Kardiologia Polska 2017; 75, 3: 261–266; DOI: 10.5603/KP.a2016.0179 ISSN 0022–9032

ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Risk factors of immunoglobulin resistance and coronary complications in children with Kawasaki disease

Elżbieta Berdej-Szczot[1], Ewa Małecka-Tendera[2], Tomasz Gawlik[3], Małgorzata Firek-Pędras[1], Lesław Szydłowski[4], Aneta Gawlik[2]

[1]Department of Paediatrics, Paediatric Endocrinology, and Diabetes, Upper-Silesian Paediatric Health Centre, Katowice, Poland

[2]Department of Paediatrics, Paediatric Endocrinology, Medical University of Silesia, School of Medicine, Katowice, Poland

[3]Department of Nuclear Medicine and Endocrine Oncology, Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Gliwice, Poland

[4]Department of Paediatric Cardiology, Medical University of Silesia, School of Medicine, Katowice, Poland

Abstract

Background: The risk of immunoglobulin resistance is still likely to occur in Kawasaki disease (KD) despite adequate treatment. The Kobayashi score (KS) is used to predict unresponsiveness to treatment although the usefulness of the score in populations other than Asian seems to be debatable.

Aim: The analysis of clinical and laboratory parameters predisposing to immunoglobulin resistance and coronary complications in children hospitalised due to KD.

Methods: The data of children hospitalised due to KD between 2003 and 2016 underwent analysis. Clinical and laboratory parameters were analysed, including all parameters present in KS in relation to the risk of intravenous immunoglobulin (IVIG) resistance and the occurrence of coronary complications in the form of aneurysms and dilatations.

Results: Seventy-three children (51 boys; aged 1.5–135 months) with KD were hospitalised. In eight (11%) patients IVIG resistance was observed. We reported aneurysms or coronary dilatations in 13 (17.8%) children. The criterion for increased risk of IVIG resistance based on KS (≥ 4 points) was fulfilled by 21 (29%) children. Resistance to IVIG and coronary complications were observed in four (19.1%) and two (9.5%) children with the score ≥ 4 points, respectively, and four (7.7%) and 11 (21.6%) from the group < 4 points in KS, respectively. The prevalence of IVIG resistance and coronary artery complications was not different between the group with ≥ 4 and the group with < 4 points ($p = 0.22$, $p = 0.32$, respectively). A higher risk of IVIG resistance was confirmed in children with a longer duration of fever (13.0 days with IVIG resistance vs. 9.2 days with a good response to IVIG, $p = 0.04$). For the prediction of the occurrence of coronary artery aneurysms the following were of great importance: the day of diagnosis (which was usually the day of the beginning of treatment), the number of symptoms, and the maximal platelet count ($p = 0.001$; $p = 0.019$ and $p = 0.026$, respectively).

Conclusions: In our study population we did not demonstrate the usefulness of KS to predict IVIG resistance or the risk of the occurrence of coronary artery aneurysms. However, prolonged fever, late diagnosis, poorly symptomatic course of the disease, and a high platelet count at the time of the follow-up remain independent risk factors.

Key words: Kawasaki disease, Kobayashi score, immunoglobulin resistance, coronary artery aneurysms

Kardiol Pol 2017; 75, 3: 261–266

Address for correspondence:
Elżbieta Berdej-Szczot, MD, Department of Paediatrics, Paediatric Endocrinology, and Diabetes, Upper-Silesian Paediatric Health Centre, ul. Medykow 16, 40–752 Katowice, Poland, e-mail: elaberdej@poczta.onet.pl

Received: 19.09.2016 **Accepted:** 08.11.2016 **Available as AoP:** 16.12.2016

INTRODUCTION

Kawasaki disease (KD) is an acute self-limiting inflammatory disease involving medium-sized arteries and occurring mostly in children under the age of 4. Currently the disease is considered one of the major causes of acquired heart disease in children in developed countries and it is the second commonest systemic vasculitis after Henoch-Schönlein purpura [1, 2]. The highest incidence is reported in Japan and other countries of Far East Asia and also in individuals of Asian origin who live in different regions of the world [3]. If untreated, the disease results in the occurrence of coronary artery abnormalities in the form of aneurysms or dilatations. Before intravenous immunoglobulin (IVIG) treatment was administered, the prevalence of coronary complications in both Japanese and American populations had been estimated at as much as 25% of patients [4, 5].

