

Category : **Sepsis/septic shock: management**

A100 - IgM/IgA-enriched immunoglobulins – more than an IVIg: about multimeric IgA, IgM & J-chain

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Introduction:

Severe infections are still a major health burden. Beneficial effects of treatment with IgM/IgA-enriched immunoglobulins compared to standard IVIg were reported and attributed to the additional IgM and IgA component [1]. Nevertheless, the molecular structure of such complex preparations is not fully understood. Especially in focus of respiratory diseases are multimeric IgM and IgA species that could be transported to mucosa [2]. The aim of our work was to characterize an IgM/IgA-enriched immunoglobulin with focus on IgA, IgM and the presence of J-chain which enables immunoglobulin transport to mucosa.

Methods:

We characterized the IgM/IgA-enriched immunoglobulin Pentaglobin® (76% IgG, 12% IgA, 12% IgM) by measuring the ratio of IgG and IgA subclasses. Relative distribution of monomeric and multimeric immunoglobulins was analyzed by size exclusion chromatography. Specific detection of IgG, IgA, IgM and J-chain was performed by western-blot. J-chain was quantified by ELISA.

Results:

The immunoglobulin distribution reveal the presence of several immunoglobulin isotypes (IgG/IgA/IgM) as well as IgG and IgA subclasses. Molecular size distribution reveal multiple multimeric species. Subsequent western-blot analysis shows pentameric IgM and dimeric IgA with J-chain, as well as monomeric IgG and IgA (Figure 1). J-chain ELISA quantifies a notable portion of IgA and IgM molecules that is associated with J-chain.

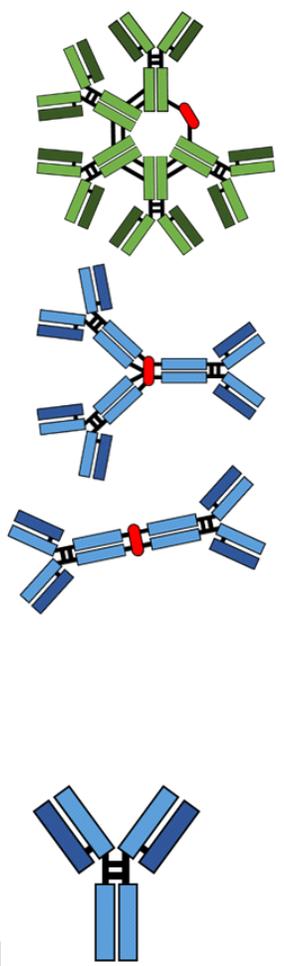
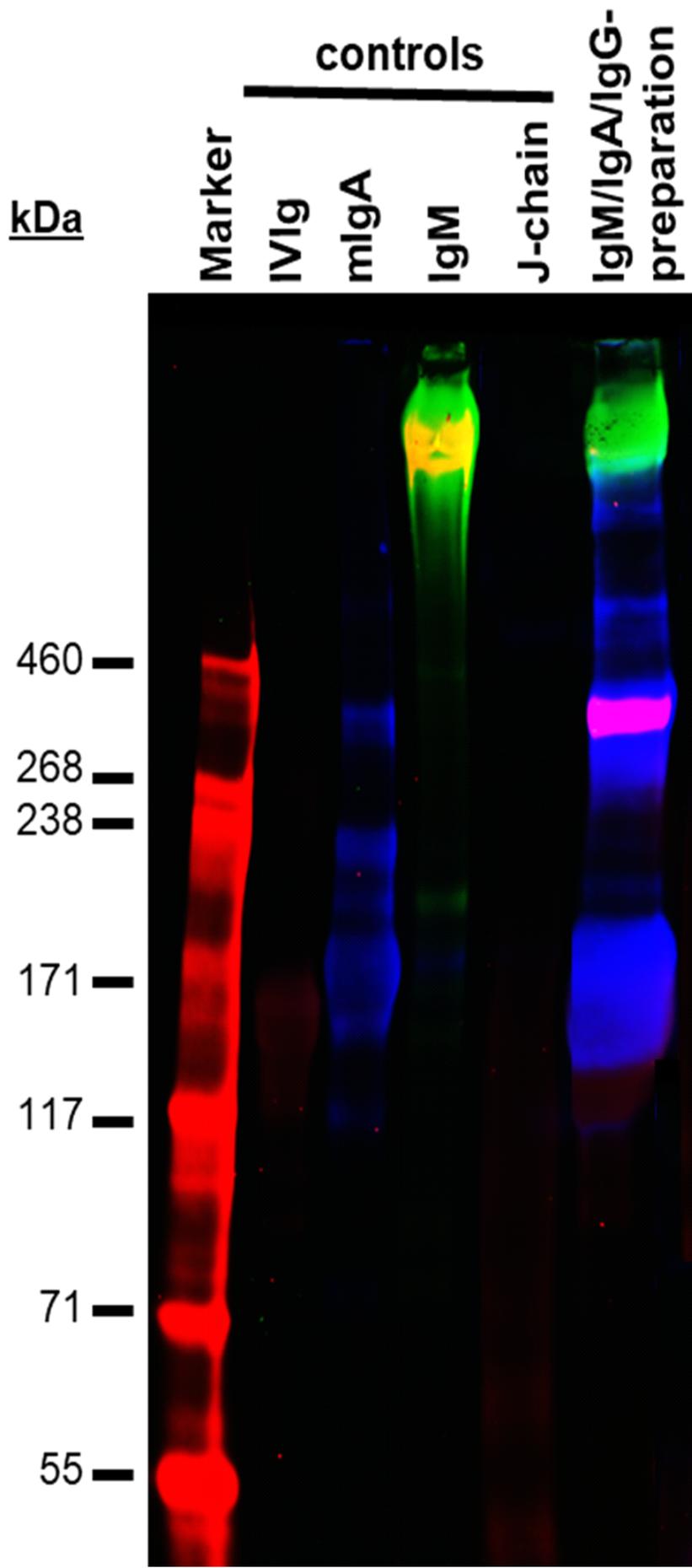
Conclusion:

