Kanglaite Injection plus 5-fluorouracil, Cisplatin and in Combination with radiotherapy in the Treatment of Advanced Pancreatic Cancer

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From May 1997 to December 2000, the authors applied Kanglaite Injection (KLT) plus small dose of FP regimen (5-FU+cisplatin) and local radiotherapy in treating 22 cases of advanced and inoperable pancreatic cancer (their lesion only localized at pancreas and its surrounding organs, regional lymph nodes, local peritoneum, but having infiltration at the confluent area between superior mesenteric vein and portal vein, celiac trunk or superior mesenteric artery) and obtained rather good therapeutic results.

1. Materials and Methods

1.1 Clinical data

Among 22 cases in the group, male accounted for 14 cases, and female 8 cases; Age: 42 ~ 66 years old, median age 58; TNM staging classification: T1b 10 cases, T2 8 cases, T3 4 cases; contrast-intensifying CT examination didn’t show definite evidence of remote metastasis. All the patients in the group were confirmed by cytological examination, duct cell carcinoma 7 cases, acinar cell carcinoma 1 case, unclassified 14 cases; clinical symptoms: jaundice 17 cases, pain 18 cases, abdominal distention 16 cases; all the patients in the group haven’t received any other chemo- or radio-therapies; their Karnofsky scale score was above 70 points, their peripheral WBC, blood platelets counts and functions of heart, lung, liver and kidney were all normal.

1.2 Treatment methods

KLT 100ml, iv. d1 ~ d28; DDP 10mg, iv. 5 times/week for 4 consecutive weeks; 5-FU 0.25, iv. (slowly) d1 ~ d28, infusion time > 8h, 28 days as a treatment course, with an interval of 4 weeks then repeated the treatment for a total of 3 treatment courses; radiotherapy 6MV2X local D10 Gy / (20f 28 d−1) , 5 times/week, which was applied simultaneously with the 1st cycle of chemotherapy. During the treatment blood picture, hepatic and renal functions were periodically checked, and symptomatic treatment such as drug to raise blood cells, metoclopramide, diazepam, etc. was applied, CT was re-examined four weeks after the end of each treatment course to assess the therapeutic as well as toxic and side effects. All the patients were followed-up until death to evaluate long-term therapeutic results.

1.3 Evaluation Criteria

Short-term therapeutic results were evaluated according to WHO (1981) Criteria [1].
2. Results

2.1 Therapeutic results

The results of Kanglaite Injection (KLT) plus small dose of FP regimen (5-FU+cisplatin) and local radiotherapy in the treatment of advanced pancreatic cancer could be summarized as follows: CR 2 cases, PR 12 cases, overall response rate (RR) 63.6% (14/22), survival time: shortest 5 months, longest 27 months, median survival time 13.5 months. 1-year, 1.5-year, 2-year survival rates were 59.1% (13/22), 27.3% (6/22), 9.1% (2/22) respectively. Clinical symptom improvement rate 95.5% (21/22).

2.2 Toxic and side effects

Leucopenia 81.8% (18/22), among them grade III~IV leucopenia accounted for 4.5% (1/22), thrombocytopenia 18.2% (4/22), all of them belonged to grade I, the incidence of gastro-intestinal reactions such as loss of appetite, nausea and vomiting, diarrhea was 86.4% (19/22), most of them were below grade II, the incidence of phlebitis was 77.3% (17/22), all of them were mild, and no hepatic and renal impairment had been seen.

3. Discussion

In accordance with the reports in the literature the effective rate of localized but irresectable pancreatic cancer treated by single drug chemotherapy was ≤17%, and by a combination chemotherapy could reach 48%, the median survival time in single radiotherapy was 5.5 months, while in radiotherapy combined with chemotherapy was 5.5 ~11.5 months, no ideal therapeutic results had been obtained in prolongation of survival period with all existing therapeutic regimens, their value remained between 6~10.3 months [1].

European-American and Japanese scholars have reported that the response rate of 5-FU continuous iv drip combined with small-dose DDP in the treatment of pancreatic cancer could reach 40~50%. The methods: 5-FU 320mg/m$^2$, iv drip for 24h for a total of 4 weeks; DDP 3.5~7.5mg/m$^2$ per day, 5d/w for 4 weeks, then followed by 4 weeks of rest. Cisplatin has a similar action as alkylating agents at high dosage, while plays a biochemical modulation (BCM) at small dosage. In FP regimen, cisplatin embodies its action of biochemical modulation, while small dosage of DDP prevents methionine from entering into cells by its combination with methionine transferring protein at cellular membrane, thus destroying the biosynthesis of DNA in the body. 5-FU, as an antimetabolite, affects the biosynthesis of DNA in the body, and interfering the synthesis of protein. The anti-tumor effect of 5-FU is basically relying on the combination of its metabolite, FdUMP, reduced tetrahydrofolic acid (5, 10CH$_2$F$_4$) and thymidine (TS) into a triple complex, thus hindering the synthesis of DNA in tumor cells [2]. The possible mechanism of interaction between 5-FU and DDP includes the increase of DDP-mediated reduced folic acid, thus strengthening the damage of DNA and interfering the repair of a DDP - DNA complex [3]. In addition, both of DDP and 5-FU are radiosensitizer, 5-FU can strengthen the cytotoxicity of ion irradiation, inhibit the repair of DNA and the accumulation of phase S
cells. DDP’s radiosensitization may accelerate the proliferation of tumor clonal cells, strengthen DNA's injury following radiation and inhibit the repair of sub-lithal injury caused by radiation and the repair of potential lethal injury [3].

Kanglaite Injection is an anti-tumor formulation prepared by extracting the active component from a TCM herb Coix seed. Its pharmacodynamics and clinical study have verified that this preparation has obvious inhibitory effect on various tumors and definite therapeutic results, the mechanisms of its actions are inhibiting tumor's angiogenesis, inducing apoptosis of tumor cells, anti-cachexia, reversing multi-drug resistance, achieving chemosensitization, enhancing body’s immunity and radiosensitization. Especially it has definite effect in raising comprehensive therapeutic effect and improving patients’ quality of life [4]. The authors applied KLT plus small-dose FP regimen and local radiotherapy in treating 22 cases of inoperable locally-advanced pancreatic cancer. Moreover, the toxic and side effects were tolerable without affecting the treatment course, and no treatment-related complications and apparent hepatic and renal impairment were found.

References