

Macro forms exist for other analytes. There appear to be a lack of guidelines in the literature for investigating suspected macroanalytes with the exception of macroprolactin where several have been published.

Aim

To provide guidelines for testing macroanalytes, in particular for macroprolactin, including when to request, how they should be analysed, quality controls, interpretation and necessary follow-ups.

Audit method

A detailed questionnaire was circulated within the Thames Audit Group and responses received from 22 laboratories and of these, 12 were from district general hospitals,7 from teaching hospitals and 3 from specialist hospitals.

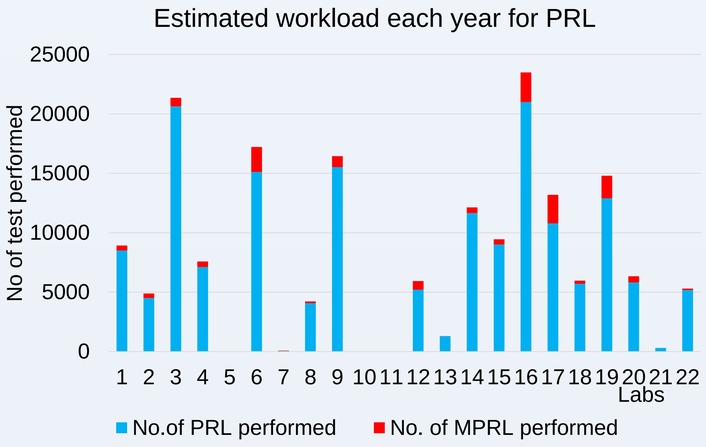
Results

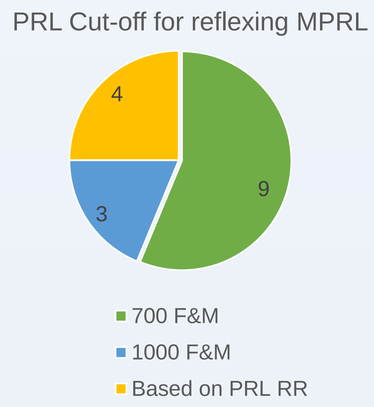
These showed a variation in practice for both macroprolactin (MPRL) analysis and reporting.

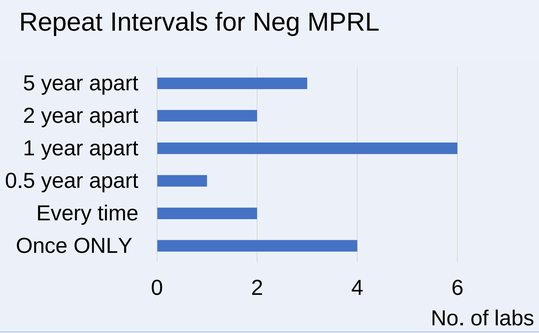
- A wide range of analytical platforms were adopted.

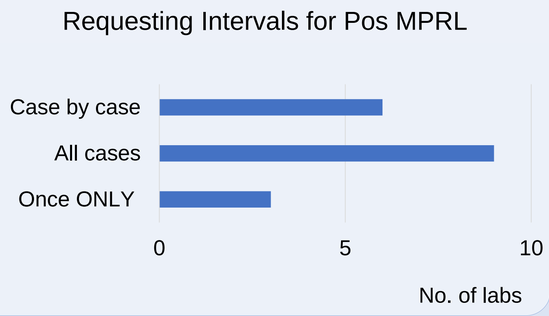
Analytical Platforms
Roche (n=12)
Abbott (n=3)
ADVIA Centaur (n=2)
Beckman (n=1)
Siemens (n=2)
Referral to other labs (n=2)

- Macroprolactin workload varied, depending on the workload of the prolactin (PRL) requests ,the cut-off and repeat intervals for reflexing for macroprolactin.

