Aspirin Dose and Prevention of Coronary Abnormalities in Kawasaki Disease

Frederic Dallaire, MD, PhD, Zoe Fortier-Morissette, MD, Samuel Blais, BSc, Anita Dhanrajani, DNB, Dania Basodan, MBBS, Claudia Renaud, MD, Mathew Mathew, BSc, Astrid M. De Souza, MSc, Audrey Dionne, MD, Joel Blanchard, BSc, Harrison Saulnier, BSc, Kimberley Kaspky, MD, Soha Rached-d’Astous, MD, Nagib Dahdah, MD, Brian W. McCrindle, MD, MPH, Derek G. Human, BM, Rosie Scuccimarr, MD

BACKGROUND: Acetylsalicylic acid (ASA) is part of the recommended treatment of Kawasaki disease (KD). Controversies remain regarding the optimal dose of ASA to be used. We aimed to evaluate the noninferiority of ASA at an antiplatelet dose in acute KD in preventing coronary artery (CA) abnormalities.

METHODS: This is a multicenter, retrospective, nonrandomized cohort study including children 0 to 10 years of age with acute KD between 2004 and 2015 from 5 institutions, of which 2 routinely use low-dose ASA (3–5 mg/kg per day) and 3 use high-dose ASA (80 mg/kg per day). Outcomes were CA abnormalities defined as a CA diameter with a z score ≥2.5. We assessed the risk difference of CA abnormalities according to ASA dose. All subjects received ASA and intravenous immunoglobulin within 10 days of fever onset.

RESULTS: There were 1213 subjects included, 848 in the high-dose and 365 in the low-dose ASA group. There was no difference in the risk of CA abnormalities in the low-dose compared with the high-dose ASA group (22.2% vs 20.5%). The risk difference adjusted for potential confounders was 0.3% (95% confidence interval [CI]: −4.5% to 5.0%). The adjusted risk difference for CA abnormalities persisting at the 6-week follow-up was −1.9% (95% CI: −5.3% to 1.5%). The 95% CI of the risk difference of CA abnormalities adjusted for confounders was within the prespecified 5% margin considered to be noninferior.

CONCLUSIONS: In conjunction with intravenous immunoglobulin, low-dose ASA in acute KD is not inferior to high-dose ASA for reducing the risk of CA abnormalities.

WHAT’S KNOWN ON THIS SUBJECT: Controversies remain regarding the appropriate acetylsalicylic acid (ASA) dose to be used during treatment of Kawasaki disease (KD). The anti-inflammatory dose of ASA is recommended in acute KD, but it has never been proven to reduce the incidence of coronary artery abnormalities.

WHAT THIS STUDY ADDS: This multicenter study suggests that an antiplatelet dose of ASA is not inferior to higher doses in reducing the risk of coronary artery abnormalities when administered concomitantly with intravenous immunoglobulin in acute KD.
Kawasaki disease (KD), an acute, self-limited vasculitis of unknown origin, is the most common cause of acquired heart disease in children in developed countries.\(^1,2\) Coronary artery (CA) dilatation and aneurysms may develop in \(~15\%\) to \(25\%\) of untreated children, putting them at risk for future CA complications such as thrombosis and myocardial infarction.\(^1,2\) Prompt diagnosis and early treatment with intravenous immunoglobulin (IVIg) significantly reduce the risk of CA involvement. Studies in the 1980s demonstrated that IVIg combined with acetylsalicylic acid (ASA) had a significant impact on morbidity, mortality, and CA aneurysm risk.\(^3,5\) ASA was used before the IVIg era for both its anti-inflammatory and antithrombotic effects.\(^6\) Studies to date have failed to demonstrate any benefit of the anti-inflammatory dose of ASA in preventing CA abnormalities.\(^6,9\) Two separate meta-analyses showed that CA abnormalities were dependent on the total IVIg dose but were independent of the ASA dose.\(^10,11\) A Cochrane review boldly stated that there was insufficient evidence to indicate whether children with KD should continue to receive ASA as part of their treatment regimen.\(^12\) Despite all this, controversies remain on the appropriate dose of ASA to be used in the treatment of acute KD.\(^13,14\) Avoiding an anti-inflammatory dose of ASA has the theoretical advantage of preventing serious side effects from high-dose ASA therapy, such as Reye syndrome, raised liver enzymes, gastrointestinal bleeding, and sensorineural hearing loss.\(^14\) On the other hand, the anti-inflammatory effect of high-dose ASA could reduce the duration of fever, which has been shown by some authors,\(^7,15\) but not all.\(^6,8,9\)

In Canada, ASA dose varies from institution to institution. At least 2 Canadian pediatric tertiary care institutions routinely and systematically use ASA at an anti-platelet dose during treatment of acute KD, whereas most other medical centers use an anti-inflammatory dose. We therefore included these institutions in a multicenter retrospective cohort study and sought to evaluate if the routine use of low-dose ASA during treatment of acute KD was noninferior to high-dose ASA in reducing the risk of CA abnormalities.