The results of this study show the biochemical complexity of polyvalent IgM/IgA-enriched immunoglobulins. The data highlight a substantial portion of multimeric IgM and IgA species. The presence of J-chain indicates the potential secretion of IgA and IgM onto mucosa. These observed biochemical properties could explain the beneficial effects of IgM/IgA-enriched immunoglobulins compared to standard IVIg in therapy of severe infections.

References:

- [1] L. Kakoullis et al. *J. Crit. Care*, vol. 47, pp. 30–35, Oct. 2018.
- [2] D. Sterlin and G. Gorochoy, *Pharmacology*, pp. 1–11, Sep. 2020.

Image :



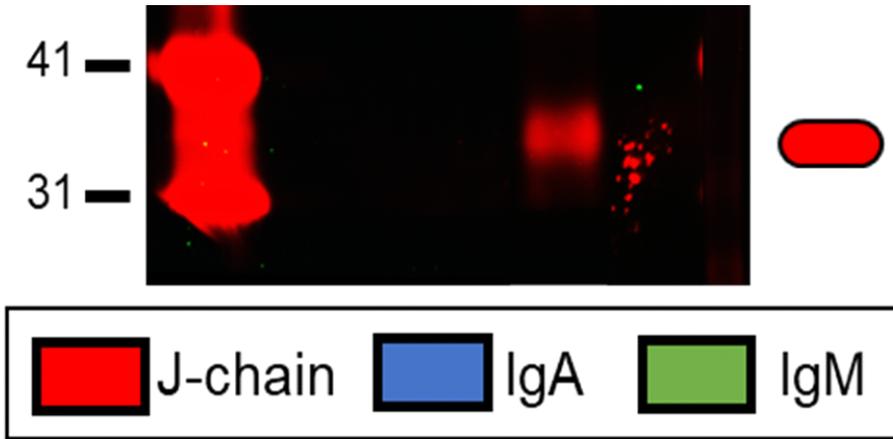


Fig. 1: Non-reducing Western-Blot analysis of IgM/IgA-enriched immunoglobulin preparation. Indicated samples were separated by SDS-PAGE and transferred to nitrocellulose membrane. Specific detection antibodies and fluorophore labeled secondary antibodies were used for detection of J-chain (red), IgA (blue) and IgM (green). Presumed structure of different immunoglobulin species is indicated. Abbreviations: Marker – HiMark™ Protein Standard; IVIg – Intravenous Immunoglobulin (Intratect®); mIgA – monomeric IgA; IgM/IgA/IgG-preparation – IgM/IgA enriched immunoglobulin (Pentaglobin®).