Effect of nifedipine combined with Magnesium Sulfate on oxidative stress, hemorheology, platelet active substances and renal function in patients with pregnancy-induced hypertension

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ABSTRACT

Objective: To investigate effect of nifedipine combined with Magnesium Sulfate on levels of oxidative stress, blood rheology, platelet active substance and renal function in patients with pregnancy-induced hypertension. Methods: A total of 99 cases of patients with pregnancy-induced hypertension were selected as the study object, according to random data table, they were divided into control group (n=50) and observation group (n=49), patients in control group were treated with Magnesium Sulfate, while patients in the observation group received Magnesium Sulfate combined with nifedipine treatment, levels of blood pressure and oxidative stress, blood rheology, platelet activity and renal function index before and after treatment of both groups were compared. Results: There were no significant difference of the level of DBP, SBP, TAc, MDA, SOD, high/low shear blood viscosity, PV, HCT, CD62P, CD63, GP IIb/IIIa, SCr and BUN before treatment between control group and the observation group. Compared with intragroup before treatment, the levels of DBP, SBP, MDA, high/low shear blood viscosity, PV, HCT, CD62P, CD63, GP IIb/IIIa, SCr and BUN after treatment of the two groups were significantly decreased, and the levels of the observation group after treatment was significantly lower than those in the control group, the difference was statistically significant; Compared with level of SOD and TAc, after treatment, the levels of SOD and TAc of the two groups were significantly higher than those in the same group before treatment, and levels of the observation group was significantly higher than in the control group, the difference was statistically significant. Conclusion: Nifedipine combined with magnesium sulfate treatment of pregnancy-induced hypertension, which can effectively reduce the blood pressure level of patients, improve the levels of oxidative stress, blood rheology and platelet active substance, protect renal function, with an important clinical value.

1. Introduction

As special complication of female during pregnancy, pregnancy-induced hypertension was one of main reasons of pregnant women and perinatal infants death[1]. Most of clinical manifestations of pregnancy-induced hypertension were hypertension, proteinuria, edema, abnormal blood rheology and hyperactive state of platelet, in addition, related research pointed that there usually appeared different degree of oxidation and anti-oxidation unbalance in patients, which was harmful to fetus[2−4]. Anti-hypertensive drug therapy could improve results of pregnancy, with critical value for decreasing cesarean section rate and death rate of maternal and child[5]. This research analyzed from oxidative stress, blood rheology, platelet active substance and renal function, in order to define the efficacy of combined therapy by nifedipine and magnesium sulfate.
2. Material and method

2.1. General data

A total of 99 cases of patients with pregnancy-induced hypertension were selected as research subjects, all being pregnant women admitted in our hospital from December 2015 to July 2017 who were confirmed to related diagnostic criteria of pregnancy-induced hypertension[6]. All of them was single birth, primipara. Divided them into control group (n=50) and observation group (n=49) according to random data table. In control group aged from 26-35 years old, average gestational weeks (33.65±1.84) weeks; In observation group aged from 25-34 years old, average gestational weeks (34.06±1.77) weeks. Exclusion: (1) multiple pregnancy; (2) allergic constitution, taboos about research drug; (3) with history of hypertension or took anti-hypertension drug orally in recent; (4) combined with diabetes, coagulation dysfunction, cardiopulmonary and hepatic and renal dysfunction; (5) chronic nephritis, patients with active stage; (6) bad compliance, incomplete clinical data and did not accept treatment. Age, gestational weeks and other data in both groups were no difference (P>0.05), it was comparable. Research was accorded with related criteria of ethics committee.