**METHODS**

**Study Design and Patient Population**

This was a multicenter, nonrandomized, retrospective, noninferiority cohort study. The target population comprised all children between 0 and 10 years of age diagnosed with complete or incomplete acute KD between 2004 and 2015 in 1 of the 5 Canadian participating institutions. Two of these institutions have been routinely prescribing low-dose ASA (3–5 mg/kg per day) in acute KD. The 3 remaining institutions have been routinely prescribing high-dose ASA (80 mg/kg per day). There was no change in the routine dose of ASA prescribed during treatment of acute KD throughout the study period in any of the participating institutions. All KD cases were identified through local clinical databases and medical archives and then screened for eligibility. Eligible subjects were children with a first episode of KD diagnosed and treated with IVIg and ASA within 10 days of fever onset. Given that the diagnosis of KD cannot be confirmed, subjects were eligible if the clinical suspicion of KD was such that treatment with IVIg was deemed clinically indicated by the treating physician. Subjects were followed from diagnosis until 12 months postdiagnosis.

Exclusion criteria were as follows: subjects whose final diagnosis of KD was clearly rejected by the treating physician; subjects with structural cardiac disease at baseline other than cardiac disease secondary to KD; subjects with recurrence of KD (second episode not included); and subjects with follow-up <6 weeks or with incomplete echocardiographic studies during follow-up.

Research ethics board approval was granted at each participating institution. Only anonymous retrospective data were gathered for this study, and the requirement for patient consent was waived by the research ethics boards.

**ASA Treatment Definition**

To test our main hypothesis, we used an approach analogous to an intent-to-treat analysis in which the treatment group was based on the dose of ASA routinely used by the institution where the subject was admitted.\(^16\) In this analysis, subjects admitted in 1 of the 2 institutions routinely prescribing low-dose ASA (3–5 mg/kg per day) during treatment of acute KD were assigned to the low-dose group, irrespective of the actual dose received. Patients admitted to 1 of the 3 institutions routinely prescribing high-dose ASA (80 mg/kg per day) during treatment of acute KD were assigned to the high-dose group.

Additionally, we compared the risk of CA abnormalities according to the dose of ASA that was actually prescribed, irrespective of the institution where they were admitted. In this analysis, low-dose ASA was defined as a prescribed dose <10 mg/kg per day during the acute febrile phase. Prescribed ASA doses \(\geq 10\) mg/kg per day were defined as high dose. There were <1% of subjects who received a moderate ASA dose (10–79 mg/kg per day) and these were included in the high ASA dose category.

**Primary and Secondary Outcomes**

The primary outcome was the risk of any CA abnormalities, defined as any main CA segment with an
internal diameter z score ≥2.5 at any time during follow-up (thus including small, medium, and giant CA aneurysms). CA z scores were calculated as previously described.17

Our secondary outcomes were as follows: any CA abnormalities except mild dilatation of the left main CA (isolated left main CA z scores <5 were not considered abnormal); persistent CA abnormalities (any CA segment z score ≥2.5 present at the 6-week follow-up or later); medium or larger CA aneurysms (any CA segment z score ≥5.0); giant CA aneurysms (z score ≥10.0 or absolute diameter >8 mm); resistance to treatment (defined as the requirement for further treatment after the first dose of IVIg); and fever duration.

Data Collection

The following data were collected from the medical charts: demographic information (sex, age at diagnosis), clinical information at diagnosis (KD symptoms, date of fever onset, duration of fever, routine laboratory results), initial treatment (IVIg doses and treatment course, IVIg brand, initial ASA dose, any other rescue treatment), follow-up treatment, and echocardiography data from diagnosis until follow-up at 12 months (weight and height at echocardiography, and all coronary internal diameter measurements). Information on side effects of ASA was not specifically collected. Data collected were entered by using the web-based data capture tool REDCap (Vanderbilt University, Nashville, TN).18

Statistical Analysis

We used a noninferiority design to assess whether the risk difference of CA abnormalities between treatment groups would stay within the 95% confidence interval (CI) of a predefined clinically acceptable margin.19 Low-dose ASA was considered noninferior to high-dose ASA if the 95% CI of the risk difference for CA abnormalities was ≤5.0%.

