

Role of Salicylates in Kawasaki Disease

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Kawasaki disease (KD) is a systemic vasculitis predominantly affecting young children. The disease is associated with cardiac complications such as cardiac aneurysm and thrombosis in a significant proportion of cases. Salicylates are commonly used in KD because of their anti-inflammatory activity. In general, the salicylate use is limited in other childhood conditions because of potential risk of complications like Reye's syndrome. This systematic review attempted to evaluate the available evidence on the effectiveness of salicylates in treating and preventing long-term cardiac consequences of KD in children.

SUMMARY

Only one multicentric (16 centers) randomized-controlled-trial (RCT) from Japan was found to be eligible for inclusion in this review. This was a three-arm trial comparing acetyl salicylic acid (ASA) alone with intravenous immunoglobulins (IVIG) and ASA treatment, and with IVIG alone; only last two arms (including 102 children) were included for this review. The dose of IVIG was 200mg/kg daily for five days, and of ASA was 30 to 50mg/kg/day in three divided doses until the fever had subsided, then 10 to 30 mg/kg/day once a day until "the acute reaction had also disappeared." Children were enrolled if they presented within seven days of onset of symptoms, and two dimensional echocardiography was performed three times a week until 60 days after the onset of symptoms. Any abnormalities on echocardiography were followed by selective

coronary angiography. No significant difference was found in the incidence of coronary artery lesions up to 30 days from onset of symptoms (RR 0.97; 95% CI 0.43 to 2.19) or prevalence after 30 days post onset of symptoms (RR 1.30; 95% CI 0.37 to 4.56). The authors concluded that there is insufficient evidence to indicate whether children with KD should or should not continue to receive salicylate as part of their treatment regimen.

COMMENTARY

Are the results valid?

The clinical question raised by this systematic review is relevant. The search strategy was primarily designed to study the outcome of coronary artery lesions. For this updated version, only specialized registers and central registers of the Cochrane group were searched for, and no additional studies were found. In the only included study, randomization method was uncertain and blinding was not done. The outcome assessed is functionally important but it would have been helpful if the other important outcomes such as duration and intensity of fever, patient comfort, and duration of hospitalization were also included. The sample size is also less for studying the outcome of coronary lesions because of their relative rarity in IVIG treated patients.

How precise and clinically significant is the treatment effect?

Although the included study reported no benefit in terms of incidence of new coronary artery lesions up

KEY MESSAGE

- The role of salicylates in further reducing the coronary complications in IVIG treated children with Kawasaki disease is uncertain.

to day 30 and their prevalence after day 30, the confidence intervals were wide thus not ruling out possibility of benefit or even harm. The other outcomes such as duration and intensity of fever were not reported in this review. Any adverse effects of salicylates, the primary concern for their usage, were also not reported in this review.

Implications for Practice and Policy

IVIG has become a standard treatment modality for children with KD because of their proven role in reducing the coronary complications(1). It appears that salicylates have no additional advantage of further reduction in these complications. However, these results are valid only for patients who are also receiving simultaneous IVIG therapy and can not be extrapolated for those not receiving IVIG because of any reason. Also, the results of the review are based on relatively small number of patients.

In the absence of a clear cut evidence of benefit or harm with salicylates, it appears unlikely that the current practice of using salicylates as well as IVIG would change on the basis of these results. Moreover, some other studies (not included in this review because of methodological concerns or not

meeting inclusion criteria) have reported the advantage of salicylates in reducing the duration of fever(2,3). Good quality and adequately powered multicentric RCTs would be required to provide a clear cut recommendation on this issue. Also, the other patient oriented outcomes such as fever clearance time and cost issues need to be studied in future trials.

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