The implementation of treatment in the 1980s using a high dose of immunoglobulins and acetylsalicylic acid decreased the risk of coronary artery abnormalities to 1–3% [6]. However, the following years brought observations related to ~20% resistance to treatment [7]. Consequently, researchers started to search for other, more effective therapeutic methods and tried to identify factors which might favour IVIG resistance. As a result, a few scoring systems came into existence, i.e. Kobayashi, Sano, and Egami [7–9]. The scoring systems assess increased risk of unresponsiveness to IVIG treatment. When these scores are used in the Japanese population, they are characterised by high sensitivity and specificity.

The Kobayashi score (KS) is the most widely developed, and it includes unfavourable prognostic factors, i.e. disease symptoms occurring within four days, age < 12 months, hyponatraemia, hypertransaminasaemia, high C-reactive protein (CRP), low baseline platelet count, and a high percentage of neutrophils. Unresponsiveness to therapy is related to an increased risk of coronary artery abnormalities due to persistent inflammation (Table 1).

Establishing a prognosis and thereby selecting a group of children with an increased risk of coronary complications due to unresponsiveness to the initial treatment offers the possibility to introduce corticosteroids as early as in the initial phase. The effectiveness of such an approach was reported by Kobayashi et al. [10] in a multicentre prospective study done in 2012 on a group of several hundred children with an increased risk of treatment resistance (≥ 5 KS). These authors reported that the addition of corticosteroids statistically significantly decreased the risk of aneurysms (3% vs. 23%, $p < 0.0001$). However, in single studies related to populations other than Japanese, the authors did not demonstrate high usefulness of KS to assess the risk of resistance to KD treatment [11, 12].

The aim of the study is a retrospective analysis of clinical and laboratory risk factors of resistance to IVIG treatment and the occurrence of coronary artery aneurysms (CAAs), including the verification of the usefulness of KS in a group of children of Caucasian origin with KD treated in one clinical centre.

Table 1. Kobayashi scoring system

Kobayashi scoring	Points
≤ 4 days of disease	2
ALT ≥ 100 U/L	1
≤ 300 000 PLT	1
CRP ≥ 10 mg/dL	1
Age ≤ 12 months	2
Na ≤ 133 mmol/L	2
≥ 80% neutrophils	2
Risk of IVIG resistance	≥ 5 points

ALT — alanine aminotransferase; CRP — C-reactive protein; IVIG — intravenous immunoglobulin; Na — sodium; PLT — platelet count

METHODS

We analysed the data records of patients with KD, who were hospitalised from May 2003 to March 2016 at the Department of Paediatrics, Paediatric Endocrinology, and Diabetes of the Medical University of Silesia. The data were collected from the archives of medical records of patients hospitalised at the centre. The diagnosis of fully symptomatic KD was established based on the diagnostic criteria of the American Heart Association. An incomplete syndrome was diagnosed with the presence of a lower number of symptoms, absence of fever, and elevated markers of inflammation with the presence of coronary artery abnormalities such as dilatations or aneurysms.

All children were administered IVIG infusion in the cumulative dose of 2 g/kg and acetylsalicylic acid at a dose of 30–100 mg/kg in divided doses within 24 h after diagnosis. Resistance to IVIG was defined as the maintenance or recurrence of fever > 36 h after IVIG administration.

Echocardiography was done by an experienced cardiologist in each child with confirmed KD, to assess the changes in coronary arteries in accordance with the guidelines [13].

In all patients the available clinical and laboratory parameters were analysed. The clinical parameters included age, time of diagnosis, which was also the day of the initiation of treatment, clinical symptoms typical of KD, the time of symptom occurrence from fever onset, response to IVIG, and the diagnosis of coronary artery complications. The laboratory parameters included in KS were as follows: determination of alanine aminotransferase (ALAT) activity, CRP concentration, sodium concentration, baseline platelet count, and the percentage of neutrophils.

We analysed the influence of the above clinical and laboratory parameters on the risk of IVIG resistance and the occurrence of CAAs. As in the case of American and British authors, we verified the usefulness of KS (≥ 4 would be indicative of an increased risk of IVIG resistance) [11, 12].

Statistical analysis

For the purpose of the statistical analysis the following tests were used: student's t-test (with a separate variance estima-

tion, when necessary), two-tailed Fisher exact test to assess the differences of fractions, and logistic regression analysis. Differences at the level of $p < 0.05$ were considered statistically significant. Statistica for Windows v 12.0 (Stat Soft Inc. Tulsa, OK, USA) was used for calculations.

