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Usefulness of Our Newly Designed Supplements for Reducing the High Risk of Pancreatic Cancer

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Abstract

Early detection of pancreatic cancer became possible by analyzing micro RNA (miRNA) from peripheral blood. We report our new preventive intervention method to reduce the risk of pancreatic cancer by using our original supplements for patients with high risk of pancreas-bearing cancer.

Purpose; The risk determination of pancreatic cancer by using miRNA from blood was examined, and it was investigated whether it was effective to decrease the high risk of pancreatic cancer by using supplements that we newly devised.

Materials and Methods; For 14 adults who are not sick, the miRNA was extracted from the blood. They consisted of 7 men and 7 females, aged between 64 and 78 years old, averaging 67.6 years old. The encompassing analysis was performed using the next generation sequencer, and the risk of pancreatic cancer was calculated as expression score (ES). After confirming the absence of visible tumor, three months of our supplements (P-glucan and Methyl-resveratrol) were subjected to take.

Then the risk determination was carried out repeatedly by analyzing miRNA from blood samples. Changes in tumor-bearing risk treated by our tumor risk-reduction supplements were evaluated by ES calculated by next Generation sequencer before and after intervention and examined by Wilcoxon test.

Results; By the proactive intervention method of the tumor-bearing reduction supplements, the expression scores, in 11 cases (79%) in 14 cases, were reduced significantly (Wilcoxon test; $p<0.0052$) after taking supplements. Furthermore, 14 cases were divided into A group (N=8) who showed higher ES than the healthy mean average, and B group (B=4) who showed lower ES than the mean average of healthy persons. In A group 8 out of 8 (100%) showed significant ($p<0.009$) reduction of ES. While, in group B, no significant reduction of ES were obtained ($p = 0.465$) .

Conclusion; For those who have high risk of pancreatic cancer, we found it possible to reduce ES perfectly by means of our newly designed supplements. This shows an effective practice of preemptive medicine.

Keywords:

MicroRNA;

Pancreatic cancer;

Cancer risk;

Supplements;

Preemptive medicine.

1. Introduction

Diagnosis of pancreatic cancer in its early stage is difficult. Since pancreatic cancer usually found in Stage IV, there is no effective therapy for it [1]. The 5-year survival rate among patients with pancreatic cancer is 9%, which is the lowest among all cancers. Therefore, early detection of pancreatic cancer is desirable. Early detection of pancreatic cancer has become possible by analyzing microRNA (miRNA) from the peripheral blood [2]. Analysis of miRNA allows for detection of pancreatic cancer foci as small as 0.1 mm in diameter. The sensitivity of this test is more than 96% [3]. Because of this sensitivity and specificity of the test, the location of the tumor may not be indicated by conventional radiologic modalities such as CT, MRI, and PET-CT. Thus pancreatic cancer is often not found by imaging, it is a problem that the technical innovation of the diagnostic technology using miRNA analysis does not relate to treatment at once.

In order to make effective use of the early diagnosis method of high sensitivity, we found a method for reducing the risk of cancer bearing.

We examined the ability to determine the risk of pancreatic cancer using miRNA from blood. At the same time, we also investigated whether our newly developed supplements can efficiently decrease the risk of pancreatic cancer.

We will report here our new preventive intervention method to reduce the risk of pancreatic cancer using our original supplements for patients with a high risk of pancreatic cancer.

2. Materials and Methods

The approval to perform this study was obtained from ethical committee of Southern Tohoku General Hospital. Documented informed consent were obtained by each subject.

Blood samples were obtained from 14 healthy adults for miRNA extraction. The patients consisted of seven men and seven women ranging in age from 64 to 78 years (average, 67.6 years).

RNA extraction was performed using standard protocol of commercial miRNeasy 96 Kit (Qiagen, Netherland). Total RNA concentration was evaluated by Nanofrop2000 spectrometer (Thermo Scientific, USA). Quality assessment of total RNA samples was performed using Agilent 2100 Bioanalyzer (Agilent Technologies, USA). Small RNA libraries were prepared using TruSeq Small RNA Sample Preparation (Illumina) according to the manufacture's protocol with 1 ug RNA input per sample followed by RNA 3' adapter ligation, RNA 5' adapter ligation, cDNA synthesis, PCR amplification using unique barcode sequences for each sample and gel size-selection of small RNA library. The yield of sequencing libraries was assessed using the Agilent 2100 Bioanalyzer (Agilent Technologies). Multiplexed libraries were sequenced on Ion GeneStudio S5 next-generation sequencing platform (Thermo Fisher Scientific, Japan), and the risk of pancreatic cancer was calculated as the expression score (ES).

