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Penicillin clearance in diabetic children

By

L. MADÁCSY, M. BOKOR and L. MATUSOVITS

Municipal Children's Hospital, Szeged

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The clearance of crystalline penicillin G was found to be significantly higher in children in the early period of diabetes than in age-matched healthy controls. The therapeutic importance of the finding is emphasized.

Several authors [4, 11] have reported on an inverse correlation between glomerular filtration rate (GFR) and the half-life of penicillin.

It has been shown earlier [5] that GFR was increased in early childhood diabetes. It seemed therefore interesting to examine how the elimination of antibiotics was affected by the increased GFR. To settle the question, we have determined the clearance of penicillin G in diabetic and in healthy children.

MATERIAL AND METHOD

Twelve diabetic and ten healthy children, ranging in age from 6 to 14 years, in apparent metabolic equilibrium and free from renal disease, were examined. The duration of diabetes ranged between two months and five years. Examinations were performed in the morning hours, the children being in bed. The diabetics received their usual daily dose of insulin two hours prior to the experiment. The clearances of penicillin G and inulin and the blood sugar level were registered continuously. Determination of penicillin G clearance was made according to BARNETT et al. [1] Measurement of penicillin level in serum and urine was performed using the microbiological procedure of IVÁN et al. [3]. The clearance of inulin was estimated as described earlier [5] and the blood sugar level by the o-toluidine method [12].

The first 500 IU/kg dose of crystalline penicillin G was given intravenously and the maintenance dose of 250 IU/min was administered in a continuous drip infusion. The latter corresponded to the product of the expected plasma concentration and the clearance value. Drip infusion and urine collection were continued for 180 minutes. Venous blood samples for penicillin determination were taken at intervals of 30 minutes.

RESULTS

Results are summarized in Tables I and II. Clearance values are shown for 1.73 m^2 body surface. In the diabetic group, mean inulin clearance was 165.8 ± 22 ml/min/1.73 m^2; and in the control group, 132.8 ± 17 ml/min/1.73 m^2 ($p < 0.01$).

Mean penicillin G clearance was 700.8 ± 142 ml/min/1.73 m^2 in dia-

TABLE I

Diabetic patients

Name	Sex	Age, year	Duration of diabetes	Body surface, m^2	Blood sugar level, mg/100 ml	Serum penicillin level IU/ml	Diuresis, ml/min	Penicillin clearance, ml/min/ 1.73 m^2	Inulin clearance ml/min/ 1.73 m^2
M. L.	male	14	2.5 years	1.28	235—177	0.93—0.76	1.0	513.6	153.9
L. I.	male	9	3 months	0.96	125— 85	1.23—1.13	1.22	530.0	142.6
R. I.	male	8	3 years	1.06	320—232	0.75—0.33	1.5	735.0	158.0
B. S.	male	8	3 years	1.12	322—254	0.80—0.53	1.78	640.0	157.7
B. E.	male	13	2 months	1.16	210—110	0.70—0.60	2.2	860.0	194.0
H. F.	male	14	1 year	1.31	290—230	0.85—0.60	2.1	775.0	155.5
B. J.	male	7	6 months	0.86	250—180	0.63—0.48	2.1	895.0	192.0
F. J.	male	13	6 months	1.55	160— 90	0.81—0.53	1.22	516.0	138.0
F. S.	female	14	5 years	1.35	320—280	0.73—0.61	3.56	765.0	161.8
S. I.	female	6	2 months	0.74	165— 80	0.90—0.53	3.1	570.0	143.4
H. A.	female	12	2 months	1.19	238—104	0.80—0.58	1.55	740.0	198.0
T. J.	female	14	5 years	1.4	280—200	0.73—0.63	2.0	870.0	194.7

