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HEART LYMPH : ELECTROLYTE COMPOSITION AND CHANGES INDUCED BY CARDIAC GLYCOSIDES

N.-H. ARESKOG,* G. ARTURSON and G. GROTTE

Departments of Paediatric Surgery, Plastic Surgery, Physiology, Clinical Physiology and Clinical Chemistry, University of Uppsala, Sweden

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Abstract—The electrolyte content of heart lymph was compared with that of plasma in heart-lung preparations of dogs. The lymph was collected from a cannula in a lymph vessel, mainly draining the left ventricle. The potassium, sodium and calcium contents of lymph and plasma were determined by flame photometry. Changes of the potassium balance were provoked by rapid-acting cardiac glycosides. The time relations and magnitudes of changes in lymph and plasma were studied. The average potassium content in lymph was 5·80 m–equiv./l and in plasma 3·90 m–equiv./l. In contrast, no significant difference was shown between plasma and lymph sodium content. Cardiac glycosides provoked a potassium loss from the myocardium which appeared more rapidly in the lymph than in the plasma. The potassium concentration change was of the same order in both the fluids, indicating that most of the potassium loss induced by the glycoside emanated from the heart in the heart-lung preparation.

It is concluded that myocardial potassium changes are adequately and sensitively reflected in cardiac lymph.

THE HEART is a good object for lymph studies, since it produces a high flow due to its continuous activity. Using a heart-lung preparation, it is possible to adjust the venous and arterial pressures and the heart rate, in order to get a good, steady, lymph flow. Previously only one study of cardiac lymph seems to have been reported.[1] The sodium, potassium or calcium contents of the heart lymph were, however, not studied. In general, the data on the electrolyte composition of lymph are very scanty. It is supposed to be similar to the electrolyte content of plasma.[2] An exception, however, is the renal capsular lymph, which has been shown to have a higher sodium content than plasma.[3]

It is well-known from animal and human studies that the working skeletal muscle loses potassium. This can be detected as an increase of the potassium concentration of the venous blood from the actual muscle. On the other hand the continuously working heart muscle is the best object in which to detect an early disturbance of the potassium metabolism (ECG changes, arrhythmia). It therefore seemed of value to study the lymph fluid from the extravascular space of the heart, which might be a sensitive indicator of electrolyte changes between the extra- and intracellular compartments.

In the present study cardiac lymph from dog heart-lung preparations (HLP) has been investigated with regard to (a) normal content of potassium, sodium and calcium,

* Present address: Department of Clinical Physiology, Regionsjukhuset, Linköping, Sweden.

compared with that of plasma and (b) changes of the electrolyte balance, induced by cardiac glycosides.

MATERIAL AND METHODS

The experiments were performed on eight mongrel dogs weighing 12–28 kg. They were anaesthetized with Nembutal-Abbott,® administered intravenously in a dose of 30 mg/kg body weight. To prevent clotting, heparin in a dose of about 5 mg/kg body weight was injected before switching on to HLP. A Starling pump performed artificial positive-pressure ventilation. In order to get a steady pH of about 7·40 and a good oxygenation throughout the experiments 2·7–3·0% CO_2 in O_2 was used as the inspired gas mixture. For further details of the HLP method see [4].

The circulating blood volume in the HLP system was about 400 ml and the heart weight 85–215 g. The same lymph vessel as described earlier[5] was cannulated and the lymph was collected continuously, the test tubes being changed as a rule every 5–10 min. The lymph vessel used mainly drains the left ventricle. Before the start of the HLP the cannulas and the connecting tube on the venous side were filled with Salidex®.*

Arterial and venous pressures, temperature, heart rate, lymph flow and, in most of the experiments, ECG and cardiac output (minus coronary blood flow), were recorded.

The potassium, sodium and, in two cases, calcium concentrations of plasma and lymph taken from the venous cannula reaching the right atrium, were analyzed by flame photometry. In some cases consecutive samples of lymph were pooled to get a sufficient amount for the analysis.

In three experiments cardiac glycosides were given, Convallatoxin (Convalyt, Dr. Madaus & Co., Cologne) in a dose of 0·005 mg/kg or Dihydro-Ouabain (Sandoz Ltd, Basle) in a dose of 0·02–0·04 mg/kg body weight of the intact dog.

