Effect of dopamine combined with dobutamine on target organ function indicators and molecular indicators in children with renal damage after neonatal asphyxia

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Abstract

Objective: To analyze the effect of dopamine combined with dobutamine on target organ function indicators and molecular indicators in children with renal damage after neonatal asphyxia. Methods: A total of 40 cases of children with renal damage after neonatal asphyxia were randomly divided into observation group and control group, control group received conventional therapy, observation group received conventional therapy + dopamine + dobutamine therapy, and then differences in levels of renal blood flow parameters, urine trace proteins and serum renal function-related parameters were compared between two groups after the treatment. Results: Vmax, Vmin and TAMX levels of observation group after treatment were higher than those of control group while RI and PI values were lower than those of control group; urine α1-MG, Alb, RBP, IgG and TRF levels were lower than those of control group; serum BUN, Cr, ET-1 and Cystatin C levels were lower than those of control group. Conclusion: Dopamine combined with dobutamine is a reliable way to treat renal damage after neonatal asphyxia, and plays a positive role in the optimizing renal blood flow and renal function.

1. Introduction

Neonatal asphyxia trends to occur in premature infants, and the systemic blood flow is redistributed after asphyxia to mainly secure blood supply to the heart, liver and other important organs, leading to relatively reduced renal blood flow and renal tissue ischemia hypoxia and dysfunction[1]. The incidence rate of renal damage after neonatal asphyxia is above 50%, and early detection and positive intervention is the most reliable method to reverse renal function reduction and avoid permanent renal damage[2]. Dopamine can act on the kidneys and dilate renal blood vessels and increase renal blood flow; dobutamine can excite heart β2 receptor, has directly positive inotropic effect, will not increase the oxygen consumption, and can increase systemic blood supply. In the study, dopamine and dobutamine were used together in the treatment of children with renal damage after neonatal asphyxia, and the changes in levels of renal blood flow parameters and renal function-related indexes in blood and urine were mainly stated.

2. Information and methods

2.1. General information

A total of 40 cases of children with renal damage after neonatal asphyxia treated in our hospital from August 2012 to August 2015 were divided into observation group and control group (n=20) according to random number table. Control group included 11 male cases and 9 female cases, the gestational age was 35-39 weeks, the average was (38.12±1.34) weeks, the birth weight was 2.21-3.35 kg and the average was (2.78±0.41) kg; observation included 10 male cases and 10 female cases, the gestational age was 34-39 weeks, the average was (38.09±1.41) weeks, the birth weight was 2.26-
3.24 kg and the average was (2.72±0.45) kg. The two groups were not statistically different in the distribution of gender, gestational age and birth weight (P>0.05) and could be subsequently compared.

2.2. Treatment methods

Control group received conventional therapy, including oxygen uptake, correcting water and electrolyte balance, diuresis, nutritional support, etc. Based on conventional treatment, observation group received dopamine combined with dobutamine treatment, specifically as follows: dopamine hydrochloride injection (10 mg/mL Guilin Pharmaceutical Co., LTD., approved by H45020091), initial dose 5 μg/(kg•min) was dissolved in 20 mL 5% glucose liquid, continuously infused by micro-pump and could be increased to 20 μg/(kg•min) according to the conditions; dobutamine hydrochloride injection (10 mg/mL, Chengdu List Pharmaceutical Co., LTD., approved by H20058536), initial dose 2.5 μg/(kg•min) was dissolved in 20 mL 5% glucose liquid, continuously infused by micro-pump and could be increased to 10 μg/(kg•min) according to the conditions. The treatment was conducted 1 time a day for consecutive 7 d.

2.3. Observation indexes

2.3.1. Renal blood flow

7 d after treatment, color Doppler ultrasound was used to detect the state of renal blood flow of two groups of children, the children took lateral position in a quiet condition and aligned the renal artery through the lateral waist and renal coronary section, the angle between beam and blood flow was <60°, and bilateral renal arterial peak systolic velocity (Vmax), end-diastolic velocity (Vmin), mean velocity (TAMX), resistance index (RI) and pulsatility index (PI) were detected.

2.3.2. Urine trace proteins

7 d after treatment, fresh urine of two groups was collected, biological automatic analyzer was used to determine the absorbance change and calculate the levels of urine α1-microglobulin (α1-MG), microalbumin (Alb), retinol-binding protein (RBP), immunoglobulin (IgG), transferrin (TRF) and so on.

