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Novel Approaches to Treat Unresectable Pancreatic Cancer Patients in South Korea: A comprehensive Review including Those Treatments and Researches

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Abstract

Pancreatic cancer arises from an abnormal growth of cells in the pancreas, an organ located behind the lower part of the stomach. Most of these tumors are unresectable, leaving patients with poor survival rates and limited life expectancy still in search of treatments and medications. However, comprehensive studies reviewing these treatments and medications for patients with unresectable pancreatic cancer are scarce. This study focused on treatments and research conducted in South Korea specifically for patients with unresectable pancreatic cancer. By utilizing various online resources, including Google Scholar, PubMed, RISS, and KCI, several treatments and medications that have shown meaningful effects were identified, although they remain largely unknown to patients both in South Korea and other countries. Nonetheless, certain limitations associated with traditional medicine were noted, such as liver side effects, credibility issues, and constraints related to the duration of experiments and sample sizes.

Keywords: Pancreatic cancer, Unresectable pancreatic cancer, Traditional Korean Medicine (TKM), Traditional Chinese Medicine (TCM)

1. Introduction

Pancreatic cancer originates from an abnormal proliferation of cells in the pancreas, an organ situated behind the lower stomach. This gland produces enzymes essential for digestion and hormones that regulate blood sugar levels. The predominant form of this cancer is pancreatic ductal adenocarcinoma (Mayo Clinic, 2024). Reports indicate that only 15 to 20 percent of pancreatic tumors in patients are resectable, and the 5-year survival rate for pancreatic cancer is only 12 percent (Johns Hopkins Medicine). Despite low survival rates and life expectancy, patients with unresectable pancreatic cancer from various countries have actively sought ways to treat their symptoms. However, there has been a lack of studies introducing these studies and treatments, particularly those conducted especially for patients with unresectable pancreatic cancer.

Therefore, this study provides a comprehensive review of pancreatic cancer treatment in Korea and presents a variety of relevant data. It is common knowledge that pancreatic cancer has a poor prognosis and that there are few treatment options, including surgery, chemotherapy, and radiation (Mizrachi et al., 2013). This study was motivated by the need to address the growing concern over deadly cancers and to provide assistance to individuals affected by cancer and their families. Traditional cancer therapies in Korea, particularly those that do not involve surgery, were identified as a unique and underreported area (PHIL HOSPITAL of KOREAN MEDICINE). The lack of information on traditional and oriental pancreatic cancer treatments specific to South Korea made awareness of the necessity of this review to support patients seeking treatment alternatives without surgery.

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Certain treatments have previously been certified and are documented (PRODUCT - GC Cell), and a number of traditional treatments have actually worked for real cancer patients in the past (Yun, et al., 2013). However, there are many skeptics wondering, "Is the use of traditional and oriental medicine as effective as Western and modern treatments in curing pancreatic cancer?" (Yoon, et al., 2013). To address this controversy, over twenty sources were collected. A search of academic libraries for traditional and oriental cancer treatment methods, particularly those related to pancreatic cancer, identified that most relevant articles had been published recently.

2. Method

Google Scholar was primarily used to find research papers regarding Korean traditional treatments and medicine. Most of the studies included in this review summarize previously published results and theses. Sources were gathered from databases such as PubMed and Google Scholar, using common keywords such as 'pancreatic cancer' and 'traditional medicine.' For studies originally published in Korean, databases including KISS, RISS, and KCI were frequently referenced. The articles that state benefits of incorporating various natural products to treat pancreatic cancer carried out their research through in-vitro and in-vivo (Son, et al., 2013; Matsushita, et al., 2018). Another study that was conducted through in-vitro commercially purchased reagents were used to synthesize the compounds, the reactions were identified using TLC and column chromatography, and the compound structures were analyzed by NMR spectroscopy. MIAPaCa2 pancreatic cancer cells were cultured and treated as the synthesized compounds, and cell death was observed using the EZ-CYTOX kit. Additionally, apoptosis was analyzed by staining with annexin-V-FITC and propidium iodide, and using flow cytometry. The sphingosine kinase inhibition and PP2A activity were respectively measured using the Echelon SK activity kit and Millipore PP2A activity kit (Park and Baek, 2022). In the next journal written on the effects of the cudrania tricuspidata leaf, the extract was prepared by extracting the leaves with ethanol to produce the Cudrania tricuspidata extract(CTE), and the PANC-1 and AsPC-1 cell lines were cultured. After treating the cells with various concentrations of CTE, morphological changes of the cells were observed using a microscope, and cell viability and toxicity were assessed using MTT and LDH assays. Additionally, the proliferation ability of the cells was analyzed through a colony formation assay, and apoptosis was confirmed using Hoechst 33342 staining (Kang, et al., 2011).

