COMMUNICATIONS IN PROLACTIN RESEARCH

SPECIAL ARTICLE

Call for Submissions: Macroprolactinaemia

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Keywords

Macroprolactinaemia, autoantibodies, immunoglobulins

Abbreviations

PRL, prolactin; PEG, polyethylene glycol; Ig, immunoglobulin

Citation

Triebel, J. *Communications in Prolactin Research*, 2025, September 19, https://doi.org/10.63701/cpr.4

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Besides monomeric prolactin (PRL) at 23 kDa, additional fractions of human serum contain immunoreactive PRL, such as big-PRL (50 kDa) and big-big PRL (>150 kDa). These fractions comprise PRL dimers and/or multimers, and complexes of PRL and immunoglobulins of the immunoglobulin G (IgG)- and immunoglobulin A (IgA)-type, referred to as macroprolactin (1–3). Macroprolactinaemia is usually defined as PRL levels above the upper threshold of the reference range due to the presence of Ig-type macroprolactin at normal levels of monomeric PRL. Thus, the presence of Ig-type macroprolactin can impact the measurement of monomeric PRL and cause false-high PRL levels, if not properly addressed by polyethylene glycol (PEG) precipitation. As neatly summarized recently by Michael N. Fahie-Wilson, there is widespread consensus that (a) macroprolactinaemia is common; (b) its clinical significance is its ability to produce false-high PRL levels indicating hyperprolactinaemia of monomeric PRL; and (c) that it is biologically inactive *in vivo* (4). It has been concluded from clinical studies, including a longitudinal cohort study, that macroprolactinaemia is a benign condition with no pathological significance (5). Anti-PRL autoantibodies are the major cause of macroprolactinaemia, although other binding types have also been discussed (6). Much of the attention on macroprolactinaemia has been focused on its prevalence and methodological issues (such as reducing the macroprolactin cross-reactivity of PRL assays) while investigating the true endocrine nature of macroprolactinaemia has received less attention. As demonstrated by the research of Naoki Hattori et al., major epitopes for anti-PRL autoantibodies are located at the N- and C-terminal residues of the PRL molecule (7). The PRL–IgG complex increases the half-life of PRL in the circulation as it hinders renal elimination (8). Due to its size, it may prevent PRL from entering target tissues. Macroprolactin has been found in cord-blood and amniotic fluid (9) and can be detected in the serum of pregnant women (10). PRL may dissociate from IgG, regaining its full biological activity (11). In addition, a distinct group of individuals with normal PRL levels also have significant fractions of IgG-bound PRL, indicating that macroprolactinaemia can occur across the full range of circulating PRL levels. (6). Should the definition of macroprolactinaemia include these cases, and if yes, is there a clinical relevance? Given the absence of autoimmune disease in subjects with macroprolactinaemia, which is the true physiological origin and context of anti-PRL autoantibodies? Does binding to IgG/IgA block cleavage of the PRL molecule by proteases? This journal provides the ideal framework for communicating any work on these subjects. A set of recommended literature is presented in Table 1. Submit your manuscript, or find out more about Communications in Prolactin Research here: https://www.communications-in-prolactin-research.com/

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Table 1 Selected Recommended Literature.

Title	Study Type	Authors	Reference
Macroprolactin; High Molecular Mass Forms of Circulating Prolactin	Review	Fahie-Wilson, John, Ellis	(12)
Clinical Relevance of Macroprolactin	Review	Gibney, Smith, McKenna	(13)
Serum Total Prolactin and Monomeric Prolactin Reference Intervals Determined by Precipitation with Polyethylene Glycol: Evaluation and Validation on Common Immunoassay Platforms	Original Research	Beltran, Fahie-Wilson, McKenna, Kavanagh, Smith	(14)
The natural history of macroprolactinaemia	Original Research / Clinical Study	Hattori, Adachi, Ishihara, Shimatsu,	(15)

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