2.2 Treatment method

Both groups were given conventional treatment, including: limited movement, proper left lateral position, strictly control diets, sufficiently supplement calcium (at least 1 g/d), in order to reduce risk of preeclampsia. On this basis, control group was given magnesium sulfate (Zigong Honghe pharmaceutical Co. Ltd, approved number: H51021263, specification: 500 g/bag), method: added 20 mL 25% magnesium sulfate solution in 20 mL 10% glucose solution, mixed evenly, intravenous drip was less than 0.5 h, then added 60 mL 25% magnesium sulfate solution in 100 mL 5% glucose solution, maintained speed of intravenous drip at 2 g/h, regulated speed according to actual blood tension, 1 time/d. Observation group took nifedipine orally on the base of control group (Guangdong South China pharmaceutical Co. Ltd, lot number: 201708108, specification: 10 mg×100 s), generally starting dosage was 10 mg/time, 3 times/d, maintained dosage at 10-20 mg/time, 3 times/d, both groups were treated for 5 d. In process of treatment, payed attention to vital sign of patients and prevented poisoning.

2.3 Observation indexes

Compared diastolic blood pressure (DBP) and systolic blood pressure (SBP) level in both groups before and after treatment. Extracted fasting periphery venous blood of patients before and after treatment of 5 d, part of blood deal with water bath and following by centrifuge, collected supernatant for detection. (1) Observation of oxidative stress level: Total anti-oxidant capacity (TAc), serum malondialdehyde (MDA), superoxide dismutase (SOD), measurement method was ELISA, respectively detected by TAc kits, MDA ELISA kits and SOD ELISA kits, they were purchased from Shanghai Meilian biotechnology Co., Ltd. (2) blood rheology indexes: whole blood hypshear viscosity, whole blood hypershear viscosity, plasma viscosity (PV) and hematokrit (HCT), full Auto-hemorheological analyzers was used to detection; (3) platelet active substance: platelet granule membrane glycoprotein (CD62P,CD63) and platelet glycoprotein (GP IIb/IIIa), detected by platelet functional analyzer; (4) renal function: Serum creatinine (Scr) and urea nitrogen, adopted full automatic biochemical analyzer. Operation was strict with kits introduction.

3. Results

3.1. Comparison of DBP and SBP level of both groups

There was no difference in DBP and SBP level of both groups before and after treatment (P>0.05). After treatment, DBP and SBP level in observation group respectively were (77.82±8.93) mmHg and (125.29±11.69) mmHg, compared with intragroup before treatment, both level decreased obviously (P<0.05), moreover which was lower dramatically than control group after treatment [(91.26±10.03) mmHg and (141.72±11.85) mmHg], the difference was statistically significant (P<0.05). As shown in Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment</th>
<th>DBP (mmHg)</th>
<th>SBP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>50</td>
<td>Before treatment</td>
<td>105.28±12.41</td>
<td>159.97±18.18</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>91.26±10.03</td>
<td>141.72±11.85</td>
</tr>
<tr>
<td>Observation group</td>
<td>49</td>
<td>Before treatment</td>
<td>105.24±13.25</td>
<td>160.77±19.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>77.82±8.93</td>
<td>125.29±11.69</td>
</tr>
</tbody>
</table>

Note: compared with before treatment, #P<0.05, compared with after treatment, *P<0.05.
3.2 Comparison of oxidative stress of both groups

Before treatment, there was difference in TAc, MDA, SOD level (P<0.05). After treatment, TAc and SOD level in control group were (9.65±1.54) μmol/L and (83.06±6.56) μmol/L, which was higher than intragroup before treatment (P<0.05); both level in observation group were (12.03±1.63) μmol/L and (94.49±7.27) μmol/L, higher obviously than intragroup before treatment, moreover dramatically higher than control group after treatment, the difference was statistically significant (P<0.05). MDA level of both groups after treatment was significantly decreased compared with before treatment, MDA level after treatment of both groups were decreased, moreover observation group [(22.49±2.36) μmol/L] was lower than control group [(23.61±2.72) μmol/L], the difference was statistically significant (P<0.05). As shown in Table 2.

Table 2. Comparison of oxidative stress of both groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment time</th>
<th>DBP (mmHg)</th>
<th>SBP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>50</td>
<td>Before treatment</td>
<td>105.28±12.41</td>
<td>159.97±18.18</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>91.26±10.03</td>
<td>141.72±11.85</td>
</tr>
<tr>
<td>Observation group</td>
<td>49</td>
<td>Before treatment</td>
<td>105.24±13.25</td>
<td>160.77±19.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>77.82±8.93</td>
<td>125.29±11.69</td>
</tr>
</tbody>
</table>

Note: compared with before treatment, *P<0.05, compared with after treatment, "P<0.05.

