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Effect of sites for blood sampling in determination of the galactose elimination capacity

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The galactose elimination capacity was calculated from both arterial and capillary or peripheral venous curves in twenty patients. The capillary curves on the average were delayed 1·4 min in relation to the arterial curves. No significant difference was found between the calculated galactose elimination capacity from either curve. On the average the slope of the venous curves was smaller than that of the arterial curve, and their time delay was very variable (from 1·55 to 5·27 min). Galactose elimination capacity calculated from venous curves was smaller than those calculated from arterial curves, especially in patients with a high galactose elimination capacity. Capillary blood sampling may replace arterial puncture for routine use, whereas venous blood sampling introduces a significant bias.

Key-words: capillary blood; distribution; elimination curves; galactose; liver diseases; liver function; sampling; venous blood

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The theory for calculation of the galactose elimination capacity from blood disappearance curves after a single intravenous injection of galactose is based on the assumption of parallelity between the arterial concentration curve and the curve representing the mean concentration in the body during the defined interval of measurement [6]. Experiments have indicated that the arterial concentration curve is displaced in relation to the hypothetical mean concentration curve by on the average 7 min. This displacement enters the calculation of the galactose elimination capacity from the arterial concentration curve.

The requirement for sampling of arterial blood limits the general usefulness of the method. It has been shown by Lindskov [5] that the galactose concentrations of capillary blood were in closer agreement with those of arterial blood than the concentrations in blood from a peripheral vein, and that the calculated galactose elimination capacity was slightly, but insignificantly, lower. The purpose of the present work was to compare the errors of arterial, venous and capillary blood sampling for determination of the galactose elimination capacity in order to estimate under which conditions the simpler sampling techniques can be expected to give sufficiently accurate results.

MATERIAL AND METHODS

The material consists of an unselected series of patients subjected to determination of the galactose elimination capacity according to the routine procedure of the department, including arterial sampling. In ten cases (group A) galactose concentrations were also determined in capillary blood, and in ten cases (group B) in peripheral venous blood. Nineteen patients were studied (one patient was included in both group A and B). There were eleven males and seven females, their mean age was 50 years (range 30–72 years) and mean body weight 68 kg (range 45–92 kg), eleven suffered from alcoholic cirrhosis, eight of them had ascites, three had cryptogenic cirrhosis, two primary biliary cirrhosis, one portal venous thrombosis, one intermittent intrahepatic cholestasis of unknown origin, and one Gilbert's syndrome. The material of group A and B did not differ significantly with respect to clinical data or galactose elimination capacity according to the standard method.

The intravenous injection of galactose, 0·5 g per kg body weight, was given in the course of 5 min. From 25 to 60 min after start of the injection 1 ml of blood was sampled from an indwelling needle in the brachial artery with intervals of 5 min into small test tubes with dry heparin.

In group A capillary blood was drawn from an ear lobe, in which a puncture 2–3 mm deep and about 2 cm wide had been made with a pointed surgical blade. Bleeding from the wound was provoked by slight pressure, the first drop of blood was removed and the time noted. The following drops were collected in dry heparinized glass tube, 95 mm in length with an opening of 1 mm at one end and 3 mm at the other. The tube was filled to about three quarters of its length (about 150 μl). Sampling time was kept below 1 min. The tube was immediately emptied into a small test tube, with dry heparin. In group B 1 ml of venous blood was collected from an indwelling needle in an anticubital or antibrachial vein without stasis.

Arterial and venous or capillary blood was drawn by separate technicians. No attempt was made to synchronize sampling from different sites, but they followed the same general scheme. Galactose was measured in whole blood and urine (collected 3 h after start of the injection), using the galactose dehydrogenase method [4].

The slope of blood concentration-time curves was calculated by linear regression, omitting samples with a concentration lower than 2 mmol/l. Comparison of regression lines as to residual variation, slope and horizontal distance was performed by standard methods [1]. The galactose elimination capacity was calculated as $I - U/t_{c=o} + 7$, where I is the amount injected, U is the amount excreted into the urine, $t_{c=o}$ is the intercept of the concentration time curve with the time axis, and 7 is the correction for uneven distribution [6].