RESULTS

Kawasaki disease was diagnosed in 73 patients, i.e. in 51 (70%) boys and 22 (30%) girls. All patients were of Caucasian origin. At the time of diagnosis, the age of patients was 1.5–135 months (median age 26 months). The number of patients < 12 months of age was 16 (22%) and < 60 months of age was 62 (85%). The male-to-female ratio was 2.3:1. Sixteen (22%) children were admitted to our centre after day 10 of the disease.

Sixty-five (89%) children responded to the treatment. We observed resolution of fever and clinical symptoms and normalisation of inflammatory markers (two patients were treated at the Department of Paediatric Cardiology due to CAAs before the implementation of treatment, diagnosed after day 10 of the disease). However, in eight (11%) patients recurrence of fever was observed with persistently elevated inflammatory markers. Five of these patients were administered another IVIG infusion, and one patient was given IVIG and methylprednisolone/prednisolone at a dose of 1 mg/kg. All patients responded well to the second-line treatment except for one child who developed haemophagocytic syndrome. The presence of aneurysms and coronary artery dilatations was diagnosed in 13 (17.8%) patients.

The application of KS

Analysing all patients based on KS, we noted a maximum number of 8 points (in three patients). Of 73 patients, 21 (29%) children were assessed ≥ 4 points. Of these children, only four (19.1%) did not respond adequately to standard treatment. However, of the remaining 52 (71%) patients who did not fulfil the criteria for risk of IVIG resistance based on KS (< 4), recurrence of fever was reported in four (7.7%) cases after the first infusion. This difference was not statistically significant ($p = 0.22$). No significant differences in the prevalence of unresponsiveness to IVIG treatment were found when different cut-off points were adopted in KS (1–8: $p = 1$; $p = 1$; $p = 0.71$; $p = 0.22$; $p = 1$; $p = 0.58$; $p = 1$; $p = 1$, respectively).

In relation to the risk of aneurysms, as in the case of IVIG resistance, no statistically significant differences were found regarding the prevalence of aneurysms in groups ≥ 4 KS and < 4 KS (2, 9.5%, and 11, 21.6%, respectively; $p = 0.32$). As in the case of IVIG resistance when different cut-off points were adopted in KS, no significant differences between groups were observed (1–8: $p = 0.44$; $p = 0.76$; $p = 0.06$; $p = 0.32$; $p = 0.27$; $p = 0.67$; $p = 0.57$; $p = 1.0$, respectively).

In one (12.5%) patient with IVIG resistance, the presence of aneurysms was simultaneously confirmed. Aneurysms occurred in 12 (18.5%) patients among the remaining group (responding to IVIG). No significant difference was observed between these groups ($p = 1.0$).

Analysis of the influence of all clinical and laboratory parameters (independently of KS) on the risk of IVIG resistance and/or CAAs

The duration of fever was the only statistically significant difference between children who were IVIG resistant and the group of children with a good response to therapy (13.0 vs. 9.2 days, respectively; $p = 0.04$). However, compared to patients with no coronary complications, the group of children diagnosed with CAAs was characterised by later diagnosis (13.8 vs. 8.1 days, $p < 0.001$), a lower number of symptoms (3.4 vs. 4.3, $p = 0.02$), and a higher baseline platelet count (586.5 vs. 431.1 G/L, $p = 0.018$). A higher maximal platelet count at the follow-up was on the border of statistical significance (850.1 vs. 686.5 G/L, $p = 0.09$).

Analysing the influence of all the clinical variables using logistic regression analysis, only the day of diagnosis (in the majority of cases it was also the day of the beginning of treatment) were the number of symptoms and the maximal platelet count at follow-up significant for prediction of CAAs ($p = 0.001$; $p = 0.019$ and $p = 0.026$, respectively). Each day of delay in diagnosis increased the risk of aneurysms (odds ratio [OR] 1.55; 95% confidence interval [CI] 1.20–2.02). With each increase in the maximal platelet count by 100 G/L, an increase in the risk of aneurysm was also reported (OR 1.67, 95% CI 1.07–2.62). However, with each additional symptom of the disease, the OR for the occurrence of aneurysms decreased significantly (OR 0.34, 95% CI 0.14–0.83).