There was a couple of studies where the treatment was tested on real patients, like the article that organized patients diagnosed with unresectable lung cancer, and analyzed their survival rates when they treated them with Wheel Balanced Cancer Therapy (Jeon, et al., 2015). One study targeted a 63-year-old female patient with recurrent pancreatic cancer which involved two periods of integrative treatment in 2022, combining Korean traditional medicine and chemotherapy. The Korean traditional medicine treatments included various herbal medicines, acupuncture, herbal acupuncture, and moxibustion. The chemotherapy regimen consisted of irinotecan, oxaliplatin, and TS-1. Furthermore, in another study, a researcher team extracted 500 types of herbal medicines by adding 100 ml of methanol solvent to 5g of each herbal medicine and keeping them at room temperature for three days, through filtration using filter paper. As a result, they were able to select 13 herbal extracts with cytotoxic effects. Among these 13, they finally selected Astilbe rubra, which exhibited high anticancer activity against pancreatic cancer cell lines(based on the literature review) and had not been previously reported.

Moreover, a research team analyzed 47 pancreatic cancer patients for one year. The patients were divided into three cohorts based on the presence or absence of liver metastasis and the type of surgery they got. Survival rates, changes in tumor markers, and disease-free survival rates were analyzed. Recurrence was confirmed using CT and ultrasound (Kim, et al., 2004). In addition, one study evaluated the anti-cancer effects of Phellodendri Cortex water extract on the pancreatic cancer cell line MIA PaCa-2. In the study, researchers prepared and analyzed the extract by using cell culture, MTT assay, FACS analysis, fluorescence microscopy, DNA fragmentation analysis, and Western blot to measure cell viability, apoptosis, and reactive oxygen species generation (Lee, et al., 2013).

3. Results

The reviewed articles presented various findings. One article listed many natural products that were capable of

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inducing apoptosis, the most prominent one being Agaricus Blazei, which is a type of fungi that yields the ability to treat pancreatic cancer when it is extracted in hot water (Matsushita, et al., 2018; Kim, et al., 2021). Another plant that was used in traditional medicine to treat diseases such as malaria was Pulsatilla saponin, commonly known as the Korean pasque flower, was found to have apoptosis effects. Not only that, it was also proven to be capable of cell proliferation and angiogenesis (Son, et al., 2013). Treatments using such plants were unique to a few countries like South Korea before it was discovered as new drugs and the use was expanded globally. Furthermore, a recently published newspaper reported that a South Korean pharmaceutical company had used polytaxel to create a painless treatment for pancreatic cancer. This treatment method was tested on six animals, and it was possible to analyze that the cancer in four out of the six animals had reduced or completely disappeared after the injection of the drug (Yoon, 2020). Lastly, a hospital in Daejeon, South Korea produced a study suggesting that the Wheel Balance Cancer Therapy may have a positive effect on improving the quality of life and preventing metastasis in patients who were diagnosed with various types of cancers such as breast, stomach and even pancreatic cancer (Son, et al., 2013; Jeon, et al., 2015).

This study utilized Donguibogam, materials from the National Library, online articles, and peer-reviewed studies to investigate various researches focusing on special therapies not covered by national insurance for pancreatic cancer patients, with a particular emphasis on traditional Korean medicine treatments. The following conclusions were drawn from the analysis.

Firstly, according to the study, A Case Report of Unresectable Pancreatic Carcinoma Patient for Relieving Cancer Related Pain and Improving Quality of Life by Korean Medical Treatment, a combination of acupuncture therapy, wild cultivated ginseng medicine acupuncture, ginsenoside and anti-cancer agent B-based Korean medicine treatment significantly improved cancer pain and associated symptoms, enhancing patient quality of life (Yun, et al., 2013). Additionally, the study, A Case Report of Traditional Korean Medicine Based-Integrative Oncology of Recurrent Pancreatic Cancer, reported that a patient with recurrent pancreatic cancer after partial pancreatectomy maintained stable tumor size without enlarging the size through combined cancer treatment based on traditional Korean medicine, including anti-cancer drug use, acupuncture, and chemotherapy (Joo, et al., 2022).

