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GAMMA GLOBULIN THERAPY IN KAWASAKI DISEASE

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The objectives of this study were to evaluate the therapy protocol of gamma globulin (GG) re-treatment without steroids. Patients. From Jun. 1994 to Jun. 2001, 220 typical patients were enrolled within 8 days of illness. They had no coronary artery dilatation at admission and before GG treatment. Their risks were evaluated by the Iwasa's risk score system. Of 220 patients, 66% were selected as high-risk patients and 80% were treated with GG. Initial dose of GG was single 2g/kg for the high-risk patients and 1g/kg for the low-risk patients with prolonged fever, 49 patients had GG re-treatment. Maximum dose of GG was 8g/kg and mean dose of GG was 1.8g/kg per patient. Dose of re-treatment after Sep. 1996 was decided by WBC and CRP before and after GG treatment. Results. Of 220 patients, 13 patients had coronary artery lesions (CAL, over 3 mm in diameter) in acute stage and 3 patients had CAL at 30th days of illness, which were all transient dilatation. In high-risk female patients, 51 patients treated with GG had no CAL. In high-risk male patients from Jun. 1994 to Jun. 1999, 60 patients were treated with sulfonated GG (Sulfo-GG) or GG prepared by propylene glycol (PEG-GG). And CAL (8/31) in Sulfo-GG group was significantly higher than CAL (1/29) in PEG-GG group (p=0.017). In high-risk male patients after Jul. 1999, when we did not use Sulfo-GG, 1/22 had CAL. The other 3 CAL patients, whose CAL were under 3.1 mm in diameter, were high-risk patient without GG, low -risk patient without GG and high-risk patient with GG. Persistent fever over 10 days of illness occurred in 20/159 patients before Jun. 1999, but 3/61 after Jul. 1999. Duration of fever after Jul. 1999 was significantly shorter than that before Jun. 1999 (p = 0.039). Repetition of PEG-GG treatment can reduce CAL.

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GAMMAGLOBULIN FAILURE AND RETREATMENT IN KAWASAKI DIS-EASE

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Background: Several cases of Kawasaki disease, (KD), up to 15%, were unresponsive to the initial treatment with intravenous immunoglobulin (IVIG). We retrospectively analyzed all children admitted for KD to determine the occurrence and variables associated with the initial IVIG treatment failure. **Methods**: All patients who fulfilled the criteria for KD and were treated with a single dose (2g/kg) of IVIG between January 1995 and December 2000 were enrolled. An analysis of patients who had initially failed to respond to IVIG and patients who had coronary artery aneurysm (CAA) was conducted. **Results** : A total of 113 patients were enrolled during the study period. There were 65 boys (57.5%). Thirteen patients (11.5%) were found to be unresponsive to initial IVIG treatment. Patients who were anemic (Hb < 10 gm/dl), had high leukocyte (wbc) counts (>12,000/mm3), and high neutrophil count (>75%) were at risk for failure to response to a single dose of IVIG. We found no correlation between age, gender, days of starting IVIG treatment and ESR with failure of initial IVIG treatment. There were 23 patients (20.3%) who developed CAA. Male gender, lower hemoglobin (<10 g/dl), higher neutrophil count (>75%), higher ESR (>100mm/hr), prolonged fever and failure to respond to a single dose of IVIG were associated with a higher risk of developing CAA. **Conclusions**: The failure of a single dose of IVIG treatment could be seen in up to 11.5% of our Kawasaki patients. We found that low hemoglobin (<10g/dl), high wbc counts (>12,000/mm3) and high neutrophil counts (>75%) were associated with retreatment of a second dose of IVIG.

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KINETICS OF SERUM IMMUNOGLOBULINS IN KAWASAKI DISEASE: ARE THEY PREDICTORS FOR CORONARY OUTCOME ?