The following logistic regression equation was obtained: logit P = 6.00 (± 2.58) – 0.44 (± 0.13)*day of diagnosis + 1.01 (± 0.45)*number of symptoms – 0.51 (± 0.22)*platelet count max, where P is the probability of the non-occurrence of aneurysms; equation coefficients given with adequate standard errors.

Receiver operating characteristic (ROC) curve analysis was performed (Fig. 1) after attributing the probability of the development of CAAs to each patient (see the above equation).

Among the patients with $p > 0.9$ (46), aneurysms were not detected in any of the children (sensitivity 100%, specificity 78%, accuracy 82%); for the cut-off point 0.69 the test reached the sensitivity of 85%, specificity 90%, accuracy 88.8%; in all children with $p < 0.15$ the presence of aneurysms was confirmed (specificity 100%, sensitivity 38%, accuracy 88.8%).

None of the measured clinical parameters was significant in terms of the influence on the treatment response in the logistic regression analysis.

DISCUSSION

Seventy-three patients with KD were hospitalised during a 13-year follow-up. The incidence in Europe and among

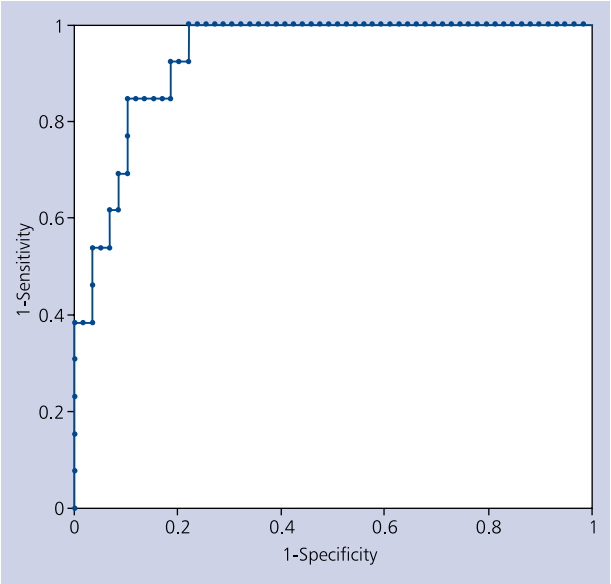

Figure 1. Receiver operating characteristic (ROC) curve demonstrating the properties of the proposed test classifying the probability of the occurrence of coronary artery aneurysms in patients with Kobayashi scoring

the Caucasians is significantly lower as compared to the epidemiological data from Japan, where it is estimated to be 8/100,000 in Europe in children < five years of age and 265/100,000 in Japan [1, 3]. Our material confirms higher incidence in children < 60 months of age (85% of patients, median age 26 months), which is consistent with American observations (24–26 months) [2]. Our study also confirms a preponderance of male over female patients (2.3:1).

Immunoglobulin infusion at the recommended dose did not result in resolution of fever in 11% of hospitalised children. However, only in one of these patients did CAAs develop in the further disease course (1 point in KS). In our study group the prevalence of IVIG resistance confirms the data from the literature. In the majority of cases patients presented with disease recurrence or even no resolution of fever after the first IVIG infusion [14–16]. Single observations indicated a significantly higher risk of unresponsiveness to treatment, periodically exceeding 30% [17].

Coronary artery abnormalities in the form of dilatations or aneurysms were observed in 17.8% of patients. A relatively late time of diagnosis probably influenced a significant number of complications. In 22% of patients the diagnosis was established after day 10 from fever onset, and in 50% of these cases CAAs had already been diagnosed on admission. Recently some improvement has been noticed in the detection of KD. Consequently, children are referred to our centre more quickly even with an incomplete form of the disease.

Data analysis of our patients in relation to the usefulness of KS to assess the risk of treatment resistance (scoring ≥ 4 as a factor of an increased risk of resistance) demonstrated that 21 (29%) of these patients fulfil the criteria for IVIG resistance [11, 12]. In fact, only four of these patients did not respond to IVIG therapy, although none of the patients developed coronary artery abnormalities. Our analysis confirmed that the risk of IVIG resistance was not significantly different between the group of children with ≥ 4 scoring results and the group with a lower score (KS). It indicates poor usefulness of KS in relation to the prediction of risk of inadequate treatment response in terms of our patient population. Additionally, we did not find a significant difference in relation to the response to IVIG therapy even when any other cut-off point in KS was considered. American and British researchers presented similar observations concerning the application of the scoring scale as a predictor of response to IVIG therapy [11, 12]. Sleeper et al. [11] in a prospective randomised study on a group of 99 patients with KD demonstrated high specificity (85–87%) but low sensitivity (33–42%) of Japanese scoring systems in the assessment of the risk of IVIG resistance in relation to the North American population (14% of subjects were of Asian origin) [11]. The Egami score was also of little usefulness in the prediction of the risk of resistance in relation to the San Diego population [17]. However, a retrospective assessment of KD patients hospitalised in the United Kingdom, which was based on KS, demonstrated both low sensitivity (58%) and specificity (33%) in predicting immunoglobulin resistance [12].

