Effect of Dahuang Mudan Decoction to Supplement the Treatment of Acute Appendicitis and its Effect on Serum TNF-α level

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Abstract: Objective: To supplement Dahuang Mudan Decoction therapeutic formula in the surgical treatment of acute appendicitis, and to observe its effect on patients’ serum TNF-α levels. Methods: 60 patients with acute appendicitis who underwent laparoscopic appendectomy were divided into two groups (admitted in January-October 2023) by randomization grouping method; the control group was supplemented with conventional treatment, and the observation group was supplemented with Dahuang Mudan Decoction treatment. Comparison of traditional Chinese medicine (TCM) evidence points, postoperative gastrointestinal recovery, inflammatory factor levels, and postoperative complication problems were compared between the two groups. Results: After treatment, all TCM evidence points, inflammatory factor levels, and complication rates of the observation group were lower than those of the control group, and the recovery time of postoperative bowel sounds, the time of the first flatulence and defecation were shorter than those of the control group (P < 0.05). Conclusion: The effect of Dahuang Mudan Decoction plus a reduction in the adjuvant treatment of acute appendicitis is reliable, can actively reduce the serum TNF-α level, and promote faster and better recovery of patients.

Keywords: Acute appendicitis; Dahuang Mudan Decoction; TNF-α level

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1. Introduction

Appendicitis is a kind of acute abdominal disease with a very high incidence, mainly manifested by pain in the right lower abdomen, accompanied by fever, nausea and vomiting and other undesirable signs and symptoms, most appendicitis is due to bacterial infection, which can be seen as an abnormal blood supply to the lumen of the appendix, and requires proper treatment as soon as possible, otherwise, it may cause infectious shock, or secondary bacterial peritonitis [1], which may cause continuous harm to the body, and even threaten the life. Laparoscopic appendectomy is the main method of treating acute appendicitis, and it is often accompanied by anti-infective treatment with Western medicines after the operation, but complications may still occur after the operation, with varying degrees of recovery. Traditional Chinese medicine (TCM) has a deeper knowledge of
appendicitis, stating that appendicitis is caused by the accumulation of heat and poison in the body, which leads to intestinal carbuncle pus, and the stasis does not persist, which in turn obstructs intestinal operation. Disease then starts to occur, and in addition to surgical treatment, it is necessary to strengthen the detoxification and dissipation of toxins and activation of blood circulation and elimination of static blood, and so on. Dahuang Mudan Decoction belongs to traditional Chinese medicine prescription, many herbs play various effects, and acute appendicitis is mostly accompanied by an inflammatory reaction. This paper will analyze the effect of Dahuang Mudan Decoction to assist in the treatment of acute appendicitis, as well as the effect on the patient’s serum TNF-α level, where a total of 60 patients were included.

2. Information and methods

2.1. Data

60 patients suffering from acute appendicitis were screened as the subjects of this study (admission time: January–October 2023), and all of them were subjected to laparoscopic appendectomy and were divided into 30 cases of the control group and 30 cases of the observation group by randomized grouping method.

In the control group, there were 17 males and 13 females, with ages ranging from 22 to 58 (39.15 ± 7.14) years old, and onset times ranging from 12 to 68 (40.25 ± 10.13) hours. Seventeen of the cases had simple appendicitis, 10 had suppurative appendicitis, and 3 had perforated appendicitis.

Observation group: 18 males and 12 females, age 21-59 (39.27 ± 7.21) years old, onset time 10–69 (40.41 ± 10.29) hours, of which 16 cases were simple appendicitis, 10 cases were suppurative appendicitis, and 4 cases were perforated appendicitis.

The data of the two groups were statistically analyzed, and it was concluded that $P > 0.05$.

Inclusion criteria: (1) meeting the clinical diagnostic criteria of acute appendicitis, (2) belonging to the type of heat and toxicity, (3) first-time onset of disease, (4) no other intestinal diseases as well as serious medical and surgical diseases, (5) complete clinical data.

Exclusion criteria: (1) in special periods, such as pregnancy, breastfeeding, etc., (2) combined with mental illness or the existence of cognitive disorders, (3) the existence of immune dysfunction, coagulation dysfunction, (4) at the same time to participate in other medical research projects.