2.3.3. Serum renal function–related parameters

7 d after treatment, peripheral venous blood was extracted from two groups, let stand and then centrifuged to get supernatant, and radioimmunoassay was used to determine blood urea nitrogen (BUN), creatinine (Cr), endothelin (ET-1), cystatin-2 (Cystatin C) levels in it.

2.4. Statistical methods

Obtained data was input in SPSS 21.0 for analysis and processing, measurement data was in terms of average ± standard deviation (Mean ± SD), comparison between two groups was by t test, and P<0.05 was the standard of statistical significance in differences.

3. Results

3.1. Renal blood flow parameter values

The most intuitive manifestation of renal damage after neonatal asphyxia is the change of renal blood flow and flow velocity, color Doppler ultrasound was used in the study to detect the values of bilateral renal arterial peak systolic velocity (Vmax), end-diastolic velocity (Vmin), mean velocity (TAMX), resistance index (RI) and pulsatility index (PI) and other renal blood flow parameters of two groups 7 days after treatment, and the specific results were as follows: Vmax, Vmin and TAMX levels of observation group after treatment were higher than those of control group while RI and PI values were lower than those of control group (P<0.05), shown in Table 1.

3.2. Urine trace proteins

Neonatal kidney damage can be directly reflected in the change of related protein levels in the urine, biological automatic analyzer was used in the study to determine the levels of 1-MG, Alb, RBP, IgG, TRF and other trace proteins in urine of two groups 7 days after treatment, and the specific results were as follows: urine 1-MG, Alb, RBP, IgG and TRF levels of observation group after treatment were lower than those of control group (P<0.05), shown in Table 2.

3.3. Serum renal function–related parameters

Serum levels of renal function-related parameters undergo a

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Vmax (cm/s)</th>
<th>Vmin (cm/s)</th>
<th>TAMX (cm/s)</th>
<th>RI</th>
<th>PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>20</td>
<td>0.32±0.04</td>
<td>0.08±0.01</td>
<td>0.19±0.02</td>
<td>0.62±0.07</td>
<td>1.07±0.14</td>
</tr>
<tr>
<td>Control</td>
<td>20</td>
<td>0.26±0.03</td>
<td>0.05±0.01</td>
<td>0.11±0.01</td>
<td>0.78±0.09</td>
<td>1.53±0.17</td>
</tr>
<tr>
<td>t</td>
<td></td>
<td>5.383</td>
<td>5.293</td>
<td>6.281</td>
<td>5.483</td>
<td>6.495</td>
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<tr>
<td>p</td>
<td></td>
<td>&lt;0.05</td>
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</tbody>
</table>
series of changes in children with renal damage after neonatal asphyxia, and they are the objective indexes for disease treatment effect, peripheral blood serum was obtained from two groups after treatment in the study, radioimmunoassay was used to determine the levels of BUN, Cr, ET-1, Cystatin C and other illness-related molecules, and the specific results were as follows: serum BUN, Cr, ET-1 and Cystatin C levels of observation group after treatment were lower than those of control group (P<0.05), shown in Table 3.

4. Discussion

Multiple organ dysfunctions may occur after neonatal asphyxia, renal damage accounts for more than 50%, the great difficulty in the neonatal urine testing causes that the significant clinical manifestation of oliguria is easily ignored, and the vast majority of non-oliguria renal dysfunction is more difficult to be early diagnosed[3,4]. Blood flow redistribution and renal vasoconstriction after neonatal asphyxia lead to sharp decline of kidney blood flow, and it is the core cause of renal function injury in children. Renal damage is reversible in early stage of the disease, and without timely treatment, it will lead to permanent glomerular and renal tubular damage, and even acute renal failure[5,6]. Oxygen uptake, water and electrolyte balance adjustment, nutrition support and so on are by far the most commonly used methods in treatment of renal damage after neonatal asphyxia, but they are not kidney-targeted, and have limited effect on restoring the renal blood flow and optimizing the renal function. How to effectively alleviate the severity of renal damage after neonatal asphyxia and save the children’s renal function is the key of the clinical research, the foreign studies have reported that dopamine and dobutamine play a positive role in the improvement of kidney function[8]. Dobutamine is dopamine homologue, direct acts on cardiac β1 receptor and exerts positive inotropic effect, increases the stroke volume without increasing myocardial oxygen consumption, and helps to guarantee blood supply of important viscera in children with neonatal asphyxia[9,10]. In the study, dopamine and dobutamine were used together in the treatment of children with renal damage after neonatal asphyxia and expected to achieve the effect of increasing heart stroke, reducing circulation resistance and increasing renal blood flow, and the analysis of their specific therapeutic effect was further elaborated in the following paragraphs.