In the case of our study, the use of KS did not have practical application in the context of predicting the occurrence of CAAs, which is consistent with American and British reports [11, 12].

The availability of the clinical data and the laboratory examination results allowed further analysis in the search for markers useful in everyday clinical practice. In fact, CAAs were related to late diagnosis and a lower number of symptoms. It should be stressed that both these parameters (time of diagnosis, number of symptoms), though logically correlated, have a significant influence independently of each other. Observation of higher baseline and maximal platelet count at the time of hospitalisation as a factor increasing the risk of coronary lesions is interesting. Each delay in establishing diagnosis, each increase in the maximal platelet count by 100 G/L, and each additional symptom are related to the OR of the occurrence of aneurysms by 1.5, 1.67, and 0.34, respectively. The logistic regression equation was formed to assess the vascular risk. Patients with the probability of > 0.9 did not present with aneurysms (sensitivity 100%, specificity 78%, accuracy 82%). However, in all patients with $p < 0.15$ the presence of aneurysms was confirmed.

Duration of fever was the most significant and the only parameter in the case of response to IVIG therapy. Duration

of fever was significantly longer in children unresponsive to treatment, which was obviously a result of late diagnosis and consequently late implementation of treatment.

Based on the previous observations, it is difficult for us to recommend the use of corticosteroids in the treatment of KD in our population. Neither American nor European guidelines have recommended corticosteroids as the first-line treatment [1, 2]. Only one of our patients was given second IVIG therapy in addition to corticosteroids due to the recurrence of fever and persistently elevated markers of inflammation after the first infusion. The second IVIG therapy resulted in good clinical effect. In a six-month follow-up the patient did not develop coronary complications. However, the recent literature data are not promising. Sleeper et al. [11] did not demonstrate benefits of corticosteroid therapy in decreasing the risk of coronary complications.

CONCLUSIONS

Attempts to search for markers of the prediction of the risk of treatment resistance and the occurrence of coronary artery complications in patients with KD are fully substantiated. The consequences of KD are grave and carry a burden throughout life in the case of our patients. Despite certain limitations (retrospective study, small sample of patients, late hospitalisation/diagnosis), our study confirms the reports of other centres analysing patients mainly of Caucasian origin [11, 12]. It seems that a high sensitivity and specificity of KS may be adequate only in the case of the Japanese population [7, 10]. It is possible that such different observations and experience may be the result of a late diagnosis, which, in turn, may be caused by much less frequent occurrence of KD in the European population and consequently less experience of medical health workers related to this issue.

The authors thank Arkadiusz Badziński MA for the assistance in the translation of the manuscript.

