

Chemotherapy combined with regional hyperthermia in locally advanced unresectable pancreatic cancer: clinical and anthropological benefits

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Today the adenocarcinoma of the pancreas shows a significant increase of incidence, mainly in western countries. This tumor tends to affect mainly the male population, smokers and has a marked effect in proportion to the increase of age. Recent studies have shown a correlation between pancreatic cancer and diets high in animal fat and protein, and the role of coffee is discussed. The symptomatology is often delayed and is mostly characterized by obstructive icterus, in the case of localization in the head, and of pain for involvement of nerve fibers both in the retroperitoneal tumors of the head and body-tail. It frequently turns out to be the weight loss caused by maldigestion to reduced synthesis and transit of pancreatic enzymes. The prognosis of this cancer is poor, with lower survival than 12 months. Regardless of treatment, these tumors are often surgically inoperable forcing the surgeon to palliative shunt, moreover chemotherapy and radiation therapy are of little prognostic impact. The clinical radiofrequency hyperthermia (HT) shows, in recent experimental studies, to have anti-tumor effects in combination with chemotherapy based on new drugs. The treatment with capacitive hyperthermia (HT) shows antitumoral effects associated with chemotherapy (CHT) treatment which consists of gemcitabine (GEM) alone or it is in association with oxaliplatin, cisplatin, or 5-FU (1, 2, 3, 4, 5). This method presents a considerable operational simplicity and a very low incidence of complications, as well as, with equipment of recent introduction excellent tolerability by patients. The interest in hyperthermia has been growing in recent years, as it has been shown that drugs commonly used in cancer therapy may have greater efficacy at the same dose, or retain the same efficacy with lower doses when administered in association with hyperthermic techniques.

The advantages of the results can be summarized as follows: a more simple use of chemotherapy and radiotherapy, then undoubtedly better tolerated by patients, and in a stimulation of the immune reactivity, notoriously depressed in neoplastic patient. For these reasons the radiofrequency hyperthermia is considered a viable technique of enhancement of the action of other therapies (chemotherapy, immunotherapy, radiotherapy) allowing in many cases a stoppage phases of the disease for a more or less long time, allowing the maintenance of conditions of survival satisfactory, and in some cases even a reduction of the tumor mass. The current technology has allowed the development of highly sophisticated equipment, equipped with liquid-cooled and flexible antennas, thus allowing us to prolong the treatments without discomfort for patients and with no particular side effects.

The aim of this study was to evaluate the action of CHT associated with regional Hyperthermia (HT) tested on a group of 25 patients suffering from locally advanced unresectable pancreatic carcinoma (LAPC).

Materials and methods

We used a radiofrequency hyperthermia equipment SYCHROTERM RF 13.56 MHz, equipped with a liquid-cooled flexible antennas with a diameter of 26 cm, positioned in epigastrium-mesogastrio at the Center for Clinical Hyperthermia, Policlinico Tor Vergata, University of Rome "Tor Vergata". The treatment was based on a median of 3 cycles structured in 8 sessions of 45 minutes each, on alternate days, using about 250 W for a session. The group of 25 patients treated (12 male and 13 female) was selected on the basis of the characteristics of inoperability of the tumor (locally advanced unresectable pancreatic cancer) with a life expectancy of ≤ 12 months. At the same time patients underwent chemotherapy based on gemcitabine and fluorouracil, in period from 02/2001 to 07/2009. The outcome of the treatment was determined by CT, preliminary and 20 days after the last session of chemo-hyperthermia. We considered responding patients who reported reduced or stable disease.

Results

The study was performed on 25 patients, at our center clinical hyperthermia in the period 01/2001-07/2009, suffering from locally advanced unresectable pancreatic cancer (LAPC). The group consisted of 12 males and 13 females with a mean age of 64 years. All patients received chemotherapy according to the protocol

gemcitabine-oxaliplatin. Median overall survival (OS) was 16 months in the group CHT+HT vs 8-11 months as reported in literature.

Survival was 19 patients (76%) at 12 months, 12 patients (48%) at 18 months, 11 patients (44%) at 24 months of and 9 patients (36%) over 24 months (see Table 1.).

n.	Survival	n. patient	%
1	Survival 12 th month:	19 pts	76%
2	Survival 18 th month:	12 pts	48%
3	Survival 24 th month:	11 pts	44%
4	Survival over 24 th month:	9 pts	36%

Table 1.

We did not observe effects or increase toxicity in CHT.

Conclusion

Anticancer nucleoside Gemcitabine, Oxaliplatin and 5 FU have dose limiting toxicities (DLT) Major side effects of Gemcitabine include bone marrow suppression, flu-like syndrome and severe hepatic toxicity. (6, 7, 8, 9, 10)

The application of Regional Hyperthermia (HT) on this restricted group of patients has given out very interesting results. The HT + CHT can reduce the tumoral increase, can raise the survival of the patients and, above all, the HT can improve general conditions of the patients that have been treated with this kind of associated therapy. The results justified further evaluation in a large number of patients to confirm the benefit.

The Hyperthermotherapy improved the quality of life of all responding patients.

Compared to the severe physical, existential and esthetic impact of the chemotherapy alone, patients with Hyperthermia do not experience particular side effects. As a consequence of that, patients are less anxious in facing the treatment; they establish a fruitful empathic relation with cares and doctors. So, the anguish proceeding the moment of cares (CHT) turns now into a necessary but not threatening and foreboding moment (11, 12, 13, 14, 15). Physiotherapy intervention, too, has something to offer throughout the whole cancer journey, including for patients who are not curable and whose life is limited.

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