# Immunomodulatory treatments with intravenous immunoglobulin

This is an excerpt from the full technical report, which is written in Norwegian.

The excerpt provides the report's main messages in English.

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Review of systematic reviews

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Norwegian Knowledge Centre for the Health Services summarizes and disseminates evidence concerning the effect of treatments, methods, and interventions in health services, in addition to monitoring health service quality. Our goal is to support good decision making in order to provide patients in Norway with the best possible care. The Centre is organized under The Norwegian Directorate for Health, but is scientifically and professionally independent. The Centre has no authority to develop health policy or responsibility to implement policies.


We would like to thank all contributers for their expertise in this project. Norwegian Knowledge Centre for the Health Services assumes final responsibility for the content of this report.


Norwegian Knowledge Centre for the Health Services
Oslo, July 2008

# Key messages



**Immunomodulatory treatments with intravenous immunoglobulin**

The objective of this report was to summarise clinically relevant effects of immunomodulatory treatments with intravenous immunoglobulins (IVIG).

We searched systematically for systematic reviews evaluating the effectiveness of IVIG for autoimmune diseases and other conditions causing harmful immunological and inflammatory reactions. The searches were performed in the international databases Cochrane Library and Centre for Review and Dissemination Database. We were interested in systematic reviews that compared IVIG with other interventions, no intervention or placebo. Two reviewers assessed inclusion criteria and methodological quality independently. We also rated our confidence in the effect estimates.

The literature search identified 254 unique references. Of these, 11 systematic reviews met our inclusion criteria. All the included reviews had high methodological quality. They focused on the following indications for IVIG: dermatomyositis/polymyositis, carditis in rheumatic fever, myasthenia gravis, haemolytic disease in neonates, multiple sclerosis, Guillain-Barré syndrome (GBS), Kawasaki disease in children, acute myocarditis, sepsis, chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy.

Well documented effects of immunomodulatory treatments with IVIG were reduced risk of coronary artery abnormalities the first 30 days after treatment of children with Kawasaki disease, and improvements in disability in CIDP patients. It was also well documented that IVIG and plasma exchange have equivalent effectiveness for GBS.

There is a need for further research on several of the included indications for IVIG. Further, many of the included systematic reviews need to be updated. It would also be of interest to summarise randomised controlled trials of the effectiveness of IVIG for idiopathic thrombocytopenic purpura (ITP), for which IVIG is a commonly used intervention.

# Executive summary



**Immunomodulatory treatments with intravenous immunoglobulin**

## BACKGROUND

The use of immunomodulatory treatments with intravenous immunoglobulins (IVIG) is increasing in Norwegian hospitals to down regulate harmful immunological and inflammatory responses in autoimmune diseases and other conditions in people with an originally normal immune system. Common indications for IVIG are:

- idiopathic thrombocytopenic purpura (ITP)
- Guillain-Barré syndrome (GBS)
- Kawasaki disease
- myasthenia gravis (MG)
- multiple sclerosis (MS)
- rheumatoid arthritis
- systemic lupus erythematosus (SLE)
- sepsis
- myocarditis
- dermatomyositis
- chronic inflammatory demyelinating polyneuropathy (CIDP)

IVIG is an expensive intervention and its accessibility is limited because it is produced by plasma from blood donors. It is important to know what kind of documentation there is for the effectiveness of IVIG for the various relevant conditions. The objective of this report was to summarise clinically relevant effects of immunomodulatory treatments with IVIG.

## METHODS

We searched Cochrane Library and Centre for Review and Dissemination Database for systematic reviews evaluating the effectiveness of IVIG for autoimmune diseases and other conditions causing harmful immunological and inflammatory reactions. We were interested in reviews that compared IVIG with other interventions, no intervention or placebo. Two reviewers assessed inclusion criteria and methodological quality independently. The methodological quality of the reviews was assessed by a standardised checklist for systematic reviews. We also rated our confidence in the effect estimates with the assessment tool GRADE.

## RESULTS

The literature search identified 254 unique references. Of these, 11 systematic reviews met our inclusion criteria. All the included reviews had high methodological quality. They focused on the following indications for IVIG: dermatomyositis/polymyositis, carditis in rheumatic fever, myasthenia gravis, haemolytic disease in neonates, multiple sclerosis, Guillain-Barré syndrome (GBS), Kawasaki disease in children, acute myocarditis, sepsis, chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy.

We found high quality pooled effect estimates for three indications: Kawasaki disease in children, CIDP and GBS. A combination of IVIG and aspirin gave fewer children with coronary artery abnormalities after 30 days than placebo and aspirin in Kawasaki disease (RR 0.74; 95 % CI 0.61-0.90). More CIDP patients achieved disability improvements with IVIG than with no intervention (RR 3.17; 95 % CI 1.74-5.75). There was no difference between IVIG and plasma exchange in disability improvements in GBS patients. Also, there was no difference between IVIG + aspirin and placebo + aspirin in coronary artery abnormalities after more than 30 days in Kawasaki disease.

All other effect estimates were of moderate or low quality.

## CONCLUSIONS

Well documented effects of immunomodulatory treatments with IVIG are reduced risk of coronary artery abnormalities after 30 days in children with Kawasaki disease, and disability improvements in CIDP patients. IVIG and plasma exchange are equally effective for GBS.

Other effects of IVIG are less well documented. There is a need for further research and more randomised controlled trials (RCTs) on immunomodulatory treatments with IVIG for most of the relevant conditions. There is also a need for updates of the included systematic reviews. Finally, researchers should make an effort to summarise RCTs of the effectiveness of IVIG for ITP.

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