Electrophysiological changes of Papillary Muscles in Guinea Pigs with iron deficiency anemia and heart failure

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ABSTRACT

Objective: To investigate the changes of left ventricular papillary muscle action potentials in guinea pigs with iron deficiency anemia and heart failure. Methods: A total of 20 cases of iron deficiency anemia with heart failure were treated with experimental group and 10 normal guinea pigs as control group. Blood samples were collected to determine hemoglobin content, red blood cell number and whole blood iron index, and the changes of cardiac function and hemodynamics were detected by 6 240 biological signal collection system to determine whether the model was successful or not. Intracellular microelectrode technique was used to determine the action potentials of the papillary muscles in the model group and the control group. The potential amplitudes (APA), overshoot values (APA), maximum depolarization rate (Vmax), 20 % of repolarization, 50 % and 90 % of repolarization (APD50, APD90 and APD90) and the average velocity of repolarization were measured. Compare statistical difference between the model group and the control group. Results: 14 cases of model group survived completely, compared with control group, APD50 and APD90 prolonged, and the average velocity decreased. Conclusions: the action potential repolarization duration in the guinea pig papillary muscle of iron deficiency anemia with heart failure is prolonged, and the average repolarization velocity is slow.

1. Introduction

In the clinic, anemia and heart failure is a common disease, but the electrophysiological effects of anemia and heart failure in the papillary muscle not reported so far, we pre established successfully with heart failure model in guinea pig iron deficiency anemia, in order to explore the effects of anemia and heart failure papillary muscles, the experimental design.

2. Objects and Methods

2.1 Experimental subjects

30 guinea pigs, both male and female, weighing 350-450 g, were provided by the experimental animal center of Hebei North University. During the experiment, the daily illumination time was controlled for 12 h, the temperature of the feeding environment was 22-25 °C, and the room was ventilated and dry.

2.2 Methods

2.2.1 Grouping

Healthy guinea pigs were randomly divided into two groups, a group of 20, the experimental group (iron deficiency anemia complicated with heart failure group): feeding a low iron diet, iron...
containing about 11.7 mg/kg, drinking deionized water[4]; 1 mg/ (kg-d) was injected subcutaneously with isoproterenol for 2 weeks, after 2 weeks increase the dosage to 2 mg/ (kg-d) gradually, the total treatment time was 6 weeks[5]. Another group of 10 was the control group: feeding iron rich feed, iron content of about 144 mg/kg, drinking tap water; daily subcutaneous injection and experimental group dosage of physiological saline, the time is consistent with the experimental group.

2.2.2 The indexes of anemia and cardiac function were measured

After 6 weeks of feeding on guinea pig right common carotid artery intubation survival, determined by RM6240 biological signal acquisition system: heart rate (HR), blood pressure (BP), left ventricular systolic pressure (LVSP), left ventricular diastolic pressure (LVEDP), left ventricular end diastolic pressure (LVDP), left ventricular systolic maximum velocity (+dp/dtmax) and left ventricular diastolic maximum rate (-dp/dtmax). After hemodynamic measurement, the carotid artery was bled 1ml, the concentration of hemoglobin, the number of red blood cells and the iron index of whole blood were measured. Hemoglobin concentration was determined by cyanide high iron method. The number of erythrocytes was counted by the red cell count plate and counted by the low power microscope. The iron index of whole blood was determined by atomic absorption spectrometry.

2.2.3 Preparation of papillary muscle specimen and its potential guidance

After cardiac function and carotid artery blood collection were taken out, the heart was removed quickly, and the papillary muscle was removed and placed in O₂ saturated modified Locke solution (NaCl 0.157 mol/L, KCl 0.56×10⁻² mol/L, CaCl₂ 21×10⁻⁵ mol/ L, NaHCO₃ 18×10⁻³ mol/L, Glucose 0.56×10⁻² mol/L). Specimen preparation see literature[6]. The prepared specimens with stainless steel needle is fixed in the groove on the filling of silicone rubber, with (36±0.5) °C modified Locke solution of constant temperature, constant speed c perfusion, the flow rate is 5 mL/min, with continuous filling of pure O₂ fluid, pH 7.4. The action potential of ventricular myocytes was recorded by standard glass microelectrode and intracellular guidance technique. The glass microelectrode is filled with saturated KCl electrode liquid, and the DC resistance is 10-20 M. The guiding electrode was inserted into the ventricular myocytes of the specimens, and the stimulating electrodes were placed on the myocardium of the specimens, giving square wave stimulation of wave width, 2 ms, 1 Hz, and two times the threshold intensity (YC-2 stimulator, Chengdu instrument factory). The action potential by SWF-1B type microelectrode amplifier (Chengdu instrument factory) amplified by RM6280C multi-channel physiological signal acquisition system (Chengdu instrument factory) computer input, automatic display signals, and analyze the parameters of action potential.

2.3. Statistical methods

Software SPSS version 17.0 was used for statistically analysis. Mean ± SD was used to express the measurement data. Software SPSS version 16.0 was used to carry out the test of homogeneity of variances. Data of homogeneity of variance (P>0.10) in multiple groups were compared using One-way ANOVA, and student’s t-test was used for the comparison of two groups. P<0.05 was considered statistically significant.

3. Results

3.1. Changes of cardiac function and hemodynamic indexes

Compared with the control group, the BP of the model group decreased significantly (P<0.01), the absolute values of LVSP, LVDP, and +dp/dtmax and -dp/dtmax decreased significantly (P<0.01) and LVEDP increased significantly (Table 1) (P<0.01).