3.3 Comparison of hemorheology indexes of both group

There was no difference in whole blood hypershear/hyposhear viscosity, plasma viscosity (PV) and hematokrit (HCT) (P>0.05). Compared with before treatment, whole blood hypershear/hyposhear viscosity, plasma viscosity (PV) and hematokrit (HCT) were lower significantly than before treatment intragroup (P<0.05), moreover these level in observation group were [(4.58±0.54) mPa • s, (13.67±1.76) mPa • s, (1.55±0.31) mPa • s and (37.21±1.85)%], which was lower than control group [(5.73±0.71) mPa • s, (16.08±1.65) mPa • s, (1.95±0.33) mPa • s and (42.21±2.02)%], difference was significant (P<0.05). As shown in Table 3.

Table 3. Comparison of hemorheology indexes of both group.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment time</th>
<th>Whole blood hypershear viscosity (mPa • s)</th>
<th>Whole blood hyposhear viscosity (mPa • s)</th>
<th>PV (mPa • s)</th>
<th>HCT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>50</td>
<td>Before treatment</td>
<td>6.52±0.82</td>
<td>19.16±2.34</td>
<td>2.65±0.53</td>
<td>47.74±3.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>5.73±0.71</td>
<td>16.08±1.65</td>
<td>1.95±0.33</td>
<td>42.21±2.02</td>
</tr>
<tr>
<td>Observation group</td>
<td>49</td>
<td>Before treatment</td>
<td>6.48±0.79</td>
<td>19.13±2.33</td>
<td>2.61±0.48</td>
<td>46.33±3.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>4.58±0.54</td>
<td>13.67±1.76</td>
<td>1.55±0.31</td>
<td>37.21±1.85</td>
</tr>
</tbody>
</table>

Note: compared with before treatment, *P<0.05, compared with after treatment, "P<0.05.

3.4 Comparison of platelet active substance of both groups

Before treatment, there was no difference in CD62P, CD63 and GP II b/IIIa level of both groups (P>0.05). These three level of both groups after treatment was lower than intragroup before treatment, moreover CD62P, CD63 and GP II b/IIIa level in observation group after treatment were respectively [(2.32±0.71)%, (4.06±0.95)%, (3.41±1.05)%, which was obviously lower than control group [(3.84±0.81)%, (5.51±1.07)%, (4.98±1.32)%], difference was significant (P<0.05). As shown in Table 4.

Table 4. Comparison of platelet active substance of both groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment time</th>
<th>CD62P (%)</th>
<th>CD63 (%)</th>
<th>GP II b/IIIa (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>50</td>
<td>Before treatment</td>
<td>5.56±0.92</td>
<td>8.69±1.23</td>
<td>8.72±1.45</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>3.84±0.81</td>
<td>5.51±1.07</td>
<td>4.98±1.32</td>
</tr>
<tr>
<td>Observation group</td>
<td>49</td>
<td>Before treatment</td>
<td>5.61±1.93</td>
<td>8.72±1.24</td>
<td>8.71±1.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>2.32±0.71</td>
<td>4.06±0.95</td>
<td>3.41±1.05</td>
</tr>
</tbody>
</table>

Note: compared with before treatment, *P<0.05, compared with after treatment, "P<0.05.

3.5 Comparison of renal function indexes of both groups

There was no difference in SCr and BUN level of both groups (P>0.05). After treatment, SCr and BUN level in control and observation group were respectively (83.72±11.57) μmol/L, (72.93±12.42) μmol/L and (5.01±1.09) mmol/L, which was lower than intragroup before treatment (P<0.05), SCr and BUN level in observation group were obviously lower than control group, the difference was significant (P<0.05). As shown in Table 5.