RESULTS

Arterial versus capillary blood sampling. The residual variation of the arterial curve is smaller than that of the capillary curve in eight out of ten experiments (Table I). In one case (P.R.) the difference is significant, and the validity of the further statistical comparison of the curves thus may be questioned in this case. However, since this difference is due to an unusually low variation of the arterial curve rather than to a greater than normal variation of the capillary curve, this experiment is included in the over-all evaluation. In contrast to the arterial curves, the capillary curves show inhomogeneity of variances ($P < 0{\cdot}025$, Bartlett's test). However, the estimate of the mean residual variation of the capillary curve is not substantially greater than that of the arterial curve.

In no case is the difference between the slope of the arterial and the capillary curve significantly different, but in half of the cases, the capillary curve is significantly delayed in relation to the arterial curve. The mean delay, calculated from all the curves, amounts to 1·4 min, which is significantly different from zero ($P < 0{\cdot}01$).

Good agreement is found between the galactose elimination capacity calculated from the arterial and the capillary blood concentrations (Fig. 1). The 95% confidence limits of the regression line, with the arterial sampling as independent variate, covers the line of identity, the intercept of the line with the axes does not deviate significantly from zero, and the residual variation of the dependent variate (galactose elimination capacity calculated from capillary sampling) is less than 5% of the mean value.

TABLE I. Comparison of arterial (a) and capillary (c) blood concentration curves after a single intravenous injection of galactose

Initials	Sampling site	No. of samples	Residual variation mmol/l	*F* test	Slope mmol l^{-1}/min^{-1}	*t* test	Horizontal distance* min	*t* test
H.N.	a	8	0·145	NS	−0·091	NS	1·78	$P<0·05$
	c	8	0·121		−0·087			
R.P.	a	6	0·079	NS	−0·143	NS	−0·23	NS
	c	6	0·101		−1·151			
A.G.	a	8	0·105	NS	−0·097	NS	1·95	$P<0·025$
	c	8	0·156		−0·101			
S.S.	a	6	0·097	NS	−0·091	NS	0·79	NS
	c	8	0·139		−0·085			
L.J.	a	7	0·157	NS	−0·156	NS	1·31	NS
	c	8	0·220		−0·148			
R.I.	a	8	0·125	NS	−0·086	NS	1·49	NS
	c	6	0·174		−0·088			
A.L.	a	8	0·135	NS	−0·087	NS	4·03	$P<0·001$
	c	8	0·137		−0·080			
P.R.	a	8	0·045	$P<0·05$	−0·070	NS	2·06	$P<0·005$
	c	8	0·107		−0·071			
K.N.	a	8	0·180	NS	−0·143	NS	−0·21	NS
	c	6	0·373		−0·135			
N.B.	a	5	0·127	NS	−0·203	NS	1·22	$P<0·005$
	c	5	0·069		−0·203			
Mean	a		0·127**	NS‡	0·0018¶	NS‡	1·42	$P<0·01$
	c		0·176†		(SD, 0·0056)		(SD, 1·22)	

* positive values indicate that the capillary concentration curve is delayed in relation to the arterial curves; ** square root of pooled variance (Bartlett's test); † inhomogeneity of variance ($P<0·025$); ‡ *t* test (paired); ¶ mean difference (a−c).

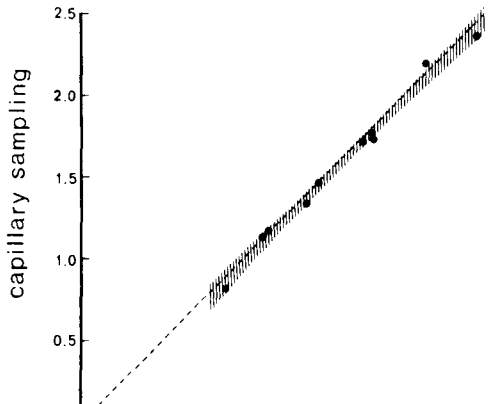

FIG. 1. Comparison of galactose elimination capacity (mmol/min) calculated from arterial (GE_a) and capillary (GE_c) blood concentration curves after a single intravenous injection of galactose ($GE_c = -0·019+0·992\ GE_a \pm 0·050$). One dot represents one patient, the dotted line is the line of identity. The 95% confidence limits (hatched area) is shown.

