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ABSTRACT

Objective: To investigate the effect of arterial interventional chemotherapy before radical operation for gastric cancer on serum tumor markers and cell growth in the lesion. Methods: 90 patients with primary gastric cancer who underwent radical operation for gastric cancer in our hospital were chosen as the research subjects and divided into the control group (n=48) (did not receive preoperative arterial interventional chemotherapy) and the arterial interventional chemotherapy group (n=42) (received preoperative arterial interventional chemotherapy). The differences in tumor markers in serum as well as proliferation and apoptosis gene expression in gastric cancer tissues were compared. Results: Before surgery started, serum CA199, CA153, CA724 and AFP levels of arterial interventional chemotherapy group were significantly lower than those immediately after admission whereas serum CA199, CA153, CA724 and AFP levels of control group were not significantly different from those immediately after admission. After surgery, proliferation genes CUL4A and NTSR1 mRNA expression in gastric cancer tissues of arterial interventional chemotherapy group were lower than those of control group whereas DADS and FAM96B mRNA expression were higher than those of control group; apoptosis genes Livin and Bcl-2 mRNA expression were lower than those of control group whereas p53, p21 and Bax mRNA expression were higher than those of control group. Conclusion: Preoperative arterial interventional chemotherapy combined with radical operation for gastric cancer can more effectively inhibit the malignant degree of tumor and delay the growth of cancer cells.

1. Introduction

In recent years, the incidence of primary gastric cancer has been on the rise in China, and radical surgery should be adopted in a timely manner after early diagnosis[1,2]. Recent studies have shown that small metastases can be left after radical operation for gastric cancer, which is the main cause of long-term tumor recurrence. Arterial interventional chemotherapy is a method of injecting high-concentration chemotherapy drugs into the local feeding arteries of tumor, which can effectively kill the small metastases and reduce the malignancy of tumor to lay a foundation for subsequent surgical treatment[3,4]. In this study, the patients who received radical operation for gastric cancer alone and those who received arterial interventional chemotherapy combined with radical operation for gastric cancer were reviewed, the differences in tumor markers and cancer cell growth vitality were compared in order to provide a reference for the selection of treatment options for similar patients in the future, and the details are as follows.

2. Data and methods

2.1 Case data

90 patients with primary gastric cancer undergoing radical operation for gastric cancer in our hospital between February 2016 and October 2017 were selected as the research subjects, and
preoperative application of arterial interventional chemotherapy or not was referred to divide them into the control group (n=48) (who did not receive preoperative arterial interventional chemotherapy) and the arterial interventional chemotherapy group (n=42) (who received preoperative arterial interventional chemotherapy). Control group included 25 males and 23 females and were 47-78 years old; arterial interventional chemotherapy group included 22 males and 20 females and were 45-79 years old. There was no significant difference in above basic data distribution between the two groups (P>0.05), and the follow-up study plan was approved by the hospital ethics committee.

Inclusion criteria: (1) those who were pathologically diagnosed with primary gastric cancer; (2) those who were in accordance with the indications of radical operation; those who were diagnosed and treated for the first time, and without history of treatment of the disease; (3) those who were ≤ 80 years old; (4) those who or whose families signed the informed consent form. Exclusion criteria: (1) those combined with other primary malignant and neoplastic diseases; (2) those with history of arterial interventional chemotherapy; (3) those with history of abdominal surgery 1 year prior to admission; (4) those combined with systemic infectious disease.

2.2 Treatment methods

Control group received radical operation for gastric cancer alone, and artery interventional chemotherapy group received preoperative arterial interventional chemotherapy combined with radical operation for gastric cancer, which were as follows: Seldinger method was referred for right femoral arterial puncture and intubation, the catheter was placed in the initial segment of celiac trunk, high-pressure injection pump was used to inject contrast agent, imaging was conducted to show the tumor feeding arteries, and then superselective intubation was done. The injected chemotherapy drugs included 150 mg/m² paclitaxel and 60 mg/m² cisplatin. Before chemotherapy, dexamethasone injection 10 mg was routinely used, and the hydration and diuresis were conducted after chemotherapy to reduce toxicity. Radical surgery was performed 7-10 d after chemotherapy.

2.3 Serum tumor marker content detection

Immediately after inclusion and before operation started (after the completion of arterial interventional chemotherapy), the peripheral blood specimens of the two groups were collected to isolate supernatant, and enzyme-linked immunosorbent assay was used to detect the serum contents of tumor markers carbohydrate antigen 199 (CA199), carbohydrate antigen 153 (CA153), carbohydrate antigen 724 (CA724) and alpha fetoprotein (AFP).