3.2 Comparison of blood anemia indexes between two groups of guinea pigs

The hemoglobin content, red blood cell count and serum iron content in the model group were smaller than those in the control group (Table 2) (P<0.01).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>The hemoglobin content (g/L)</th>
<th>red blood cell count (×10¹²/L)</th>
<th>Fe (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>10</td>
<td>146.2±15.37</td>
<td>6.19±0.53</td>
<td>451.38±51.87</td>
</tr>
<tr>
<td>Model group</td>
<td>14</td>
<td>85.13±18.55</td>
<td>4.15±0.82</td>
<td>367.41±54.63</td>
</tr>
</tbody>
</table>

Values were expressed by mean ± SD. Compared with control group, *: P < 0.05; **: P < 0.01.

Table 1.

Comparison of cardiac function indexes between two groups of guinea pigs.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>HR (time/min)</th>
<th>BP (mmHg)</th>
<th>LVSP (mmHg)</th>
<th>LVDP (mmHg)</th>
<th>LVEDP (mmHg)</th>
<th>+dp/dtmax (mmHg)</th>
<th>-dp/dtmax (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>control group</td>
<td>10</td>
<td>243.2±22.6</td>
<td>51.34±6.68</td>
<td>66.39±6.21</td>
<td>-5.28±1.51</td>
<td>1.12±0.81</td>
<td>2.986.74±493.72</td>
<td>-2.957.87±511.96</td>
</tr>
<tr>
<td>model group</td>
<td>14</td>
<td>231.3±38.7</td>
<td>40.49±6.76</td>
<td>52.57±6.81</td>
<td>-2.16±1.76</td>
<td>5.48±1.51</td>
<td>1.881.23±413.51</td>
<td>-1.868.19±403.75</td>
</tr>
</tbody>
</table>

Values were expressed by mean ± SD. Compared with control group, *: P < 0.05; **: P < 0.01.
3.3 Comparison of action potential indices between two groups of guinea pig papillary muscles

Compared with the control group, the APD\(_{50}\) and APD\(_{90}\) of the model group were significantly prolonged (\(P<0.01\)), and the mean speed of repolarization decreased significantly (Table 3) (\(P<0.01\)).

### Table 3.

<table>
<thead>
<tr>
<th>Groups</th>
<th>APA(mV)</th>
<th>RP(mV)</th>
<th>OS(mV)</th>
<th>APD(_{20})(ms)</th>
<th>APD(_{50})(ms)</th>
<th>APD(_{90})(ms)</th>
<th>Vmax(V/s)</th>
<th>the mean speed of repolarization (mV/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>119.76±3.53</td>
<td>88.71±3.69</td>
<td>31.05±1.18</td>
<td>121.98±6.77</td>
<td>216.82±5.13</td>
<td>245.63±7.12</td>
<td>218.63±5.68</td>
<td>340.83±14.75</td>
</tr>
<tr>
<td>model</td>
<td>118.23±3.38</td>
<td>88.02±3.97</td>
<td>30.19±1.05</td>
<td>124.81±9.36</td>
<td>231.7±5.89 *</td>
<td>270.91±8.08 *</td>
<td>217.71±6.37</td>
<td>280.06±13.91 *</td>
</tr>
</tbody>
</table>

Values were expressed by mean ± SD. Compared with control group, \(*: P<0.05; \*: P<0.01\).

4. Discussion

In the clinic, chronic anemia can lead to chronic heart failure, and chronic heart failure is often associated with anemia. In order to make a detailed study of the disease, we successfully established a model of iron deficiency anemia combined with heart failure in guinea pigs.

This study used a low iron diet and deionized water for guinea pigs after 6 weeks, the survival of 14 guinea pigs in the model group with slow growth and weight loss; ear, claws are evident pale; dull coat, yellow; response to stimulation is poor, poor activity, love huddled down; red blood, protein content of guinea pig red blood cell count and the content of serum iron were less than the control group; BP decreased significantly, the difference was statistically significant; the absolute value of LVSP, LVDP, \(+dp/dt\text{max}\), and \(-dp/dt\text{max}\) were significantly decreased, LVEDP increased significantly, the difference was statistically significant; the above symptoms, signs and auxiliary examination showed that the guinea pig model group appeared anemia and heart failure.

We measured the model group and the control group, and plasma of guinea pig papillary muscle action potential, found that the model group compared with control group, APD\(_{50}\) and APD\(_{90}\) were significantly prolonged (\(P<0.01\)), the average speed of repolarization decreased significantly (\(P<0.01\)), and the mechanism may be due to an increase of outward K\(^{+}\) currents and(or) decrease of inward L-Ca\(^{2+}\) current during repolarization. When the anemia associated with heart failure after neurohumor complex, When the anemia associated with heart failure after neurohumor complex, resulting in ion channel function disorder, for example, lead to hERG/IKr channel dysfunction\([7]\), myocardial cell repolarization delay. Because of the prolongation of myocardial repolarization duration, it is easy to have arrhythmia when anemia is combined with heart failure\([8]\).

Through our research showed that the anemia heart failure associated with electrophysiological properties of myocardial cells appeared abnormal, which might be one of the mechanisms to arrhythmia, its detailed mechanism needs further experimental design to study.

### Reference