Adjusted risk differences between treatments were computed by using binomial regression risk analysis.20 Only confounding variables that influenced the final adjusted risk difference by >5% were kept in the final model. Potential confounding variables considered for inclusion in the models were as follows: type of KD (complete versus incomplete), sex, need for retreatment (any rescue treatment after the first IVIg), young age (<12 months of age at diagnosis), and IVIg brand. All were kept in the final model, except IVIg brand, which had no influence on the adjusted risk difference. Differences in patients’ characteristics between treatment groups were assessed by using Student’s t test or an χ² test, where appropriate. We used SAS (version 9.4, Cary, NC) for all analyses. P values <.05 were considered statistically significant.

RESULTS

A total of 1483 subjects were identified and screened for eligibility. Of them, 270 were excluded for the following reasons: 33 did not receive IVIg or ASA, 20 had missing information on initial ASA treatment, 152 received IVIg after 10 days of fever, 42 had missing echocardiography results, 19 had structural heart defects, and 4 already had KD in the past. The 1213 remaining subjects were included in the final analysis. Among them, 848 were admitted in institutions where high-dose ASA is routinely prescribed in acute KD. The remaining 365 subjects were admitted in institutions where low-dose ASA is routinely prescribed in acute KD.

Table 1 presents the characteristics of the study population. In the high-dose ASA group, 794 subjects (93.6%) received an ASA dose ≥10 mg/kg per day. Of them, all but 2 patients received an ASA dose ≥70 mg/kg per day. In the low-dose ASA group, 341 subjects (93.4%) received an ASA dose <10 mg/kg per day. In the low-dose ASA group, there were 4 subjects (1.1%) who received an ASA dose between 11 and 70 mg/kg per day and 20 subjects (5.5%) who received an ASA dose ≥70 mg/kg per day. Treatment groups were similar for age, sex, and number of days of fever before first dose of IVIg. There were more patients with complete Kawasaki (≥24 criteria) in the low-dose ASA group (76.2% vs 69.0%). Subjects in the low-dose ASA group were slightly more likely to require a second IVIg course (27.4% vs 24.4%), less likely to receive oral steroid treatment (2.5% vs 4.0%), and more likely to receive infliximab (0.8% vs 0.2%), but these differences did not reach statistical significance. IVIg brand varied considerably between institutions (see details in Table 1). We observed a higher mean C-reactive protein concentration in the low-dose ASA group. Significant P values for differences between groups were also observed for hemoglobin, white cell count, and albumin, although the differences were small.

Our primary outcome, any CA abnormalities, was observed in 255 subjects (21.0%). Of these, there were 98 subjects (8.1%) with transient small CA dilatations (z score ≥2.5 but <5) at diagnosis that did not persist at the 6-week follow-up: 62 subjects (7.3%) in the high-dose ASA group and 36 subjects (9.9%) in the low-dose ASA group. Excluding these transient dilatations, we found 157 subjects (12.9%) with persistent CA abnormalities. Of these, there were 5.5% with medium or large CA aneurysms and 2.3% with giant CA aneurysm.