Conflict of interest: *none declared*

References

1. Eleftheriou D, Levin M, Shingadia D, et al. Management of Kawasaki disease. Arch Dis Child. 2014; 99(1): 74–83, doi: 10.1136/archdischild-2012-302841, indexed in Pubmed: 24162006.
2. Newburger JW, Takahashi M, Gerber MA, et al. Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association, American Academy of Pediatrics. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation. 2004; 110(17): 2747–2771, doi: 10.1161/01.CIR.0000145143.19711.78, indexed in Pubmed: 15505111.
3. Makino N, Nakamura Y, Yashiro M, et al. Descriptive epidemiology of Kawasaki disease in Japan, 2011-2012: from the results of the 22nd nationwide survey. J Epidemiol. 2015; 25(3): 239–245, doi: 10.2188/jea.JE20140089, indexed in Pubmed: 25716368.
4. Newburger JW, Takahashi M, Burns JC, et al. The treatment of Kawasaki syndrome with intravenous gamma globulin. N Engl J Med. 1986; 315(6): 341–347, doi: 10.1056/NEJM198608073150601, indexed in Pubmed: 2426590.
5. Kato H, Sugimura T, Akagi T, et al. Long-term consequences of Kawasaki disease. A 10- to 21-year follow-up study of 594 patients. Circulation. 1996; 94(6): 1379–1385, doi: 10.1161/01.CIR.94.6.1379.
6. Furusho K, Kamiya T, Nakano H, et al. High-dose intravenous gammaglobulin for Kawasaki disease. Lancet. 1984; 2(8411): 1055–1058, indexed in Pubmed: 6209513.
7. Kobayashi T, Inoue Y, Takeuchi K, et al. Prediction of intravenous immunoglobulin unresponsiveness in patients with Kawasaki disease. Circulation. 2006; 113(22): 2606–2612, doi: 10.1161/CIRCULATIONAHA.105.592865, indexed in Pubmed: 16735679.
8. Seki M, Kobayashi T, Kobayashi T, et al. External validation of a risk score to predict intravenous immunoglobulin resistance in patients with kawasaki disease. Pediatr Infect Dis J. 2011; 30(2): 145–147, doi: 10.1097/INF.0b013e3181f386db, indexed in Pubmed: 20802375.
9. Kobayashi T, Kobayashi T, Morikawa A, et al. Efficacy of intravenous immunoglobulin combined with prednisolone following resistance to initial intravenous immunoglobulin treatment of acute Kawasaki disease. J Pediatr. 2013; 163(2): 521–526, doi: 10.1016/j.jpeds.2013.01.022, indexed in Pubmed: 23485027.
10. Kobayashi T, Saji T, Otani T, et al. RAISE study group investigators. Efficacy of immunoglobulin plus prednisolone for prevention of coronary artery abnormalities in severe Kawasaki disease (RAISE study): a randomised, open-label, blinded-endpoints trial. Lancet. 2012; 379(9826): 1613–1620, doi: 10.1016/S0140-6736(11)61930-2, indexed in Pubmed: 22405251.
11. Sleeper L, Minich B, McKrindle E, et al. Evaluation of Kawasaki disease risk-scoring system for intravenous immunoglobulin resistance. J Pediatr. 2011; 158: 831–835, doi: 10.1016/j.peds.2010.10.031.
12. Davies S, Sutton N, Blackstock S, et al. Predicting IVIG resistance in UK Kawasaki disease. Arch Dis Child. 2015; 100(4): 366–368, doi: 10.1136/archdischild-2014-307397, indexed in Pubmed: 25670405.
13. Berdej-Szczot E, Firek-Pędras M, Szydłowski L, et al. Analysis of risk factors and prospective evaluation of cardiovascular complications of Kawasaki disease in children: a single centre study. Kardiol Pol. 2013; 71(12): 1279–1286, doi: 10.5603/KP.a2013.0180, indexed in Pubmed: 23990228.
14. Durongpisitkul K, Soongswang J, Laohaprasitiporn D, et al. Immunoglobulin failure and retreatment in Kawasaki disease. Pediatr Cardiol. 2003; 24(2): 145–148, doi: 10.1007/s00246-002-0216-2, indexed in Pubmed: 12457253.
15. Han RK, Silverman ED, Newman A, et al. Management and outcome of persistent or recurrent fever after initial intravenous gamma globulin therapy in acute Kawasaki disease. Arch Pediatr Adolesc Med. 2000; 154(7): 694–699, indexed in Pubmed: 10891021.
16. Burns JC, Capparelli EV, Brown JA, et al. Intravenous gamma-globulin treatment and retreatment in Kawasaki disease. US/Canadian Kawasaki Syndrome Study Group. Pediatr Infect Dis J. 1998; 17(12): 1144–1148, indexed in Pubmed: 9877364.
17. Tremoulet AH, Best BM, Song S, et al. Resistance to intravenous immunoglobulin in children with Kawasaki disease. J Pediatr. 2008; 153(1): 117–121, doi: 10.1016/j.jpeds.2007.12.021, indexed in Pubmed: 18571548.

Cite this article as: Berdej-Szczot E, Małecka-Tendera E, Gawlik T, et al. Risk factors of immunoglobulin resistance and coronary complications in children with Kawasaki disease. Kardiol Pol. 2017; 75(3): 261–266, doi: 10.5603/KP.a2016.0179.