Arterial versus venous blood sampling. The residual variation appears to be slightly smaller in the venous than in the arterial curves (Table II), but testing for inhomogeneity of variance for each group of curves separately as well as for all curves together gives *P* values greater than 0·1. The slope of the venous curves is significantly smaller in two experiments, and on the average it is 10% smaller ($P<0·005$). In four out of eight experiments, in which the horizontal distance between arterial and venous curves can be tested (i.e. where the slopes are not significantly different), the mean delay of the venous curves in relation to the arterial curves is not greater than that of the capillary curves (1·4 min), but the variance is much greater ($P<0·05$, *F* test), so that the mean is not significantly different from zero.

The galactose elimination capacity calculated from the venous curve is lower than that calculated from the arterial curve when the latter is higher than about 1·5 mmol/min. The regression line (Fig. 2) shows a significant

TABLE II. Comparison of arterial (a) and venous (v) blood concentration curves after a single intravenous injection of galactose

Initials	Sampling site	No. of samples	Residual variation mmol/l	Residual variation *F* test	Slope mmol/l^{-1} min^{-1}	Slope *t* test	Horizontal distance* min	Horizontal distance* *t* test
F.P.	a	8	0·206	NS	−0·095	NS	−0·32	NS
	v	8	0·177		−0·089			
M.H.	a	8	0·125	NS	−0·071	NS	−1·28	NS
	v	8	0·129		−0·062			
W.G.	a	8	0·098	NS	−0·060	NS	−1·55	NS
	v	7	0·073		−0·062			
E.H.	a	8	0·199	NS	−0·153	NS	3·79	$P<0·001$
	v	8	0·114		−0·138			
B.K.	a	8	0·097	NS	−0·093	$P<0·05$	−1·91	$(P<0·05)$**
	v	8	0·108		−0·083			
K.N.	a	8	0·168	NS	−0·111	NS	5·27	$P<0·001$
	v	8	0·098		−0·099			
T.B.	a	8	0·120	NS	−0·092	NS	4·44	$P<0·001$
	v	8	0·137		−0·080			
I.I.	a	8	0·114	NS	−0·143	$P<0·001$	3·55	$(P<0·001)$**
	v	8	0·127		−0·119			
B.M.	a	8	0·122	NS	−0·106	NS	−0·56	NS
	v	8	0·144		−0·094			
C.D.	a	8	0·077	NS	−0·110	NS	2·57	$P<0·001$
	v	8	0·084		−0·109			
Mean	a		0·139†	NS‡	0·0099¶	$P<0·005$‡	1·40	NS
	v		0·123†		(SD, 0·0073)		(SD, 2·78)	

* positive values indicate that the venous curve is delayed in relation to the arterial curve; ** test performed irrespective of significant difference between slopes; † square root of pooled variance (Bartlett's test); ‡ *t* test (paired) ¶ mean difference (a−v)

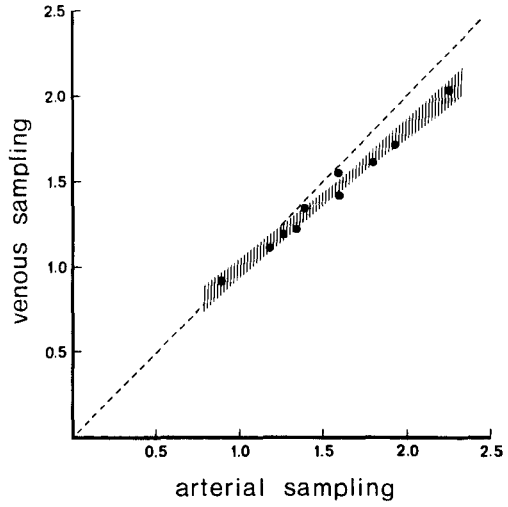

FIG. 2. Comparison of galactose elimination capacity (mmoles. min^{-1}) calculated from arterial (GE_a) and peripheral venous (GE_v) blood concentration curves after a single intravenous injection of galactose ($GE_v = 0·177 + 0·807\ GE_a \pm 0·043$). One dot represents one patient, the dotted line is the line of identity. The 95% confidence limits (hatched area) is shown.

deviation from the line of identity and a significant positive intercept with the ordinate.