Table 2 presents the proportion of subjects with CA abnormalities according to treatment groups as well as the unadjusted and adjusted risk differences. The risk of any CA...
TABLE 1 Population Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SD, or Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Subjects, N = 1213</td>
</tr>
<tr>
<td>Age, y</td>
<td>3.4 ± 2.3</td>
</tr>
<tr>
<td>Aged &lt;1y at diagnosis</td>
<td>14.4</td>
</tr>
<tr>
<td>Male sex</td>
<td>59.2</td>
</tr>
<tr>
<td>Complete Kawasaki (≥4 criteria)</td>
<td>71.2</td>
</tr>
<tr>
<td>Subjects receiving ASA dose &lt;10 mg/kg per d</td>
<td>32.6</td>
</tr>
<tr>
<td>No. days of fever at first IVIg treatment</td>
<td>6.2 ± 1.7</td>
</tr>
<tr>
<td>Fever duration, d</td>
<td>7.8 ± 3.5</td>
</tr>
<tr>
<td>IVIg brand</td>
<td></td>
</tr>
<tr>
<td>Ivecéam</td>
<td>18.2</td>
</tr>
<tr>
<td>Gammagard</td>
<td>13.4</td>
</tr>
<tr>
<td>Gamunex</td>
<td>28.7</td>
</tr>
<tr>
<td>Privigen</td>
<td>10.6</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>29.0</td>
</tr>
<tr>
<td>Other treatments</td>
<td></td>
</tr>
<tr>
<td>≥2 doses of IVIg</td>
<td>25.3</td>
</tr>
<tr>
<td>≥3 doses of IVIg</td>
<td>1.8</td>
</tr>
<tr>
<td>Steroids</td>
<td>9.9</td>
</tr>
<tr>
<td>Steroids (parenteral)</td>
<td>6.4</td>
</tr>
<tr>
<td>Steroids (enteral)</td>
<td>3.5</td>
</tr>
<tr>
<td>Infliximab</td>
<td>0.4</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>0</td>
</tr>
<tr>
<td>Hemoglobin, g/L</td>
<td>112.0 ± 13.1</td>
</tr>
<tr>
<td>White cell count, ×10³ L⁻¹</td>
<td>14.0 ± 6.6</td>
</tr>
<tr>
<td>Platelet counts, ×10³ L⁻¹</td>
<td>369.8 ± 158.3</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate, mm/h</td>
<td>59.7 ± 28.4</td>
</tr>
<tr>
<td>C-reactive protein, mg/L</td>
<td>86.4 ± 75.3</td>
</tr>
<tr>
<td>Albumin, g/L</td>
<td>35.3 ± 7.3</td>
</tr>
</tbody>
</table>

All laboratory values are at baseline, before IVIg treatment.

* Overall table probability P < .05 for IVIg brand. Individual IVIg brands were not tested.

a P value <.05 (high-versus low-dose group).

Abnormalities was similar in the high-dose and low-dose ASA groups (unadjusted risk difference of 1.7% [95% CI: −3.4% to 6.7%]). After adjustment for confounders, the risk difference for any CA abnormalities in the low-dose compared with the high-dose ASA group was close to zero: adjusted risk difference of 0.3% (95% CI: −4.5% to 5.0%). When only persistent CA aneurysms were considered, there was no significant risk difference between groups: adjusted risk difference of −1.9% (95% CI: −5.3% to 1.5%). Accordingly, our hypothesis of a noninferior effect of low ASA dose was confirmed for the primary outcome (any CA abnormalities) and for persistent CA abnormalities. Given that a z score ≥2.5 that is only observed for the left main CA can be considered a normal anatomic variation, we also analyzed CA dilations without isolated mild dilatation of the left main CA with a z score >2.5 but <5. Excluding these, we found that 19.5% and 18.9% of subjects had abnormal CA in the high- and low-dose ASA groups, respectively. The unadjusted risk difference was −0.5% (95% CI: −5.4% to 4.3%) and the adjusted risk difference was −2.0% (95% CI: −6.4% to 2.4%).

For medium or larger CA aneurysms (CA z score ≥5.0), the adjusted risk difference was statistically significant, favoring the low-dose ASA group: −4.0% (95% CI: −7.4% to −0.5%), P value = .024. There was no significant risk difference between groups for giant CA aneurysm (adjusted risk difference: −1.9% [95% CI: −4.4% to 0.5%]).

Some subjects treated in an institution routinely prescribing low-dose ASA actually received high-dose ASA (24 subjects or 6.6% of the low-dose ASA group). Also, 54 subjects (6.4% of high-dose ASA group) received low-dose ASA in the institutions routinely prescribing high-dose ASA. When risk