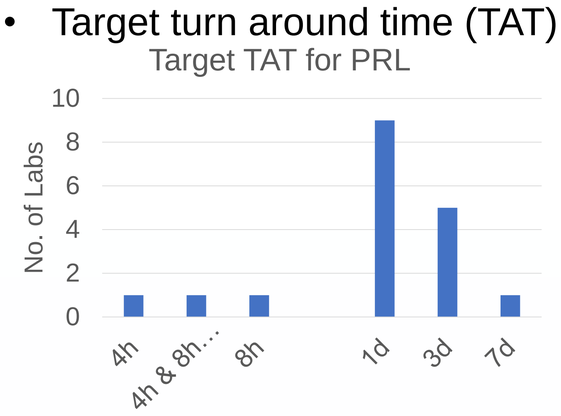


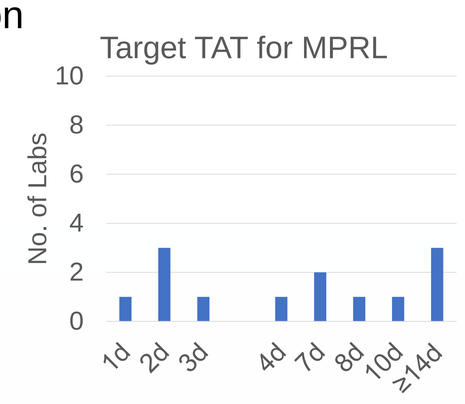




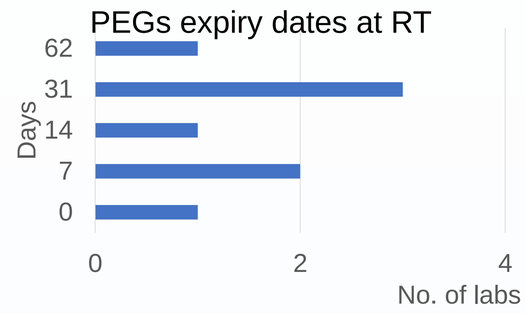


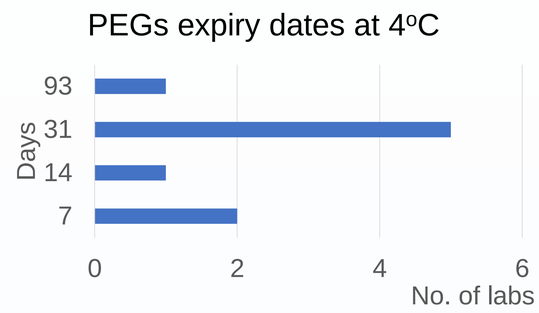
- Target turn around time (TAT) variation





- PEG stability variation: 7 laboratories stored the PEG solution at room temperature (RT) for between 7 and 62 days





- Centrifugation time ranged from 5 minutes up to 30 minutes at different speeds.
- 7 laboratories did not perform a paired sample +diluent.
- Calculations

		No. of labs
Estimated BMP	Sample PEG x dilution factor 2	9
	Sample PEG x dilution factor 2.6 or 2.7	3 &1
	BMP not reported	2
MPRL Recovery	Sample PEG /sample diluent x 100%	10
	BMP/total prolactin x 100%	6
	[100 (2z x 1.163)] / y Where z= prolactin post PEG ppt ; y= original prolactin result	1

One laboratory using the dilution factor of 2.6 corrected for dilution by the PEG solution and for recovery of monomeric prolactin but still used the reference ranges (RR) quoted by Beltran et al(2008) where a dilution factor of 2 was used to derive the RR.

- For IQC, 4 laboratories used patient samples only and 7 laboratories used commercial QC only. Only 5 used both.
- 3 Roche users included RR where sources were unknown.
- 2 laboratories used biomonomeric prolactin (BMP) RR which were higher than their RR for total prolactin.
- Only 2 laboratories had Trust guidelines available for the investigation of raised prolactin
- The majority of participants in the audit as expected investigated for macroprolactin. However, as none or very few investigated for macroamylase, macro-alkaline phosphatase, macro-CK, macrotroponin or macro-TSH, this data was not presented in the findings.

Conclusion

It is recommended that standards are drawn up for the investigation of macroprolactin and other macroanalytes.

References

- Beltran L, el all. Serum total protein and monomeric prolactin reference intervals determined by precipitation with polyethylene glycol: Evaluation and validation on common immunoassay platforms. Clin Chem 2008; 54: 1673-1681
- Fahie-Wilson MN, et al. Macroprolactin and the Roche Elecsys Prolactin assay: Characteristics of the reaction and detection by precipitation with polyethylene glycol.
- N F Jassam, el all. (2009) Macroprolactin on the Advia Centaur: Experience With 409 Patients Over a Three-Year Period. Ann Clin Biochem. 2009 Nov;46(Pt 6):501-4.
- Fahie-Wilson MN el all.. Determination of prolactin: the macroprolactin problem. Best Practice & Research Clinical Endocrinology & Metabolism 2013; 27: 725-7424.
- Gibney J, el all. . Clinical relevance of macroprolactin. Clinical Endocrinology (2005) 62,633-6432.
- Casanueva FF, el all. Guidelines of the Pituitary Society for the diagnosis and management of prolactinomas. Clin Endocrinol 2006; 65: 265-731.
- Melmed S, el all.. Diagnosis and treatment of hyperprolactinaemia: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 201; 96: 273-88

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