TABLE II

Control subjects

Name	Sex	Age, year	Body surface, m^2	Serum penicillin level, IU/ml	Diuresis, ml/min	Penicillin clearance, ml/min/ 1.73 m^2	Inulin clearance ml/min/ 1.73 m^2
S. J.	female	11	1.2	0.65—0.42	1.66	215	130
K. É.	female	9	1.0	1.49—0.83	2.28	384	124.5
S. E.	female	7	0.9	0.80—0.70	0.56	295	110
K. L.	male	9	0.89	0.93—0.81	1.28	655	160.2
M. Z.	male	8	0.95	0.60—0.48	0.33	254	105
J. Cs.	male	12	1.23	0.44—0.38	0.61	515	148.2
T. T.	male	9	0.95	1.09—0.53	0.97	565	140.0
T. A.	male	9	1.08	0.85—0.58	2.3	398	132.6
B. Gy.	male	11	1.15	1.13—0.88	3.42	380	135.0
U. Z.	male	10	1.12	1.03—0.83	1.11	380	143

betics, and 413.2±129 ml/min/1.73 m^2 in the controls. The two groups showed a significant difference ($p < 0.01$).

Discussion

Crystalline penicillin G is rapidly eliminated in unchanged form by glomerular filtration and active tubular secretion. The latter amounts to about 4/5 of the total clearance. Thus, penicillin G clearance is 4—5 times higher than that of inulin. In view of this, Eagle and Newman [2] recommended the determination of penicillin G clearance for measuring the rate of renal plasma flow (RPF).

Plaut et al. [11] studied the connection of penicillin half-life and renal function in healthy and azotaemic subjects. The reduction of renal function was found to result in a prolonged half-life of penicillin. Similar observations were reported by Kampmann et al. [4] who studied the effect of certain drugs on the half-life of penicillin.

Data regarding penicillin clearance in diabetic patients have not been found in the literature, and few papers have dealt with the penicillin clearance of healthy children [1, 2]. Barnett et al. [1] determined the clearance of penicillin G in healthy children and in preterm infants. In the latter, a low insulin clearance was associated with a low penicillin clearance.

In our experiments the mean clearance of crystalline penicillin G proved to be significantly higher in diabetics than in healthy children. These data support the observations of a close correlation between GFR and the elimination of penicillin [4, 11] as we found an accelerated elimination of penicillin with an increased GFR (Fig. 1). No correlation was observed

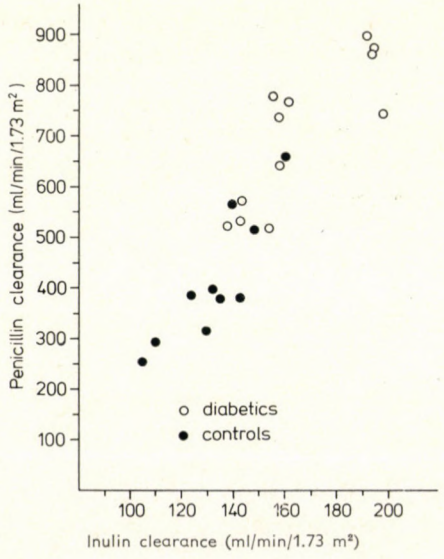

Fig. 1

between the blood sugar and the clearance values in the diabetic patients.

There is unequivocal evidence [5—9] of increased GFR in adults suffering from juvenile diabetes and in children during the early phase of the disease. Recently, MOGENSEN and ANDERSEN [10] have determined the size of the kidneys and estimated GFR and RPF in a similar patient material. They found significantly enlarged kidneys in the diabetic subjects. The enhanced GFR might thus be attributed to the enlarged glomeruli. RPF was 10% higher in the diabetic patients than in the controls but the difference was not significant statistically. In spite of this they assumed a positive correlation between GFR and RPF and the size of the kidneys in both healthy and diabetic subjects ($p < 0.01$).

These observations may serve to explain the increased penicillin clearance noticed by us.

The present findings may have some therapeutic importance. The increased elimination of crystalline penicillin in early juvenile diabetes may call for the application of higher doses, amounting occasionally even to double the usual ones.

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Dr. L. MADÁCSY
Odesszai krt. 35
H-6726 Szeged, Hungary

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