TABLE 2 Primary and Secondary Outcomes (Intent-to-Treat Analysis)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>All Subjects, n (%)</th>
<th>ASA High Dose, n (%)</th>
<th>ASA Low Dose, n (%)</th>
<th>Unadjusted Risk Difference and [95% CI]</th>
<th>Adjusted Risk Difference and [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any CA abnormalities (z score ≥2.5)</td>
<td>255/1213 (20.9)</td>
<td>174/848 (20.5)</td>
<td>81/365 (22.2)</td>
<td>1.7% [−3.4% to 6.7%]</td>
<td>0.3% [−4.5% to 5.0%]</td>
</tr>
<tr>
<td>Persistent CA abnormalities (z score ≥2.5)</td>
<td>157/1213 (12.9)</td>
<td>112/848 (13.2)</td>
<td>45/365 (12.3)</td>
<td>−0.9% [−5.0% to 3.2%]</td>
<td>−1.9% [−5.3% to 1.5%]</td>
</tr>
<tr>
<td>Any CA abnormalities excluding small isolated dilatation of the left main CA</td>
<td>234/1213 (19.3)</td>
<td>165/848 (19.5)</td>
<td>69/365 (18.9)</td>
<td>−0.5% [−5.4% to 4.3%]</td>
<td>−2.0% [−8.4% to 2.4%]</td>
</tr>
<tr>
<td>Medium or larger CA aneurysm (z score ≥5)</td>
<td>66/1213 (5.4)</td>
<td>51/848 (6.0)</td>
<td>15/365 (4.1)</td>
<td>−1.9% [−4.5% to 0.7%]</td>
<td>−4.0% [−7.4% to −0.5%]</td>
</tr>
<tr>
<td>Giant CA aneurysm (z score ≥10 or diameter &gt;8 mm)</td>
<td>28/1213 (2.3)</td>
<td>22/848 (2.6)</td>
<td>6/365 (1.6)</td>
<td>−1.0% [−2.6% to 0.7%]</td>
<td>−1.9% [−4.4% to 0.5%]</td>
</tr>
</tbody>
</table>

* Adjusted for type of Kawasaki (complete versus incomplete), sex, need for retreatment (any treatment after the first IVIg), and young age (<12 mo of age at diagnosis).
differences were computed by using the actual ASA dose received, the results were similar, with an overall slight decrease in risk differences compared with the intent-to-treat analysis. For any CA abnormalities, the adjusted risk difference was −0.7% (95% CI −5.2% to 3.8%). The adjusted risk difference of persistent CA abnormalities was −2.1% (95% CI −5.3% to 1.1%).

The risk of requiring further treatment after the first dose of IVIg was similar between groups (24.4% and 27.4% in the high- and low-dose ASA group, respectively). After adjusting for the type of Kawasaki (complete versus incomplete), sex, and age at diagnosis, the risk difference of requiring retreatment was small and not statistically significant: adjusted risk difference of 2.9% (95% CI: −2.5% to 8.4%). Fever duration was similar between high-dose and low-dose ASA groups: 7.8 ± 3.8 days and 7.9 ± 2.6 days, respectively, with an adjusted absolute difference of 0.18 days that was not statistically significant (95% CI: −0.25 days to 0.61 days).

**DISCUSSION**

The results of our study suggest that using low-dose ASA concomitantly with IVIg in acute KD is not inferior to high-dose ASA in preventing CA abnormalities. We also did not observe a significant effect of ASA dose on treatment resistance or on fever duration.

Before the IVIg era, ASA was used for its anti-inflammatory and antithrombotic effects. Although it has been the mainstay treatment of KD, studies performed at that time showed little effect of ASA on the incidence of CA aneurysms. It is only when IVIg was introduced as part of standard KD management that a significant change in the risk of CA complications was seen. In these trials, IVIg was used concomitantly with high-dose ASA. As a consequence, high-dose ASA (80–100 mg/kg per day) remained central in the treatment recommendations of acute KD in North America. However, the Japanese guidelines suggest lower doses of ASA (30–50 mg/kg per day) for the treatment of acute KD as compared with the North American recommendations. In 2013, Ogata reported that there were no differences in CA aneurysm rates between 5 institutions in the United States and Japan despite differences in ASA dose used in acute KD.

The appropriate dose of ASA to be used with IVIg in the treatment of acute KD has been the subject of debate. To our knowledge, no prospective study has shown that ASA, at any dose, reduces the incidence of CA aneurysm. There have been 3 meta-analyses that all concluded that there is no evidence that high-dose ASA decreases the risk of CA abnormalities compared with low-dose ASA.

More recently, Kuo et al compared patients receiving moderate and high-dose ASA (>30 mg/kg per day) during treatment of acute KD to patients receiving no ASA. They found no significant difference in the risk of CA lesions (17.0% vs 15.4%). In 2016, Kim et al studied a large sample of 8456 children from a retrospective survey of 116 hospitals in South Korea. They reported that compared with low-dose ASA (3–5 mg/kg per day), medium or higher dose ASA (>30 mg/kg per day) during treatment of acute KD was associated with a higher risk of CA abnormalities after adjustment for confounders. In both studies, the reasons for using low-dose ASA in settings where higher doses are routinely used was not stated. An important indication bias cannot be ruled out if low-dose ASA was prescribed to milder cases or to patients with a lower risk for the development of CA aneurysms.