Table 5. Comparison of renal function indexes of both groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment time</th>
<th>SCr (μmol/L)</th>
<th>BUN (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>50</td>
<td>Before treatment</td>
<td>94.96±12.68</td>
<td>7.67±1.22</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>83.72±11.57</td>
<td>5.75±1.16</td>
</tr>
<tr>
<td>Observation group</td>
<td>49</td>
<td>Before treatment</td>
<td>95.41±17.86</td>
<td>7.69±1.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>72.93±12.42</td>
<td>5.01±1.09</td>
</tr>
</tbody>
</table>

Note: compared with before treatment, *P<0.05, compared with after treatment, "P<0.05.
4. Discussion

According to incomplete statistics, in our country the occurrence rate of pregnancy-induced hypertension was 9.4%–10.4%, increased year by year, severely threatened health of maternal and perinatal. Hypertension of pregnancy mainly included prepregnancy hypertension, pregnancy-induced hypertension, gestational hypertension combined with proteinuria. This pathogenesis was still not clear, at present it was commonly thought that its occurrence was related with the uterine placenta ischemic, lack of vasopressin, autoimmune factors, mental state and inherit factors. Magnesium sulfate was common drug for treating pregnancy-induced hypertension in clinic, research pointed out that magnesium sulfate could expand blood vessel and lower blood pressure, prevent and reduce systemic arteriospasm, improved organ blood supply, recover organ function, improve general circulation. However, pure treatment might cause adverse effect on part of patients, its efficacy needed to be enhanced. Nifedipine was general drug for anti-hypertension, belonged to the first generation of calcium antagonists, its efficacy was sufficiently approved. It could inhibit tissue and cell excitation contraction couplings through selective inhibition of calcium channel, protect myocardial cell, expand blood vessel and improve microcirculation. Research demonstrated that regulated ability of nifedipine combined with magnesium sulfate was higher than pure magnesium sulfate treatment, results were accorded with previous report, further demonstrated the anti-pressure function of both drugs. This research was aimed to explore efficacy of both medicine on pregnancy-induced hypertension from biochemical indexes.

A lot of researches there was unbalance of oxidation and anti-oxidation commonly in patients with pregnancy-induced hypertension, clinical manifestation was low TAc and SOD level, MDA level increased, it showed that elimination ability of placental oxygen free radical was decreased, this state severely affected blood supply of fetus. Detection of TAc, SOD, MDA level was important to evaluate oxidative stress condition and prognosis of disease. This research result found that combined with nifedipine, TAc and SOD level of patients increased and MDA level decreased obviously, its effect was superior to control group, revealing that combined therapy could effectively improve oxidative stress level, whereas its reason was still further investigated.

Pregnancy-induced hypertension was closely related to systematic arteriospasm, blood viscosity increasing, insufficient blood supply often resulted in injury of heart, kidney and liver. Systematic arteriospasm was basic lesion, its early clinical manifestation was hyperactivity of platelet, platelet active substance level (CD62P, CD63, GP IIb/IIIa) was largely increased. In addition, due to blood of patients always was high viscous state, affecting by other blood indexes, platelet active substance level would be fluctuated at some degree. There was significant relevance between change of platelet active substance level and abnormal hemorheology. This research showed that both therapies could improve hemorheology index, reduce platelet active substance level, research results further demonstrated that nifedipine and magnesium sulfate were able to inhibit platelet active function. Whereas combined therapy could improve hemorheology and platelet active substance level, this might be related to additive effect of both drugs that could further inhibit uterine contraction, lower blood pressure, improve microcirculation and platelet activation. Furthermore, this paper compared with renal function level of patients after treatment, found that combined therapy could protect renal function, results were conformed to previous report.

In conclusion, efficacy of nifedipine and magnesium sulfate was better than pure magnesium sulfate, combined therapy could further decrease blood pressure, effectively regulate oxidative stress, improve hemorheology and platelet activation, protect renal function, which could improve clinical sign and be in favor of recovery, with critical clinical significance.

Reference