RESULTS

The contents of potassium, sodium and calcium in cardiac lymph compared with plasma

In all eight experiments the *potassium* content of lymph was much greater than that of plasma (Fig. 1, Table 1), being on an average 50·9 per cent higher (range 15·3–123·0 per cent). If the two extreme values are excluded, the average potassium increase in lymph, compared with plasma, was 45·0 per cent (range 31·4–70·0%). The greatest difference between the plasma and lymph potassium concentrations was obtained in an experiment in which the heart was bigger and had a much higher output than in the other experiments.

The average potassium concentration in lymph was 5·80 m-equiv./l (30 observations from eight experiments) and in plasma 3·90 m-equiv./l (31 observations from the same eight experiments). No values following the glycoside-induced electrolyte effect are included here. A few observations just before the start of the HLP, i.e. when all preparations were complete except that the aorta and inferior vena cava had not been ligated, showed the same relationship between plasma and lymph as just after the start of HLP.

* Kindly supplied by Pharmacia Ltd., Uppsala, with the following electrolyte content: Na^{+}155, K^{+}4·0, Ca^{++}3·6, Mg^{++}1·1, Cl^{-}163, and lactate 1·1 m-equiv./l.

As regards the *sodium* concentration, the differences between plasma and lymph were small and not significant. The mean sodium concentration of six experiments in lymph was 148 m-equiv./l and in plasma 144 m-equiv./l. The mean sodium increase in lymph, compared with plasma, was 2·8 per cent (range 1·3–7·2 per cent).

The *calcium* concentration was determined in only two experiments. These observations do not support the existence of any difference between plasma and lymph concentration, the average value being about 4·6 m-equiv./l for both fluids.

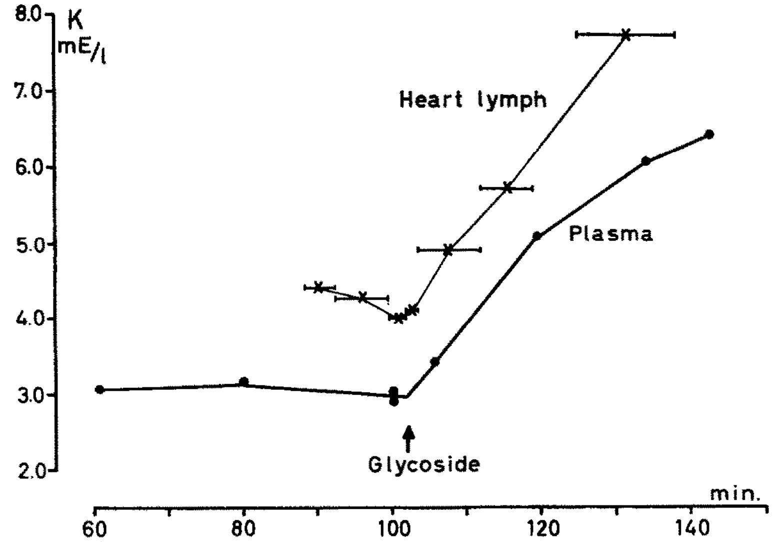

FIG. 1. Potassium concentration (K m-equiv./l) in plasma (filled symbols) and in lymph (open symbols) in relation to time after the start of HLP. Arrows indicate injection of cardiac glycoside.

TABLE 1. POTASSIUM CONCENTRATION IN LYMPH (L) AND PLASMA (P) AND THE LYMPH-PLASMA DIFFERENCE IN EIGHT HLP EXPERIMENTS

Exp. No.	Body wt. kg	Heart wt. g	n	Lymph, m-equiv./l M	Lymph, m-equiv./l Range	n	Plasma, m-equiv./l M	Plasma, m-equiv./l Range	L/P diff. m-equiv./l	L/P diff. % of P
1	15	106·5	5	4·04	3·25–4·45	4	3·02	2·90–3·15	1·02	33·8
2	12	85	7	5·21	5·00–5·65	3	3·85	3·75–4·00	1·36	35·3
3	14	97	4	5·92	4·55–6·35	8	4·32	3·40–5·05	1·60	37·1
4	14	95	2	5·90	4·80–6·90	4	3·63	3·10–4·10	2·27	62·6
5	16	100	4	6·15	4·80–7·80	4	4·68	3·90–5·30	1·47	31·4
6	17	105	4	5·13	4·30–6·00	4	4·45	3·50–5·40	0·68	15·3
7	28	215	2	7·95	7·35–8·55	2	3·58	3·40–3·75	4·37	122·0
8	19	155	2	5·83	4·65–7·00	2	3·43	3·20–3·65	2·40	70·0

As a rule, the potassium content of plasma and lymph increased during the experiment, especially preterminally (Fig. 1). These changes were not more pronounced in lymph.