In usual circumstances, comparing treatment efficacy in retrospective studies is prone to indication bias. Different clinical characteristics at presentation may influence treatment as well as outcome, thus potentially confounding the association between the two. A strength of our study lies in the fact that the participating institutions in Canada have been routinely using different ASA doses in the treatment of acute KD, thus potentially minimizing this bias. Subjects included in this study mostly received a given ASA dose according to where they lived, irrespective of their clinical characteristics. That being said, a small proportion of subjects in the low-dose group did receive high-dose ASA, possibly because of some physicians’ preference and/or a more severe disease at presentation. We elected to use a design analogous to an intent-to-treat protocol to reduce the indication bias that would be introduced if sicker patients were being prescribed higher doses of ASA. Nevertheless, when subjects were assigned to a treatment group according to the actual dose of ASA prescribed, the risk difference of CA abnormalities between treatment groups was similar to that of the intent-to-treat analysis.

Our study has limitations. Possible variations in unmeasured population characteristics between institutions may have introduced a bias. In particular, ethnic background, differential use of rescue therapy, and variation in CA imaging and measurements may have influenced the association between treatment and outcome. We did not collect information on adverse effects of ASA.

**CONCLUSIONS**

In conjunction with IVIg, our data suggest that using low-dose ASA
during acute KD is not inferior to high-dose ASA to reduce the risk of CA abnormalities. Given that ASA at any dose has never been shown to reduce the risk of CA abnormalities, our study suggests that ASA at a dose superior to 3 to 5 mg/kg per day may not be indicated in acute KD.

ACKNOWLEDGMENTS

Frederic Dallaire is supported in part by the Fonds de recherche du Québec – Santé. We thank the Fondation En Coeur for the initial support of the Registre Québécois de la Maladie de Kawasaki.

ABBRIVATIONS

ASA: acetylsalicylic acid
CA: coronary artery
CI: confidence interval
IVIg: intravenous immunoglobulin
KD: Kawasaki disease

REFERENCES


Aspirin Dose and Prevention of Coronary Abnormalities in Kawasaki Disease
Frederic Dallaire, Zoe Fortier-Morissette, Samuel Blais, Anita Dhanrajani, Dania Basodan, Claudia Renaud, Mathew Mathew, Astrid M. De Souza, Audrey Dionne, Joel Blanchard, Harrison Saulnier, Kimberley Kaspy, Soha Rached-d’Astous, Nagib Dahdah, Brian W. McCrindle, Derek G. Human and Rosie Scuccimarri
Pediatrics 2017;139;
DOI: 10.1542/peds.2017-0098 originally published online May 2, 2017;

Updated Information & Services
including high resolution figures, can be found at:
http://pediatrics.aappublications.org/content/139/6/e20170098

References
This article cites 24 articles, 6 of which you can access for free at:
http://pediatrics.aappublications.org/content/139/6/e20170098#BIBL

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Pharmacology
http://www.aappublications.org/cgi/collection/pharmacology_sub
Therapeutics
http://www.aappublications.org/cgi/collection/therapeutics_sub
Cardiology
http://www.aappublications.org/cgi/collection/cardiology_sub
Cardiovascular Disorders
http://www.aappublications.org/cgi/collection/cardiovascular_disorders_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
http://www.aappublications.org/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
http://www.aappublications.org/site/misc/reprints.xhtml

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®
Aspirin Dose and Prevention of Coronary Abnormalities in Kawasaki Disease
Frederic Dallaire, Zoe Fortier-Morissette, Samuel Blais, Anita Dhanrajani, Dania Basodan, Claudia Renaud, Mathew Mathew, Astrid M. De Souza, Audrey Dionne, Joel Blanchard, Harrison Saulnier, Kimberley Kaspy, Soha Rached-d’Astous, Nagib Dahdah, Brian W. McCrindle, Derek G. Human and Rosie Scuccimarri

Pediatrics 2017;139:
DOI: 10.1542/peds.2017-0098 originally published online May 2, 2017;

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/139/6/e20170098