Renal blood flow parameters are the most reliable and intuitive indicators to reflect the degree of renal damage after neonatal asphyxia, drug treatment efficacy and so on, and color Doppler ultrasound is the gold standard for dynamic observation of blood flow, blood flow resistance and so on[11]. In the study, color Doppler ultrasound was applied to determine renal blood flow parameters in children after treatment, and it was found that Vmax, Vmin and TAMX levels of observation group after treatment were higher while RI and PI values were lower. Renal arterial peak systolic velocity (Vmax), end-diastolic velocity (Vmin) and mean velocity (TAMX) reflect the renal blood flow, resistance index (RI) and pulsatility index (PI) reflect the renal vascular resistance, the study results showed that after dopamine combined with dobutamine treatment, renal blood flow of observation group increased and renal vascular resistance decreased, which was consistent with the pharmacological characteristics of drugs, and also suggested that the compatible drug application did improve the state of renal blood flow, and was the

| Table 2.  
<p>| Urine trace protein levels after treatment. |</p>
<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>1-MG (mg/L)</th>
<th>Alb (mg/L)</th>
<th>RBP (μg/L)</th>
<th>IgG (mg/L)</th>
<th>TRF (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>20</td>
<td>12.46±1.75</td>
<td>10.27±1.32</td>
<td>189.73±20.41</td>
<td>7.28±0.81</td>
<td>3.17±0.42</td>
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<tr>
<td>Control</td>
<td>20</td>
<td>25.81±3.09</td>
<td>14.86±1.76</td>
<td>279.66±31.42</td>
<td>15.62±1.93</td>
<td>7.81±0.85</td>
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<td>t</td>
<td>&lt;0.05</td>
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<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
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</tbody>
</table>

| Table 3.  
<p>| Serum renal function-related parameter values after treatment. |</p>
<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>BUN (mmol/L)</th>
<th>Cr (μmol/L)</th>
<th>ET-1 (mg/L)</th>
<th>Cystatin C (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>20</td>
<td>5.83±0.62</td>
<td>67.38±7.12</td>
<td>50.37±5.83</td>
<td>0.54±0.06</td>
</tr>
<tr>
<td>Control</td>
<td>20</td>
<td>7.61±0.85</td>
<td>95.47±10.21</td>
<td>64.29±7.01</td>
<td>1.03±0.12</td>
</tr>
<tr>
<td>t</td>
<td>8.394</td>
<td>11.283</td>
<td>8.394</td>
<td>5.382</td>
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</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
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</tr>
</tbody>
</table>
foundation of further optimization of renal function[12].

A series of protein components can be detected in the urine of children with renal damage after neonatal asphyxia, which is mainly because that glomerular filtration and reabsorption dysfunction after asphyxia ischemia anoxia lead to glomerular cell degeneration necrosis and the increase of filtration membrane permeability, and the middle- and high-molecular-weight proteins pass through the filtration membrane and are detected in the urine[13,14]. Urine 1-microglobulin (1-MG), microalbumin (Alb), retinol-binding protein (RBP), immunoglobulin (IgG) and transferrin (TRF) are the clinical more concerned protein molecules closely associated with renal function, and the study results showed that urine 1-MG, Alb, RBP, IgG and TRF levels of observation group were lower after treatment. 1-MG is renal tubular marker protein that can represent renal tubular damage; TRF carries less negative ionic charge, more easily passes through glomerular filtration membrane, and therefore, is a sensitive protein molecule of kidney damage; Alb, RBP and IgG have bigger molecular weight, and can be detected in the urine in the case of severe renal damage[15]. The study results indicated that after dopamine combine with dobutamine therapy, renal tubular and glomerular function were repaired in children with renal damage after neonatal asphyxia. Further detection of serum kidney function indicators showed that serum BUN, Cr, ET-1 and Cystatin C levels of observation group were lower after treatment, which further confirmed the role of dopamine combined with dobutamine in optimizing the renal function in children.

To sum up, it can confirm that dopamine combined with dobutamine is a reliable way to treat renal damage after neonatal asphyxia, and can be widely used in clinical practice in the future in order to increase renal blood flow and optimize renal function.

References


