PostScript

LETTERS

Adverse effects of methylprednisolone pulse therapy in refractory Kawasaki disease

The efficacy and safety, including arrhythmia and sudden death,[1 2] of intravenous methylprednisolone pulse (IVMP) therapy in patients with Kawasaki disease (KD) are uncertain.

We conducted a control study in KD patients with persistent or recurrent fever (≥37.5℃) 48 hours after a single infusion of initial intravenous immunoglobulin (IVIG) 2 g/kg. At enrolment (day 1), the subjects were randomised to receive IVMP (30 mg/kg/day of methylprednisolone for three days), or additional IVIG (2 g/kg). Heparin was also continuously infused (15–20 units/kg/h) in the IVMP group. The study was halted prematurely because of adverse effects of IVMP when 22 patients were recruited; they accounted for 13% of KD patients treated with initial IVIG.

The antipyretic effect of IVMP was superior to that of additional IVIG on day 2 ($p = 0.02$, repeated measures analysis), but not on day 3 and later (fig 1). The fraction of febrile patients was significantly lower in the IVMP group until day 3 (1/11 *v* 8/11, $p < 0.001$, Fisher exact test), but not on day 4 and later (6/11 *v* 6/11). Coronary artery dimensions and the prevalence of coronary artery lesions (2/11 *v* 3/11) were similar in the two groups. Regarding adverse effects, sinus bradycardia and hyperglycaemia occurred more often in the IVMP group (table 1). Hypertension occurred in 91% of the IVMP group, but the fraction did not differ significantly, probably due to the small sample size. All of the adverse effects were transient. There were no convulsions, gastrointestinal symptoms, infection, malignant arrhythmia, or sudden death in any subjects.

Table 1 Adverse effects

	IVMP (n = 11)	Additional IVIG (n = 11)	p value
Heart rate (/min)	68 (63, 76)	98 (76, 110)	0.01
Sinus bradycardia (%)	82	18	0.01
Body temperature (℃)	35.4 (0.4)	36.1 (0.5)	0.002
Hypothermia <35.0℃ (%)	9	0	1.00
Systolic blood pressure (mm Hg)	119 (8)	113 (12)	0.24
Hypertension (%)	91	55	0.15
Blood glucose (mmol/l)	7.0 (1.4)	5.4 (0.6)	0.007
Hyperglycaemia ≥7.0 mmol/l (%)	55	0	0.01
Shortening of activated partial thromboplastin time (%)	27	18	1.00
Embolism (%)	0	0	
Stool blood (%)	0	0	

We analysed continuous variables with the normal distribution, expressed as mean (SD), by the unpaired *t* test, and those with any non-normal distribution, expressed as median (first quartile, third quartile), by the Wilcoxon rank sum test. For nominal variables, we used the Fisher exact test. All statistical tests were two tailed. Heart rate and body temperature are minimum values and systolic blood pressure is the maximum value within 72 hours after the start of IVMP or additional IVIG. Bradycardia is defined as heart rate <2 percentile of the normal standard (*Pediatr Cardiol* 1979;**1**:123–52) and hypertension as systolic blood pressure >95 percentile of the normal standard (*Pediatrics* 1996;**98**:649–58.). Blood glucose level is the maximum value obtained on days 2, 4, and 7 after treatment with IVMP or additional IVIG. Shortening of activated partial thromboplastin time is defined as the minimum value on days 2, 4, and 7 <80% of the value on day 1.

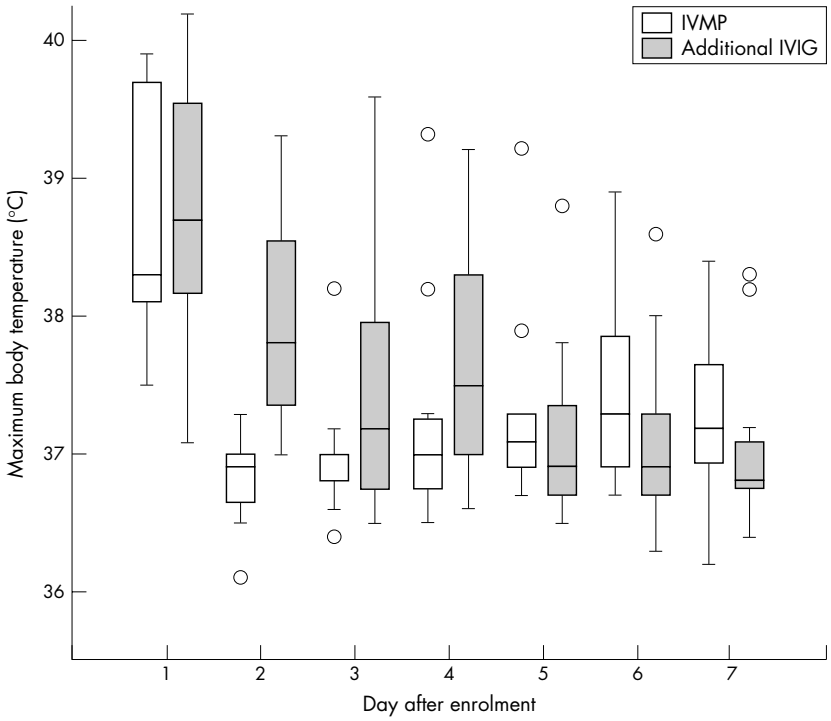

Figure 1 Changes in the maximum body temperature attained each day after treatment with IVMP or additional IVIG. The starting day of IVMP or additional IVIG was defined as day 1. Body temperature dropped more rapidly in the IVMP group than in the additional IVIG group ($p = 0.006$, repeated measures analysis); the antipyretic effect of IVMP was superior to that of additional IVIG on day 2 ($p = 0.02$, repeated measures analysis), but not on day 3 and later. The upper and lower ends of a box show the first and third quartiles, and the line inside the box the median value. The upper fence of a whisker represents the largest value within 1.5 times the interquartile range above the third quartile and the lower fence of a whisker the smallest value within 1.5 times the interquartile below the first quartile. Values beyond the fences are marked with circles.