2.4 Gastric cancer tissues

Gastric cancer lesions were collected during the operation, and fluorescence quantitative PCR was used to detect the expression of proliferation genes CUL4A, DADS, FAM96B and NTSR1 as well as apoptosis genes Livin, p53, p21, Bcl-2 and Bax in them.

2.5 Statistical methods

Tumor marker levels as well as proliferation and apoptosis gene expression were all quantitative data and recorded into SPSS25.0. The obtained statistic P was used to judge whether the differences between groups were statistically significant. P<0.05 was the criterion of statistical significance in differences in the study.

3. Results

3.1 Tumor markers

Immediately after inclusion, serum CA199, CA153, CA724 and AFP levels were not significantly different between the two groups (P>0.05). Before the surgery started, serum CA199, CA153, CA724 and AFP levels of control group were not significantly different from those immediately after admission (P>0.05), and serum CA199, CA153, CA724 and AFP levels of arterial interventional chemotherapy group were significantly lower than those immediately after admission (P<0.05). Before surgery started, serum CA199, CA153, CA724 and AFP levels of arterial interventional chemotherapy group were lower than those of control group (P<0.05), shown in Table 1.

Table 1. Comparison of serum tumor marker levels.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>CA199 (U/mL)</th>
<th>CA153 (U/mL)</th>
<th>CA724 (U/mL)</th>
<th>AFP (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Immediately after inclusion</td>
<td>Before surgery started</td>
<td>Immediately after inclusion</td>
<td>Before surgery started</td>
</tr>
<tr>
<td>Control group</td>
<td>48</td>
<td>84.39±9.12</td>
<td>83.57±9.12</td>
<td>27.46±3.05</td>
<td>28.11±3.40</td>
</tr>
<tr>
<td>Arterial interventional chemotherapy group</td>
<td>42</td>
<td>84.27±9.06</td>
<td>40.16±5.42*</td>
<td>27.38±3.17*</td>
<td>12.49±1.76*</td>
</tr>
</tbody>
</table>

Note: vs. immediately after inclusion within group, *P<0.05.
Comparison of apoptosis gene expression in gastric cancer tissues after surgery.

Table 3.

Comparison of apoptosis gene expression in gastric cancer tissues after surgery.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Livin</th>
<th>p53</th>
<th>p21</th>
<th>Bcl-2</th>
<th>Bax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>48</td>
<td>60.37 ± 8.21</td>
<td>92.64 ± 11.34</td>
<td>73.19 ± 8.53</td>
<td>110.31 ± 14.28</td>
</tr>
<tr>
<td>Arterial interventional chemotherapy group</td>
<td>42</td>
<td>43.29 ± 5.06</td>
<td>125.31 ± 14.05</td>
<td>92.17 ± 11.64</td>
<td>75.29 ± 8.12</td>
</tr>
<tr>
<td>( i )</td>
<td>&lt;0.05</td>
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</table>

3.2 Proliferation genes

CUL4A and NTSR1 mRNA expression in gastric cancer tissues of arterial interventional chemotherapy group were lower than those of control group whereas DADS and FAM96B mRNA expression were higher than those of control group. After surgery, the differences in proliferation genes CUL4A, DADS, FAM96B and NTSR1 mRNA expression in gastric cancer tissues were statistically significant between the two groups \( (P<0.05) \), shown in Table 2.

3.3 Apoptosis genes

Livin and Bcl-2 mRNA expression in gastric cancer tissues of arterial interventional chemotherapy group were lower than those of control group whereas p53, p21 and Bax mRNA expression were higher than those of control group. After surgery, the differences in apoptosis genes Livin, p53, p21, Bcl-2 and Bax mRNA expression in gastric cancer tissues were statistically significant between the two groups \( (P<0.05) \), shown in Table 3.

4. Discussion

Primary gastric cancer is a clinical more see and high degree of malignant tumor diseases, and radical surgery is the best treatment for patients with early disease. With the increase of case study, scholars have currently believed that there is the possibility of tiny tumor lesion residue after radical surgery alone, and it is necessary to apply preoperative auxiliary treatment to kill such tumor lesions in advance. Arterial interventional chemotherapy is the therapy to apply radiiagnostics techniques to inject chemotherapy drugs into the local feeding artery of tumor and achieve exterminating or killing effect on local tumor cells\(^5\)-\(^7\). In this study, arterial interventional chemotherapy was added into the overall treatment before radical operation for gastric cancer and compared with radical operation for gastric cancer alone, and the differences in their effects were discussed from serum tumor markers, gastric cancer proliferation-related and apoptosis-related gene expression in lesions and other aspects.