DISCUSSION

In order to estimate the elimination of a substance from the body by means of concentration-time curves, the concentration measured should be representative of the mean concentration of the substance in its volume of distribution at any given time. Galactose is known to be distributed in the extracellular compartement [2] and in some intracellular compartements as well (e.g. liver [3] and red blood cells [8]). The liver removes galactose from the blood stream so rapidly that concentration equilibration between the blood and extravascular compartments of distribution following a single intravenous injection of galactose can not be expected [6]. There is evidence, however, that after a mixing and distribution period, the arterial concentration and the mean concentration have a relatively well-defined relation [7]. This relation can not be applied directly to concentra-

tions in other parts of the vascular bed. During the elimination phase big concentration differences will exist between different vessels, the lowest being found in the hepatic veins, and the highest in vessels draining organs in which galactose was stored during and immediately following the intravenous injection. The galactose concentration in the latter vessels will be larger than that of the arterial blood feeding the organs, determined partly by the artery-to-vein mean circulation time (because the arterial concentration is decreasing), partly by the amount of galactose leaving the organ. Thus organs with a relatively large perfusion and a large extravascular volume will show a relatively high arterio-venous concentration difference.

The data presented show that capillary blood from the ear lobe approximates the arterial blood in respect to galactose concentrations during the phase of steady elimination, although the inhomogeneity of variance indicates that individual time-dependent circulatory or methodological factors may interfere to some extent. The mean delay time of 1·4 min probably exceeds the artery-to-ear lobe capillary mean circulation time and therefore the blood cannot be considered as completely 'arterialized' in that respect. The difference also reflects transport of galactose from tissue to blood. From a theoretical point of view it seems appropriate to use 5 min instead of 7 min as a correction for uneven distribution when capillary blood from the ear lobe (and possibly also from the finger tips) is used instead of arterial blood, but the data presented show that this makes very little difference.

The results obtained by using venous blood shows greater deviations from the arterial curves with respect to slope as well as to time delay. The difference in slope is significantly correlated with the rate of elimination, estimated from the slope of the arterial curve ($r = +0{\cdot}72$). It probably reflects that the release of galactose from the tissues drained by the superficial veins on the arm is increasing during the phase of steady elimination. This increase, however, must be quantitatively relatively unimportant, and untypical for the body as a whole, unless the absolute rate of elimination of galactose is increasing simultaneously. Otherwise the concentration of arterial blood (which represents that of mixed venous blood a mean circulation time earlier) could not show a steeper fall.

A priori, a greater time delay would be expected in venous than in capillary concentration curves. Instead, a significantly greater variation was found. For analytical reasons the time delay is more easily detected in relatively steep curves, where it also has a greater influence on the calculated galactose elimination capacity. This is in agreement with the data. Thus the difference between galactose elimination capacity calculated from venous and arterial curves is reduced if the venous curves are corrected for the time delay actually found. A systematic difference persists, however, probably due to the difference in the slope of the curves.

The variations in time delay of the venous curves cannot be fully explained from the observations presented, but it is likely to be due to variations of the rate of perfusion through the organs drained by the superficial arm veins. There is no evidence of great fluctuations of flow during the period of observation, since this would have made the concentration-time curve irregular (i.e. increased the residual variation). Nevertheless, the smaller slope of the venous concentration curves as well as great variability of the time delay makes blood sampling from the superficial veins of the arm less suited for estimation of the galactose elimination capacity after a single intravenous injection.

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