KD patients refractory to initial IVIG should be treated with additional IVIG,[3 4] because IVMP induced faster but temporary resolution of fever and more adverse effects. Further investigations with steroid therapy are necessary to determine the indication and the appropriate dose in KD.

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Blood pressure measurement in a district general paediatric A&E department

Blood pressure is a simple physiological measure routinely estimated in many paediatric clinical environments. The recommended frequency and requirement for this measure in children is debatable, particularly in casualty departments. However the rising burden to healthcare systems from hypertension should perhaps be used to review current practice.[1]

One thousand and six consecutive patient records from a district general hospital in west London from May to August 2004 were audited retrospectively. Blood pressure was measured in 9% of those 16 years or younger. By contrast aural temperature and manually estimated pulse rates were recorded in 91% of the group. Age was the largest single determinant for measurement ($p < 0.001$); triage priority, arrival time, and presenting complaint had lower impacts. Only 32% of children with a high priority triage had a measure of blood pressure. Appropriate follow up of abnormal results was patchy; 14% of raised blood pressures documented in casualty received no follow up or repeat measure. Interviews with staff indicated that there was no perceived need to check blood pressure unless specific medical directions were received. Equipment and appropriate age related normal charts were readily available and did not limit the service.

Although no evidence supports population based blood pressure screening in children, studies have suggested advantages to the measurement of blood pressure in the hospital setting.[2–4] This strategy identifies hypertension early, particularly in teenagers, who are infrequent attendees in general practice.[5] In urban British populations a hospital casualty is frequently their sole point of contact with health services (local audit results).

Following the audit period in this centre two cases of essential hypertension were subsequently identified in children aged 14 and 16 years. Neither had blood pressure measured on earlier visits to casualty. As documented recently the global burden of hypertension is likely to increase.[5] While A&E departments are not designed to carry out primary prevention, the valuable opportunity to prevent disease and improve outcomes with a simple measurement should not be overlooked.

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Intima-media thickness in obesity: relation to hypertension and dyslipidaemia

Obesity in childhood contributes to cardiovascular risk factors, such as hypertension and dyslipidaemia.[1] Exposure to these cardiovascular risk factors may induce atherogenic changes in the arteries.[1] Measurement of the intima-media thickness (IMT) of the common carotid artery (CCA) is an acknowledged non-invasive marker for early atherosclerotic changes and is a feasible, reliable, valid, and cost effective method.[2 3] It has not yet been studied whether hypertension and dyslipidaemia are related to IMT in obese children. Therefore, we measured clinical data (age, gender, degree of overweight as standard deviation score of BMI (SDS-BMI)[4]), IMT, serum lipids (triglycerides and HDL, LDL, and total cholesterol), systolic (SP) and diastolic blood pressure (DP) in 46 obese children (median age 9.6 years). The control group was comprised of 16 lean age and gender matched children. IMT was measured at CCA near the bifurcation at the far wall by B-mode ultrasound using a 14 Mhz linear transducer and compared between obese and lean children by Mann-Whitney U test, since IMT was not normally distributed. IMT as dependent variable and age, gender, SDS-BMI, blood pressure, and serum lipids as independent variables were determined in a multiple linear regression analysis. Blood pressure and lipids were compared between obese children with IMT above the upper quartile of IMT and children with IMT below or equal to the upper quartile of IMT by Student's t test for unpaired observations. Obese children showed a significant ($p < 0.001$) thicker intima media (median 0.06 cm) compared to the control group (median IMT 0.04 cm). In multiple linear regression analysis, IMT correlated significantly to triglycerides ($p = 0.023$) and systolic and diastolic blood pressure ($p < 0.001$). The children with IMT above the upper quartile (0.06 cm) showed significantly increased triglycerides ($p = 0.038$, median 142 mg/dl versus 103 mg/dl) and blood pressure ($p < 0.001$, median SP 137 mm Hg versus 119 mm Hg, median DP 71 mm Hg versus 60 mm Hg), while they did not differ significantly from the other children in respect of gender, age, SDS-BMI, and HDL, LDL, or total cholesterol.

Since IMT is increased in obese children, vascular changes in obesity seem to occur already in childhood. Childhood obesity may be a risk factor for developing atherosclerosis, since higher IMT of the CCA is reported to be predictive and is related to the severity and extent of coronary artery disease and strokes.[5 6] Our findings suggest that hypertension and hypertriglyceridaemia, which are part of the metabolic syndrome, have the highest atherogenic potential in childhood obesity.

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How to improve patients' understanding in biomedical research?

We read with interest the recent paper from Barnett and colleagues,[1] reporting the impact of different styles of informed consent forms proposed to children; it is one of the few papers on this important topic. Indeed, the content of informed consent documents (ICD) is a crucial element in the process of providing information to participants in biomedical research. Clear comprehension of this information—that is, the ability to understand its meaning and its consequences, is of great importance. However, investigators sometimes have the feeling that volunteers do not fully understand the major concepts of the study in which they are enrolled, and this issue is specifically relevant to children. This feeling has been confirmed by several studies in adults. A study conducted in two public hospitals[2] showed that 40.7% and 74.5% of patients respectively did not understand the content of the ICD for clinical studies in which they were enrolled. In a third study, 156 veterans were