Electrolyte effects of cardiac glycosides

Both in plasma and lymph a considerable increase of the potassium concentration was obtained after injection of cardiac glycosides. As regards the time course, the changes appeared to be more rapid in lymph, thus indicating a potassium loss from the myocardial cells. In a typical experiment a potassium increase from ~ 3·0 to

6·0 m-equiv./l in plasma and from 4·1 to 7·7 m-equiv./l in lymph was obtained 30 min after the glycoside injection. Thus the magnitude of the increase was the same in plasma and lymph.

No significant changes of the sodium concentration in plasma and lymph were observed. Lymph values are, however, available only from one experiment.

DISCUSSION

Compared with man, the dogs usually showed lower plasma potassium values. This might be due to species and diet factors and—to a lesser extent—the Salidex® fluid in the extracorporeal system before the start of the HLP. The same experience appeared in earlier reported, bigger experimental series of HLP.[6]

Earlier data on the electrolyte content of lymph are rare. In lymph from the cervical lymphatics and thoracic duct the values correspond well to the normal plasma contents of potassium and sodium. Simultaneous plasma data are, however, lacking.[7] As regards calcium,[8, 9] the average values were slightly lower in lymph (4·9 m-equiv./l in cervical and 4·6 m-equiv./l in thoracic duct lymph, compared with 5·8 and 5·2 m-equiv./l in plasma respectively). Renal capsular lymph has a higher sodium concentration than plasma but the same potassium concentration.[3]

The high potassium content of cardiac lymph found here might be explained in different ways. The isolated heart has a tendency to lose potassium continuously, i.e. the loss is greater than the gain of the myocardial cells. Even at the beginning of the HLP, however, there is a difference between the potassium concentration in plasma and lymph, and this might be due to the muscular activity of the heart (like the potassium loss during skeletal muscular activity). Assuming a drained heart wet wt. of 50 g, a moderate cardiac lymph flow of 2·5 ml/hr, containing about 4 m-equiv./l potassium,[10] and a lymph-plasma difference of 2 m-equiv./l, only 0·5 m-equiv./l of potassium leaves the heart via the lymphatics in one hour. In some HLPs, however, there were lymph flows of 6 ml/hr and lymph-plasma differences of 4 m-equiv./l, resulting in a more than fourfold increase of the above-mentioned potassium loss via the lymphatics but, compared with the total potassium content of the heart, this is still of minor importance.

As has been shown recently,[11] no glucose is taken up by the myocardium, when the blood glucose has fallen to a low value. This implies that the potassium gain of the myocardium will be reduced, since potassium enters the cells partly in connexion with carbohydrates. This mechanism might contribute to the potassium loss of the isolated heart and might be one of the causes of the spontaneous insufficiency of the isolated heart. Only after several hours' run of the HLP does a metabolic acidosis aggravate the potassium loss.[12] Using an inspiring gas mixture with excess of oxygen, it is possible to prevent tissue anoxia, which is yet another cause of potassium loss.

The glycoside effect on the potassium balance has been discussed in earlier reports.[6] In this study it was used to compare the time relations and magnitudes of changes in plasma and lymph. This also shows that the glycoside-induced potassium loss emanates mostly from the heart and not from the lungs in the HLP.

In conclusion we may say that the cardiac lymph, i.e. the extravascular fluid of the heart, is a suitable and sensitive object for studies of the myocardial electrolyte metabolism, especially with regard to potassium, since it is difficult, owing to the high intracellular content, to detect small intracellular variations of concentrations in tissue samples. The lymph seems probably also to be a more accurate index and to reflect more sensitively the intracellular electrolyte changes than coronary sinus blood plasma, since all the potassium loss from the tissue to the extravascular space drained by the lymph cannula, can be measured. This is not possible with intermittent samples from coronary sinus blood plasma and the coronary arteriovenous potassium difference also depend, among other factors, on the coronary blood flow per time unit. The quantitative importance of the Thebesian veins is also difficult to estimate.

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