Czynniki ryzyka oporności na leczenie immunoglobulinami i powikłania kardiologiczne u dzieci z chorobą Kawasaki

Elżbieta Berdej-Szczot[1], Ewa Małecka-Tendera[2], Tomasz Gawlik[3], Małgorzata Firek-Pędras[1], Lesław Szydłowski[4], Aneta Gawlik[2]

[1]Oddział Pediatrii, Endokrynologii i Diabetologii Dziecięcej, Górnośląskie Centrum Zdrowia Dziecka, Katowice
[2]Klinika Pediatrii i Endokrynologii Dziecięcej, Wydział Lekarski, Śląski Uniwersytet Medyczny, Katowice
[3]Zakład Medycyny Nuklearnej i Endokrynologii Onkologicznej, Centrum Onkologii — Instytut im. Marii Skłodowskiej-Curie, Gliwice
[4]Klinika Kardiologii Dziecięcej, Wydział Lekarski, Śląski Uniwersytet Medyczny, Katowice

Streszczenie

Wstęp: W chorobie Kawasaki (KD) pomimo właściwego leczenia istnieje ryzyko immunoglobulinooporności. Skala Kobayashi jest stosowana w przewidywaniu braku odpowiedzi na terapię, choć jej użyteczność w populacjach innych niż azjatycka wydaje się dyskusyjna.

Cel: Celem pracy była analiza parametrów klinicznych i laboratoryjnych predysponujących do immunoglobulinoopornosci i powikłań kardiologicznych u dzieci hospitalizowanych z powodu KD.

Metody: W badaniu uwzględniono dane dzieci hospitalizowanych z powodu KD w latach 2003–2016. Analizowano parametry kliniczne i laboratoryjne, w tym wszystkie uwzględniane w skali Kobayashi, w aspekcie ryzyka oporności na dożylne immuboglobuliny (IVIG) i powstania powikłań wieńcowych pod postacią tętniaków lub poszerzeń naczyń.

Wyniki: Hospitalizowano 73 dzieci z KD (51 chłopców) w wieku od 1,5 do 135 miesięcy. U 8 (11%) zaobserwowano oporność na IVIG. Tętniaki lub poszerzenia naczyń wieńcowych stwierdzono u 13 (17,8%) dzieci. Kryterium zwiększonego ryzyka oporności na IVIG wg skali Kobayashi (≥ 4 pkt) spełniało 21 (29%) dzieci. Oporność na IVIG i powikłania kardiologiczne prezentowało odpowiednio 4 (19.1%) i 2 (9.5%) dzieci z punktacją ≥ 4 oraz 4 (7.7%) i 11 (21.6%) pacjentów z grupy z punktacją < 4 w skali Kobayashi. Częstość oporności na IVIG oraz powikłań w naczyniach wieńcowych nie różniła się między grupą z ≥ 4 pkt. a grupą z < 4 pkt. (odpowiednio, p = 0,22 i p = 0,32). Potwierdzono wyższe ryzyko oporności na IVIG u dzieci dłużej gorączkujących (13,0 dnia z opornością na IVIG *vs.* 9,2 dnia z dobrą odpowiedzią na IVIG; p = 0,04). Dla predykcji wystąpienia tętniaków w naczyniach wieńcowych istotne znaczenie miały: dzień ustalenia rozpoznania (najczęściej też dzień rozpoczęcia leczenia), liczba objawów i maksymalna liczba płytek krwi (odpowiednio, p = 0,001; p = 0,019 i p = 0,026).

Wnioski: U badanej populacji nie wykazano przydatności skali Kobayashi do przewidywania oporności na IVIG i ryzyka pojawienia się tętniaków naczyń wieńcowych, natomiast niezależnymi czynnikiem ryzyka pozostaje długo utrzymująca się gorączka i późno postawiona diagnoza, skąpoobjawowy przebieg choroby oraz wysoka liczba płytek w trakcie obserwacji.

Słowa kluczowe: choroba Kawasaki, skala Kobayashi, immunoglobulinooporność, tętniaki naczyń wieńcowych

Kardiol Pol 2017; 75, 3: 261–266

Adres do korespondencji:
Lek. Elżbieta Berdej-Szczot, asystent, Oddział Pediatrii, Endokrynologii i Diabetologii Dziecięcej, Górnośląskie Centrum Zdrowia Dziecka, ul. Medykow 16, 40–752 Katowice, e-mail: elaberdej@poczta.onet.pl
Praca wpłynęła: 19.09.2016 r. **Zaakceptowana do druku:** 08.11.2016 r. **Data publikacji AoP:** 16.12.2016 r.