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Background: Immunoglobulins(Ig), such as IgA, have been found in affected coronary arteries in Kawasaki Disease(KD). Changes in Ig may reflect the development of coronary artery lesions(CAL). **Objectives:** To characterize changes in serum Ig during the course of KD and to determine whether Ig were predictive of coronary outcome. **Methods:** 243 KD pts(1995-2001) were included in this retrospective study. Data retrieved consisted of demographics and clinical course including lab tests from pre-treatment to 1yr post KD diagnosis(i.e. pre/post-IVIG, subacute, convalescent, 1yr). The quantitative variables were tested for their significance using the Student t test. **Results:** The mean age of pts was 3.7±2.8yrs. 66.3% were males and 33.7% were females. All received IVIG(2g/kg) and ASA. 19.3% required adjunctive therapy(multiple IVIG±corticosteroids). CAL detected at KD diagnosis, 3mos and 1yr comprised of ectasias (49.0%,31.3%,14.0%), aneurysms(3.3%,2.9%,1.2%) and giant aneurysms(0%,0.4%,0%). 93 pts had paired pre/post-IVIG Ig. Immediately post IVIG, the mean change in Ig was an increase IgG(70.9±16.8%), IgM(2.3±21.2%) and a decrease IgA(-8.5±20.4%). 43 pts had paired pre/subacute Ig. In this case, the mean change in Ig was an increase IgG(34.8±47.7%), IgM(13.7±36.4%) and a decrease IgA(-15.4±65.1%). No significant differences were noted in pts with giant aneurysms and Ig levels. Significant serologic markers associated with CAL were decreased subacute IgG&IgA(acute ectasias), increased post-IgG&decreased pre/post-IgM(persistent ectasias), and increased pre/convalescent-IgA&convalescent-IgG(persistent aneurysms). Consistent with Harada's risk factors, a lower PLT(p=0.04) and higher ESR(p=0.008) were associated with CAL. Persistent CAL were associated with a lower albumin(p=0.02) and a larger fall in the WBC post-IVIG(p=0.03). **Conclusions:** The natural history of Ig post IVIG in KD pts was an increase IgG and IgM and a fall in IgA. Patients with acute CAL had lower subacute IgA and IgG. In contrast, pts with persistent CAL had higher IgA pre-IVIG, higher IgG post-IVIG, lower IgM pre and post-IVIG, and higher convalescent IgG & IgA.

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PREDICTION OF RESISTANCE TO TWO INTRAVENOUS INFUSIONS OF HIGH-DOSE Γ -GLOBULIN IN PATIENTS WITH KAWASAKI DISEASE BEFORE TREATMENT

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Approximately 5 to 15% of patients with acute Kawasaki disease (KD) is non-responsive to intravenous γ -globulin (IVGG), which is one of critical risk factors of severe coronary artery injury. To determine how to predict IVGG-resistance before treatment, the correlation between the response to IVGG and clinical parameters at disease onset were analyzed in 112 children with acute KD treated with IVGG (1g/kg for two day) consecutively in six hospitals. Patients were classified as IVGG-responsive which was defined as defevescence within 24 hours after finishing IVGG (n=90) or IVGG-resistant as conistent fever over 24 hours after IVGG (n=22). An incident of coronary artery abnormalities during the acute phase was significantly higher (p<0.0001) in the IVGG-resistant group (50%) than in the IVGG-responsive group (11%), and so was that in the recovery phase (12% vs. 0%, p=0.0012). By an univariate analysis the IVGG-resistant group showed significantly higher serum levels of C-reactive protein (CRP), total bilirubin, aspertate aminotransferase (AST), alanine aminotransferase, lactate dehydrogeas (p<0.0001 in each), &gamma-glutamyltranspeptidase (p=0.02639) and neutrophil count (p=0.0159), as well as showed sigficantly lower serum albumin level (p=0.0181) than those in the IVGG-responsive group. A logistic regression analysis showed that as the appropriate cutoff values predicting the resistance to IVGG, a CRP level >7mg/dL (p=0.0104), a total bilirubin level >0.9mg/dL (p=0.0014) and an AST level >200IU/L (p=0.0031) were significant. Patients fitted in at least two of three cutoff values were considered resistant to IVGG (sensitivity = 77% and specificity = 86%). Alternative or additional therapy at an early stage of the disease should be considered for patients with acute KD who are predicted to be resistant to IVGG.