2.2. Methods

Both groups of patients with acute appendicitis received laparoscopic appendectomy, and the control group was treated with routine symptomatic therapy after surgery, including rehydration, fever reduction, etc., and anti-infection therapy with a mixture of metronidazole injection 250 mL and saline 250 ml under sedation, once a day for seven consecutive days.

The observation group was supplemented with Dahuang Mudan Decoction plus reduction therapy based on the treatment program of the control group. The basic formula included 6 g licorice, 10 g forsythia, 10 g mangosteen, 10 g peach kernel, 10 g honeysuckle, 15 g peony bark as well as 15 g rhubarb and 30 g Semen benincasae. Some additions can be made to the formula which includes 10 g frankincense, 10 g red peony and 10 g myrrh in patients with severe stasis symptoms and 10 g dandelion and 15 g Patrinia scabra in those with serious heat toxicity symptoms. Usage: Decoct 400 mL juice with water, divide into two parts, take one in the morning and one in the evening for seven consecutive days.

2.3. Observation indexes

(1) Compare the TCM symptom scores of the two groups. Including fever, poor appetite, nausea and
vomiting, abdominal pain, 0–3 points, the lower the score, the less severe the symptoms, the evaluation method refers to the “Colonoscopy Supplement with Traditional Chinese Medicine Treatment of Appendicitis Expert Consensus (2016 Edition)” [4].

(2) Comparison of postoperative gastrointestinal function recovery indicators. Including the recovery time of bowel sounds, as well as the time of the first flatulence emission and the time of defecation.

(3) Compare the level of inflammatory factors. Collect 3 mL of blood, obtain serum after centrifugation, and use enzyme-linked immunosorbent assay to detect TNF-α level, IL-8 level and CRP level.

(4) Comparison of postoperative complications. Possible complications include intestinal obstruction, lung infection, and incision infection.

2.4. Statistical methods
The data in the text were entered into statistical software to be analyzed (software version: SPSS25.0), and the formula of mean ± standard deviation (SD) was used to indicate the measurement data (conforming to normal distribution). [(n, %)] was used to indicate the count data, and independent samples t-test, χ² test, if the obtained P is below 0.05, it means that there is statistical significance between the comparison data.

3. Results
3.1. TCM evidence points
As shown in Table 1, the difference of each syndrome integral of the two groups of acute appendicitis patients before treatment was insignificant compared with that of the two groups, P > 0.05, after treatment, each syndrome integral of the two groups was reduced, but the magnitude of the reduction was greater in the observation group, for example, each syndrome integral of the observation group was lower than that of the control group after treatment, P < 0.05.

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases (n)</th>
<th>Fever Before treatment</th>
<th>Fever After treatment</th>
<th>Poor appetite Before treatment</th>
<th>Poor appetite After treatment</th>
<th>Nausea and vomiting Before treatment</th>
<th>Nausea and vomiting After treatment</th>
<th>Abdominal pain Before treatment</th>
<th>Abdominal pain After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>30</td>
<td>2.21 ± 0.30</td>
<td>0.95 ± 0.21</td>
<td>2.14 ± 0.51</td>
<td>0.99 ± 0.18</td>
<td>1.91 ± 0.24</td>
<td>0.69 ± 0.12</td>
<td>2.30 ± 0.27</td>
<td>0.97 ± 0.19</td>
</tr>
<tr>
<td>Observation group</td>
<td>30</td>
<td>2.25 ± 0.24</td>
<td>0.35 ± 0.16</td>
<td>2.17 ± 0.48</td>
<td>0.41 ± 0.09</td>
<td>1.96 ± 0.20</td>
<td>0.25 ± 0.07</td>
<td>2.35 ± 0.21</td>
<td>0.41 ± 0.12</td>
</tr>
<tr>
<td>t</td>
<td>-</td>
<td>0.570</td>
<td>12.448</td>
<td>0.235</td>
<td>15.786</td>
<td>0.877</td>
<td>17.347</td>
<td>0.801</td>
<td>13.649</td>
</tr>
<tr>
<td>P</td>
<td>-</td>
<td>0.571</td>
<td>0.000</td>
<td>0.815</td>
<td>0.000</td>
<td>0.384</td>
<td>0.000</td>
<td>0.427</td>
<td>0.000</td>
</tr>
</tbody>
</table>

