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Fasting Level and Epinephrine-induced Release of Free Fatty Acids in Patients with Congenital Heart Disease

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The fasting level of free fatty acids and sugar in plasma and their response to subcutaneous epinephrine administration was studied in children suffering from congenital heart disease. In cyanotic cases elevated fasting values were found for free fatty acids (14 cases); in non-cyanotics, however, the values were normal (7 cases). In non-cyanotic heart disease the rise of free fatty acids and sugar in response to epinephrine administered subcutaneously was normal, while in cyanotic patients (10 cases) it was found to be decreased. When the studies were repeated with intravenous infusion of epinephrine the cyanotic patients showed a normal response.

Der Nüchternspiegel von freien Fettsäuren und Glucose im Plasma sowie deren Reaktion auf subcutane Adrenalinapplikation wurde bei Kindern mit angeborenen Herzfehlern untersucht. Bei Herzfehlern mit Cyanose wurden erhöhte Nüchternwerte für freie Fettsäuren gefunden (n = 14), während sie bei solchen ohne Cyanose normal waren (n = 7). Der Anstieg von freien Fettsäuren und Glucose nach subcutaner Adrenalinapplikation war bei den Kranken ohne Cyanose normal, während er bei denen mit Cyanose (n = 10) vermindert war. Bei Wiederholung der Versuche mit intravenöser Adrenalininfusion zeigten auch die cyanotischen eine normale Reaktion.

In cyanotic congenital heart disease glycolysis shifts towards anaerobiosis as seen from the elevation of the lactic acid level (1). The fasting level of blood sugar and the carbohydrate tolerance after peroral administration of sugar are normal (2). Up to the present no investigation has been made of the metabolism of free fatty acids. In dogs the free fatty acid level rises during acute hypoxia and this is most probably due to an increased catecholamine production (3). A high level of free fatty acids was also found in the umbilical artery of hypoxic newborn infants (4). The present work deals with the fasting level of free fatty acids and its release provoked by epinephrine in children with congenital heart disease.

Methods

Examinations were carried out on children of 2—14 years of age suffering from congenital heart disease and on healthy children of the same age. The patients were divided into two groups: heart disease with cyanosis (right to left shunt) and without cyanosis (left to right shunt). Patients with heart failure and those receiving drugs were not included. The blood was taken after overnight fasting. The investigations with epinephrine were performed 6 hours after meal. 0.03 mg/kg, max. 0.5 mg epinephrine was administered subcutaneously and the blood samples were taken at 0, 30, 60, 90 and 120 minutes. Intravenously, 2 µg/kg/min epinephrine was infused for 30 minutes and the blood was obtained at 0, 15, 30 and 60 minutes. The free fatty acid determination was carried out by DOLE's (5) and in some cases by ANSTALL's method (6). The sugar was estimated by the method of SOMOGYI-NELSON.

Results

The fasting level of sugar is normal in all types of heart disease. The free fatty acids are normal in noncyanotic patients (table 1). In children with cyanosis the free fatty acid level is higher than in healthy children or patients exhibiting no cyanosis ($p < 0{,}01$). Since in hypoxia the levels of lactic acid and other organic acids are elevated in the blood and this might cause falsely high values for free fatty acids by DOLE's method, we repeated the examinations with ANSTALL's colorimetric method which is more specific for free fatty acids. High free fatty acid levels could be found with this method as well. There was no correlation between the haemoglobin and the free fatty acid concentration.

Tab. 1
Fasting values of plasma free fatty acids and sugar

		Plasma sugar mg/100 ml	Plasma free fatty acids (µVal/l) (DOLE)	(ANSTALL)
Healthy	n	18	20	14
	mean	72.3	862	779
	SD	± 15.9	± 298	± 247
Cyanotic	n	23	12	14
	mean	74	1380	1216
	SD	± 15.3	± 595	± 752
	p	> 0.5	< 0.01	< 0.05
Non-cyanotic	n	7	7	
	mean	84.6	762	
	SD	± 34	± 424	
	p	> 0.2	> 0.2	

In further examinations we studied the changes of plasma free fatty acids and sugar after subcutaneous administration of epinephrine (table 2). In cases with left to right shunt the response was similar to that of healthy children, while in right to left shunt the rise was smaller in respect to both free fatty acids and glucose. Since the reduced release of free fatty acids and sugar might be caused by the slower absorption of epinephrine if administered subcutaneously, we repeated the measurements in some cases after the intravenous infusion of epinephrine (table 3). In three cases out of four we found the mobilisation of free fatty acids and sugar normal, so it can thus be assumed that in cyanotic patients the

Tab. 2
Change of plasma free fatty acids and sugar in response to epinephrine administered subcutaneously. Mean values

	n	Change of plasma free fatty acids (μVal/l)				Change of plasma sugar mg/100 ml			
		30 min	60 min	90 min	120 min	30 min	60 min	90 min	120 min
Healthy	10	+ 752	+ 336	+ 120	+ 295	+ 47	+ 28	+ 8	+ 4
Cyanotic	9	+ 243	— 48	— 161	— 153	+ 27	+ 17	+ 3	0
Non-cyanotic	5	+ 776	+ 378	— 46	— 34	+ 66	+ 46	+ 14	0

Tab. 3
Free fatty acid and sugar levels in response to epinephrine administered intravenously

	Plasma free fatty acids (μVal/l)				Plasma sugar mg/100 ml			
Healthy	0 min	15 min	30 min	60 min	0 min	15 min	30 min	60 min
1.	670	840	1240	780	110	181	174	141
2.	490	840	990	440	92	136	132	108
3.	1260	2850	2100	900	100	139	172	100
4.	860	1100	1000	480	91	167	138	100
Cyanotic								
1.	1820	1880	2280	1160	89	104	107	127
2.	760	1840	2060	840	78	95	111	94
3.	1140	1680	1730	1070		130	177	136
4.	1500	970	780	780	77	82	114	90

slower absorption of epinephrine may be partially or wholly responsible for the reduced release of free fatty acids and sugar.

Discussion

Enhanced lipolysis may be one of the possible explanations for the high plasma free fatty acids found in cyanotic cases of congenital heart disease. The studies with epinephrine show that in these patients the ability of adipose tissue to release free fatty acids is not impaired, consequently the possibility of increased lipolysis cannot be excluded. In hypoxia the catecholamine level increases (7) which causes a high level of free fatty acids. This was found e. g. in phaeochromocytoma as a consequence of high catecholamine secretion (8). In cyanotic patients, however, the excretion of catecholamine metabolites in the urine increases only slightly (9), it thus seems improbable that the great increase in the free fatty acid level should be solely due to the mobilisation of catecholamines. There have been no studies carried out concerning the other hormones (growth hormone, thyroxin, glucocorticoids) influencing the free fatty acid release.

The other possible explanation is that the reesterification of free fatty acids into triglycerids is decreased. It is noteworthy in this respect that Hait and Coworkers found an increased insulin secretion in patients with cyanotic heart disease (2). If the high level of free fatty acids and insulin can really be found simultaneously it can be assumed that the adipose tissue in these patients is resistant to insulin. The measurement of plasma glycerol can provide further information on whether the high level of free fatty acids is due to increased lipolysis or decreased reesterification, since the whole quantity of glycerol released from the adipose tissue gets into the circulation, whereas a certain amount of free fatty acids is immediatly reesterificated.

Finally it can be assumed that in these patients the peripheral utilisation of free fatty acids is reduced and this might also be an explanation for the high plasma free fatty acids.

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