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THE SELECTION OF THE GROUP WITH SUFFICIENT AND INSUFFI-CIENT EFFECT TO GAMMA GLOBULIN THERAPY IN THE KAWASAKI DISEASE

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(Objective) The effectiveness of high dose intravenous gamma globulin (IVGG) therapy in the Kawasaki disease (KD) has already been established. This time, we originally produced the treatment protocol. Using this protocol, the groups with sufficient and insufficient effect to IVGG therapy were determined. In addition, frequency and characteristics of both group were analyzed. (Patients and methods) Forty five patients of starting the IVGG therapy within the seventh illness day were made to be an object. The IVGG therapy was done by following methods. The effect was judged after treatment start 48 hours. The IVGG therapy (1g/kg) was made to be an end, if there were antipyresis and improvement tendency of CRP. The effect insufficient cases added 1g/kg IVGG. As examination items, frequency of coronary artery lesions (CAL) and laboratory findings (CRP, WBC, PMN, Ht, Pl, Alb, ChE, IgG) were chosen. (Results) (1) The one time administrated group (A group) was 31 cases (69%), and the additional dosage group (B group) was 14 cases (31%). (2) The patients with CAL were 1/31 in the A group and 5/14 in the B group. (3) There was no significance at CRP, WBC, Ht, Pl, Alb in both groups. In the B group, PMN counts were significantly high, and ChE, IgG were significantly low. (Conclusions) (1) In about 70% of the cases, the sufficient effect was obtained in the single dose of 1g/kg IVGG therapy. (2) In the group with the sufficient effect, CAL could not be seldom recognized. (3) As a method of the selection of both groups, it seemed to be the most appropriate to judge the the therapy effect by the administration of 1g/kg IVGG. (4) It is possible that this therapy reduces the quantity of using IVGG, and there is an economical advantage.

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TREATMENT OF KAWASAKI DISEASE WITH INTRAVENOUS IMMUNO-GLOBULIN : A COMPARISON OF THE 2GM/KG REGIME WITH A 1 GM/KG FLEXIBLE REGIME

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Background. A meta-analysis which included six studies from Japan and U.S. showed that the prevalence of coronary abnormalities was inversely related to the total dose of intravenous immunoglobulin (IVIG). While most hospitals in Hong Kong followed the 2gm/kg IVIG treatment regime for Kawasaki disease, two hospitals adopted a flexible regime of using a starting dose of 1gm/kg IVIG followed by additional doses for persistence or recurrence of fever. This study compared the treatment effects of the two treatment regimes in terms of duration of fever and coronary complications. Method. A retrospective study of all Kawasaki disease patients admitted between 1 July 1994 to 30 June 1999 to 12 major hospitals in Hong Kong. Results. 146 patients were treated with the 1gm/kg flexible regime while 428 patients were in the 2g/kg group. There were no significant difference of the age distribution (median age: 1.58 years vs 1.59 years), sex ratio (62% boys in both groups) and the treatment starting date (5.2 vs 5.6 days after onset of fever). Whereas about 1/3 of the patients in both groups had rapid subsidence of fever within 12 hours, significantly more patients remained febrile after 48 hours in the 1 gm/kg IVIG group (24% vs 10%, p<0.001). The prevalence of coronary abnormalities at week 8 after the onset of disease was also higher in group 1 (11.6% vs 3.5%).Conclusion. 2gm/kg IVIG regime provides better protection against development of coronary abnormalities after Kawasaki disease than 1gm/kg IVIG flexible regime.