Tumor markers are the most common indicators for clinical screening of malignant tumors, and it is simple and sensitive to detect the contents of many markers in serum. CA199 is a tumor marker highly sensitive to digestive system tumors, and its content is closely related to tumor volume, lymph node metastasis, etc.\(^8\),\(^9\); CA153 is a specific tumor marker for breast cancer, and current studies have shown that it is also highly expressed in patients with gastric cancer, and can be tested together with other tumor markers to increase the diagnostic accuracy; CA724 is a good predictor of gastric cancer staging, and studies have shown that the content of CA724 in the serum of advanced gastric cancer patients with lymph node metastasis is significantly higher than that of patients with early disease\(^10\),\(^11\); AFP is a specific tumor marker of primary liver cancer, its sensitivity and specificity are both inferior to those of carbohydrate antigen in the diagnosis of gastric cancer, but its combined detection with other markers has auxiliary diagnostic function. In the study, serum levels of above tumor markers in arterial interventional chemotherapy group had been greatly reduced before the operation started, but the levels of tumor markers in control group did not change obviously, it proves that the preoperative arterial interventional chemotherapy can effectively reduce the contents of tumor markers in patients with gastric cancer, and this is an important symbol for it to reduce tumor malignancy.

The growth vitality of cancer cells in the lesions is an intuitive indicator to reflect their malignancy, including proliferation and apoptosis. The expression levels of proliferation-related genes significantly change in malignant tumor cells, it includes the abnormally high expression of pro-proliferation genes and the abnormally low expression of anti-proliferation genes, and they promote the cancer cells to obtain infinite proliferation potential and accelerate the malignant evolution of tumors together. It has been reported in different studies that CUL4A, DADS, FAM96B and NTSR1 are associated with the proliferation of malignant tumor cells, CUL4A is a member of the ubiquitin E3 ligase family and is involved in the process of cell mitosis. Studies have confirmed that the expression of this gene significantly decreases in human gastric cancer tissues, and that specific over-expression of FAM96B can inhibit the proliferation of gastric cancer cells\(^12\),\(^13\); DADS has significant inhibitory effects on various tumors, including inhibiting DNA formation, blocking cell cycle progression and inducing tumor cell apoptosis, etc.\(^14\); FAM96B plays an important role in the proliferation and migration of vascular endothelial cells and is involved in the process of cell mitosis. Studies have confirmed that the expression of this gene significantly decreases in human gastric cancer tissues, and that specific over-expression of FAM96B can inhibit the proliferation of gastric cancer cells\(^15\),\(^16\); NTSR1 is a specific affinity receptor for neurotensin, and studies have confirmed that the expression of this gene in gastric cancer tissues is significantly higher than that in normal adjacent tissues, and that its expression is positively correlated with both tumor TNM staging and...
lymph node metastasis[17,18]. In this paper, the mRNA expression levels of CUL4A and NTSR1 in gastric cancer tissues of arterial interventional chemotherpay group were relatively lower while the mRNA expression levels of DADS and FAM96B were relatively higher after operation, suggesting that the arterial interventional chemotherapy before radical operation for gastric cancer can more effectively inhibit the expression of pro-proliferation genes and increase the expression of anti-proliferation genes to finally more effectively achieve the killing effect on cancer cells.

Apoptosis is an important part of cell growth. Under physiological conditions, aging cells will perform apoptosis, a programmed death process to ensure the body’s metabolism. However, the process of apoptosis is blocked and the proliferative activity is too exuberant in malignant tumor tissues, resulting in cell canceration. Livin is a typical anti-apoptosis gene, which can inhibit apoptosis mainly by blocking the endogenous and exogenous apoptosis pathways based on apoptosis receptors and mitochondria[19,20]; both p53 and p21 are important tumor suppressor genes, which are activated under the high expression of oncogenes in cells and induce apoptosis to kill abnormal cells[21,22]; both Bcl-2 and Bax belong to the Bcl-2 family. Bcl-2 resists apoptosis while Bax promotes apoptosis, their expression levels are balanced under physiological conditions, but when cell canceration occurs, the expression of Bcl-2 increases while the expression of Bax decreases[23,24]. In this paper, the mRNA expression levels of Livin and Bcl-2 in gastric cancer tissue of arterial interventional chemotherapy group were relatively lower while the mRNA expression levels of p53, p21 and Bax were relatively higher after operation, demonstrating that the arterial interventional chemotherapy before radical operation for gastric cancer could more effectively promote the apoptosis of cancer cells and further inhibit their growth.

To sum up, it is concluded that preoperative arterial interventional chemotherapy in patients with primary gastric cancer can more effectively inhibit tumor malignancy, which is embodied in decreased levels of tumor markers, inhibited proliferation activity and enhanced apoptosis activity of cancer cells as well as other aspects. It is worthy of being popularized in future clinical practice.

References