3.2. Recovery of gastrointestinal function
As shown in Table 2, the recovery time of postoperative bowel sounds, as well as the time of the first flatulence and defecation in the patients of the observation group were shorter than that of the patients of the control group, P < 0.05.
Table 2. Indicators of gastrointestinal function recovery (mean ± SD, h)

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases (n)</th>
<th>Bowel sounds recovery time</th>
<th>First flatulence time</th>
<th>First excretion time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>30</td>
<td>13.25 ± 3.36</td>
<td>18.17 ± 3.20</td>
<td>24.28 ± 3.27</td>
</tr>
<tr>
<td>Observation Group</td>
<td>30</td>
<td>10.14 ± 2.15</td>
<td>14.28 ± 2.29</td>
<td>20.17 ± 3.16</td>
</tr>
<tr>
<td>( t )</td>
<td>-</td>
<td>4.270</td>
<td>5.415</td>
<td>4.950</td>
</tr>
<tr>
<td>( P )</td>
<td>-</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

3.3. Inflammatory factor levels
As shown in Table 3, the levels of each inflammatory factor were higher in both groups of patients with acute appendicitis before treatment, \( P > 0.05 \), after treatment, the levels of each inflammatory factor were reduced in both groups, but the magnitude of the reduction was greater in the observation group, for example, the levels of each inflammatory factor in the observation group were lower than those in the control group after treatment, \( P < 0.05 \).

Table 3. Levels of inflammatory factors (mean ± SD)

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases (n)</th>
<th>TNF-α (ng/mL) Before treatment</th>
<th>TNF-α (ng/mL) After treatment</th>
<th>IL-8 (ng/L) Before treatment</th>
<th>IL-8 (ng/L) After treatment</th>
<th>CRP (mg/L) Before treatment</th>
<th>CRP (mg/L) After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>30</td>
<td>40.25 ± 4.16</td>
<td>36.25 ± 4.29</td>
<td>36.25 ± 4.29</td>
<td>56.20 ± 5.57</td>
<td>15.41 ± 2.37</td>
<td></td>
</tr>
<tr>
<td>Observation Group</td>
<td>30</td>
<td>40.16 ± 4.29</td>
<td>36.41 ± 4.18</td>
<td>36.41 ± 4.18</td>
<td>56.41 ± 5.29</td>
<td>10.25 ± 1.14</td>
<td></td>
</tr>
<tr>
<td>( t )</td>
<td>-</td>
<td>0.082</td>
<td>0.146</td>
<td>0.884</td>
<td>0.881</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>( P )</td>
<td>-</td>
<td>0.935</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td></td>
</tr>
</tbody>
</table>

3.4. Postoperative complications
As shown in Table 4, compared with the two groups of complications, the observation group had a lower incidence rate, \( P < 0.05 \).

Table 4. Postoperative complications [n (%)]

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases (n)</th>
<th>Intestinal obstruction</th>
<th>Lung infection</th>
<th>Incision infection</th>
<th>In total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>30</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>20.00</td>
</tr>
<tr>
<td>Observation Group</td>
<td>30</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>3.33</td>
</tr>
<tr>
<td>( \chi^2 )</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4.043</td>
</tr>
<tr>
<td>( P )</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.044</td>
</tr>
</tbody>
</table>

4. Discussion
Appendicitis can occur in all ages, the onset of the disease has a variety of symptoms such as abdominal pain, due to the insidious symptoms and lack of specificity, some patients think that it is just a simple abdominal pain and do not pay attention to it, resulting in delayed treatment. The early diagnosis rate in acute appendicitis is not high, the main treatment method for it is surgery, in recent years, laparoscopic technology in surgical treatment has been widely used, laparoscopic appendectomy treatment appendicitis trauma is light, and the effect is ideal. Even though the surgical method can be a comprehensive exploration of the abdominal cavity, and offers rapid localization of appendiceal lesions, accurate treatment. However, there are still postoperative complications,
inflammatory response becomes more serious, and postoperative gastrointestinal dysfunction problems may occur. The problem of postoperative gastrointestinal dysfunction may lead to reflex spasmodic contraction of the appendiceal circular muscle, which further triggers a variety of complications. Reducing postoperative complications, promoting the recovery of gastrointestinal function, and reducing the inflammatory response are the keys to treating appendicitis after surgery.

