

---

## The prevention of coronary artery aneurysm in Kawasaki disease: a meta-analysis on the efficacy of aspirin and immunoglobulin treatment

*Durongpisitkul K, Gururaj V J, Park J M, Martin C F*

---

### Authors' objectives

To evaluate the efficacy of aspirin (ASA) and/or intravenous immunoglobulin (IVIG) in the prevention of coronary artery aneurysm (CAA) in children with Kawasaki disease.

### Searching

MEDLINE and EMBASE were searched from 1967 to 1993 with the subject heading 'mucocutaneous lymph node syndrome' and subheadings 'coronary aneurysm' and 'coronary artery aneurysm'. Additional articles were identified from bibliographies of retrieved articles.

### Study selection

#### Study designs of evaluations included in the review

Prospective and retrospective designs which included follow-up data on incidence of CAA at 14 to 60 days. No further information is given on the study designs.

#### Specific interventions included in the review

ASA alone; low IVIG (1 g/kg) and ASA; high IVIG (>1 g/kg) and ASA; single IVIG (>1 g/kg) and ASA; high IVIG and low ASA (80 mg/kg); and high IVIG and ASA (>8 mg/kg). IVIG doses ranged from 0.1 to 2.0 g/kg per 5 days.

#### Participants included in the review

Children with Kawasaki disease. Studies were only included in the review if their patients fulfilled CDC (Center for Disease Control) diagnostic criteria for Kawasaki disease.

#### Outcomes assessed in the review

The outcome assessed was the incidence of CAA at 30 and 60 days post-intervention.

#### How were decisions on the relevance of primary studies made?

The authors do not state how the papers were selected for the review, or how many of the authors performed the selection. Explicit inclusion/exclusion criteria were used relating to diagnostic criteria, and the definition of CAA.

### Assessment of study quality

Differences in the validity of the included studies were not examined. It was assumed that all studies that met the inclusion/exclusion criteria were equally valid. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

### Data extraction

The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

### Methods of synthesis

#### How were the studies combined?

Data from relevant studies were pooled to produce overall proportions with associated confidence intervals (CIs). Proportions based on pooled data were compared by calculating a CI for the difference between the proportions. No weighting of individual studies took place.

#### How were differences between studies investigated?

Homogeneity among studies was examined a priori by determining if the proportions reported in individual studies were more than two standard deviations away from the mean of all studies. Studies lying outside this interval were deemed to be drawn from a different population and excluded. This resulted in the exclusion of four studies, two retrospective and two prospective.

#### Results of the review

Twenty-four studies (18 prospective, 6 retrospective) with a total of 4,151 patients were included. The 60-day follow-up data were available for 2,547 patients and the 30-day follow-up for all patients.

Significant differences were found at 30 days of follow-up for: ASA versus low IVIG (95% CI: 0.080, 0.170,  $p<0.0001$ ); low IVIG versus high IVIG (95% CI: 0.035, 0.105,  $p<0.0001$ ); high IVIG versus single IVIG (95% CI: 0.053, 0.107,  $p<0.0001$ ); but not for high IVIG and low ASA versus high IVIG and high ASA (95% CI: -0.007, 0.084,  $p=0.097$ ).

Significant differences were found at 60 days of follow-up for: ASA versus low IVIG (95% CI: 0.017, 0.103,  $p=0.003$ ); low IVIG versus high IVIG (95% CI: 0.038, 0.096,  $p<0.0001$ ); but not for high IVIG versus single IVIG (95% CI: -0.003, 0.045,  $p=0.092$ ); or high IVIG and low ASA versus high IVIG and high ASA (95% CI: 0.025, 0.041,  $p=0.319$ ).

#### Authors' conclusions

The incidence of CAA at 30 and 60 days is significantly lower in low-IVIG than in ASA, and lower in high-IVIG than in low-IVIG groups. The incidence was lower in the single-IVIG than the high-IVIG group at 30 days only. There is no difference in the incidence of CAA at 30 or 60 days between the high-IVIG/low-ASA and high-IVIG/high-ASA groups.

#### CRD commentary

While the authors' conclusions appear to be supported by the results of the meta-analysis, it is difficult to determine the actual importance of these results, e.g. although the reported differences are significant, the absolute differences in incidence between the groups are very small. This, and the lack of information on adverse effects of the drugs, makes the overall clinical importance of these differences unclear. The actual statistical methods are also somewhat simplistic, involving a simple pooling of similar studies (though retrospective and prospective studies were pooled), and there is no examination of the validity of individual studies.

There may be an error in Table 3: the 95% CI for the difference between high-IVIG/low-ASA and high-IVIG/high-ASA groups at 60 day follow-up does not include zero, but the text indicates a non-significant difference ( $p=0.319$ ).

#### Implications of the review for practice and research

Longer-term (1 year or more) evaluations of the effectiveness of ASA and IVIG in preventing CAA in children with Kawasaki disease are required.

#### Bibliographic details

Durongpisitkul K, Gururaj V J, Park J M, Martin C F. The prevention of coronary artery aneurysm in Kawasaki disease: a meta-analysis on the efficacy of aspirin and immunoglobulin treatment. *Pediatrics* 1995; 96(6): 1057-1061

#### PubMedID

7491221

#### Indexing Status

Subject indexing assigned by NLM

**MeSH**

Aspirin /therapeutic use; Child; Coronary Aneurysm /etiology /prevention & control; Humans; Immunoglobulins, Intravenous /therapeutic use; Mucocutaneous Lymph Node Syndrome /complications /therapy; Statistics as Topic

**AccessionNumber**

11996000062

**Date bibliographic record published**

30/11/1996

**Date abstract record published**

30/11/1996

**Record Status**

This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.