Furthermore, several studies explored the anti-cancer effects of various herbal extracts on pancreatic cancer cells. In the study, Anticancer Properties of Astilbe rubra Extracts on AsPC-1 Human Pancreatic Cancer Cells, researchers conducted experiments using Astilbe rubra(ARM), and ultimately they found ARM to have anticancer activity (Park, et al., 2017). The study "Synthesis of Sphingosine Kinase Inhibitors and Its Anticancer Activity in Pancreatic Cancer Cells" synthesized new compounds using a simple method, and these compounds improved the low anti-cancer efficacy of PF-543, a sphingosine kinase(SK) inhibitor, in pancreatic cancer cells (Park and Baek, 2022). The study “Cytotoxic Effects of Leaves of Cudrania tricuspidata Bureau Extracts on Human Pancreatic Cancer Cells” demonstrates that cudrania leaf extract induces strong cytotoxicity and apoptosis in PANC-1 and AsPC-1 cells in a concentration-dependent manner. In addition, Apoptotic Effect of Phellodendri Cortex Water Extract on MIA PaCa-2 Cell shows that phellodendri cortex water extract induces apoptosis in MIA PaCa-2 cells through ROS and caspase activation, which can damage cancer cells in anti-cancer treatments (Kang, et al., 2011).

The role of apoptosis in these studies are significant as apoptosis removes unnecessary or abnormal cells, suppressing cancer cell proliferation and preventing the progression of cancer.

The study Preliminary Study for Development of Korean Medicine Clinical Practice Guideline for Pancreatic Cancer indicates that combining oriental and western medicine treatments is beneficial for pancreatic cancer treatment, and that treatment combined with herbal medicine has a positive effect on 6 months and 1 year survival rates, objective response rates, and quality of life. In particular, the research emphasizes that in case of advanced or unresectable pancreatic cancer, herbal medicine can contribute to overcoming the resistance to conventional treatments (Park, et al., 2017).

Lastly, the study, Effectiveness of Radiofrequency Hyperthermia on Hepatic Metastasis of Pancreatic Cancer, reported that radiofrequency hyperthermia in pancreatic cancer patients did not crucially improve survival rates overall, but showed meaningful survival rate improvements when liver metastases were discovered after a surgery (Kim, et al., 2004).

These diverse researches suggest the potential of Korean medicine therapies to play a significant role in treating pancreatic cancer patients. Systematic research to verify these findings is necessary to develop stable and safe

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treatment methods in future studies.

4. Discussion

Although the reviewed articles reported promising results, evident limitations may weaken the overall reliability and strength of the findings. For instance, many were limited to in-vitro studies and thus needed further experimenting in order to confirm the effects of the treatments (Son et al., 2013; Matsushita et al., 2018). Furthermore, this review article includes a number of studies from over ten years ago, presenting the possibility of the information being outdated or inaccurate (Son et al., 2013; Jeon et al., 2015). Lastly, despite the fact that it is confirmed through research that the Wheel Balanced Cancer Therapy has a positive effect on pancreatic cancer, clinical trials were only conducted on patients who were diagnosed with stomach cancer. Further research and clinical trials should be done in order for us to state the clear correlation between this treatment and pancreatic cancer (Jeon et al., 2015; Park et al., 2007).

Oriental medical treatment has long been used. It provides plenty of advantages, but it also has specific disadvantages and adverse effects. Acupuncture, moxibustion, and cupping are the main steps in the therapy of oriental medical treatment, and patients are typically given oriental medication. Individuals experiencing adverse effects following oriental medicine treatments generally experience hepatitis, hepatotoxicity, gastrointestinal distress, nephrotoxicity, and mostly other liver-related side effects (Choi, 2017).

Most oriental treatments and traditional remedies are often seen negatively by Koreans, especially the younger generation. In essence, they lack official and scientific certification as a medical treatment. It would be among the factors preventing the insurance from existing as a standard Korean insurance. Basically, the goal of Korean health insurance is to help individuals lower the majority of their medical costs. It is supposed that the government would not be able to decide to provide medical insurance for folk remedies and oriental medical treatments that are uncertified, have severe side effects, and are not supported by the public. Acupuncture, moxibustion, and cupping are among the treatments that can be covered by medical insurance because the outlook is generally improving and more people are seeking out oriental medical care (Duzon Oriental Medicine Hospital, 2021).

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