Conventional Western medicine adopts symptomatic therapy, including antipyretic, anti-infection, etc., but the overall effect is relatively general. According to Chinese medicine, acute appendicitis should be categorized as “intestinal carbuncle” [5], which is related to dietary disorders, unhealthy emotions, and invasion of “external evils”, which can be seen in the damage of the spleen and stomach, and the blood circulation needs to be activated to remove blood stasis and clear the “heat” as well as detoxification in the treatment. Dahuang Mudan Decoction is from “Synopsis of the Golden Chamber” (edited by Zhang Zhongjing), which can activate blood circulation, disperse knots, and expel heat and eliminate stasis [6]. In the formula, *Glycyrrhiza glabra* (licorice) is used, which can remove heat and toxins, strengthen the spleen and nourish the stomach, while forsythia, peach kernel, honeysuckle and peony bark can remove heat and toxins, dissipate heat to eliminate carbuncles, and cool the blood to eliminate stasis. Mirabilite can accumulate and disperse, rhubarb can remove toxins through laxative effect, and it is very ideal to activate blood circulation and eliminate stasis, and lastly, *Semen benincasae* (Dongguazi) has a significant effect in removing diuresis and removing body heat [7]. In short, Dahuang Mudan Decoction can promote blood circulation and eliminate stasis, strengthen the spleen and benefit the “Qi”. On this basis, some other components can be added to the formula, such as dandelion and *Patrinia scabra*, can remove heat and toxins, and frankincense, red peony, and myrrh can further enhance the effect of promoting blood circulation and eliminating blood stasis [8].

A total of 60 patients suffering from acute appendicitis were selected for this study and divided into two groups, both of which underwent laparoscopic appendectomy, the control group was supplemented with conventional symptomatic treatment in Western medicine after surgery, and the observation group was supplemented with Dahuang Mudan Decoction methods after surgery. Even though Western therapy can improve the disease symptoms and promote the recovery of gastrointestinal function to a certain extent, the effect is more ideal after adding the formula of Dahuang Mudan Decoction. Postoperative recovery indicators of acute appendicitis can also be judged by the level of inflammatory factors, including TNF-α, IL-8, and CRP. TNF-α has an important role in macrophage and immune T-cell differentiation, which will exacerbate inflammatory reactions, leading to severe disease and unfavorable to postoperative recovery, IL-8 belongs to a neutrophil activation factor, which will increase the degree of inflammatory reaction, further damaging the organ tissues, and is also unfavorable to the body’s recovery. On the other hand, CRP belongs to acute inflammatory mediators, which will be involved in the development of appendicitis, triggering fever, abdominal pain and other related symptoms [9,10]. As seen in this study, the levels of the above three inflammatory factors of the patients in the observation group were lower than those of the patients in the control group after treatment, which indicated that the inflammation control effect was more satisfactory after adding the formula of Dahuang Mudan Decoction, and the probable reason for this is that peony bark in Dahuang Mudan Decoction that contains terpenoids, phenols and other components, which can inhibit capillary dilation and secretion of inflammatory factors [11], and honeysuckle contains organic acids, flavonoids and other components, which can destroy the bacterial cell structure and play an antibacterial effect while also act on the MAPK signaling pathway to play an anti-inflammatory effect [12]. So, after adding rhubarb and red peony, the overall anti-inflammatory effect is stronger, and after the reduction of the inflammatory response of the organism, the relevant complications are reduced, such as various types of infections, and the inflammation is reduced. Complications and symptoms were reduced, such as various types of infections, and the results in the article
also showed a reduction in the symptoms of the observation group than that in the control group, further indicating the good utility of Dahuang Mudan Decoction.

In conclusion, appendicitis is a high clinical morbidity, acute appendicitis in the implementation of laparoscopic appendectomy and postoperative conventional treatment, supplemented with Dahuang Mudan Decoction formula can further control inflammation, promote the recovery of gastrointestinal function, and is conducive to the patient’s postoperative recovery, and the effect is very satisfactory.

Disclosure statement
The author declares no conflict of interest.

References

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