The presence of tumors was evaluated by radiographic images such as CT (160 channels, GE, USA), 3T -MRI (Signa, GE, Japan) and PET-CT (GE, USA). After confirming the absence of visible tumor, the patients took our newly designed supplements orally for 3months. The supplements consisted of beta-glucan (Meshima, 2 g/day) and methyl-resveratrol (pterostilbene; 2 caps/day).

Risk determination was then carried out repeatedly by analyzing miRNA from the patients' blood samples. Changes in the tumor-bearing risk after treatment with our tumor risk-reduction supplements were evaluated by the ES as calculated by next generation sequencing, just before and after the intervention and followed up 8 months after treatment, then the results were examined by the Wilcoxon test.

3. Results

The average ES before and after the intervention was -718 and -965, respectively.

After the proactive intervention of our tumor risk-reduction supplements, the ES significantly declared in 11 (Wilcoxon test, $p < 0.0052$) of 14 patients (79%) (Fig.1). Furthermore, the 14 patients were divided into Group A ($n = 8$), who shown a higher ES (mean; -564) than the average ES (-900) of healthy persons, and Group B ($n = 4$), who shown a lower ES (mean; -1007) than the average ES of healthy persons. In Group A, all eight patients (100%) showed a significant reduction of the ES ($p < 0.009$) (Fig. 2). In Group B, however, no significant reduction of the ES was obtained ($p = 0.465$) (Fig.3).

Supplement for 3 months in group A, without adding further intervention, and 8 months after completion of supplementation, ES were measured in three patients and found it remained unchanged.

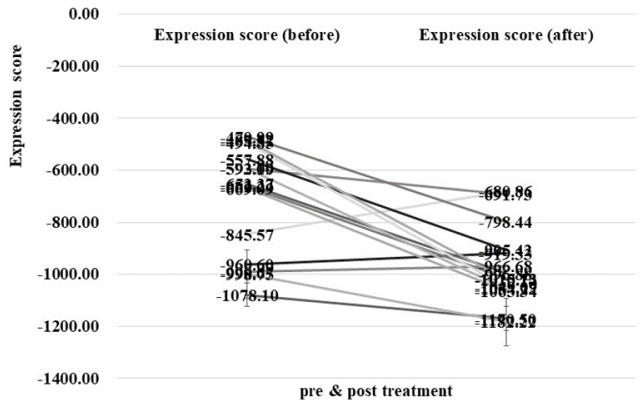

Fig.1 , Change in risk before and after intervention in all cases

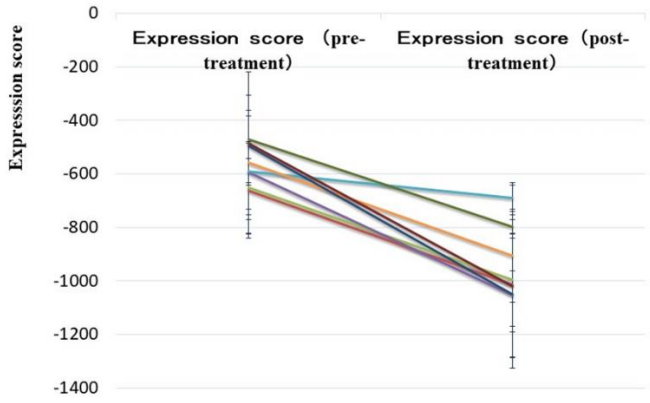

Fig.2, Changes in high risk before and after intervention

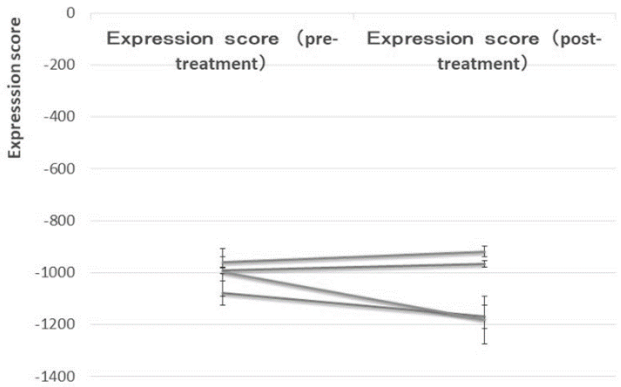

Fig.3, change in risk among low-risk individuals before and after intervention

4. Discussion

Pancreatic cancer remains one of the most lethal malignant neoplasms that caused 432,242 new deaths in 2018 (GLOBOCAN 2018 estimates). Globally, 458,918 new cases of pancreatic cancer have been reported in 2018, and 355,317 new cases are estimated to occur until 2040. Despite advancements in the detection and management of pancreatic cancer, the 5-year survival rate still stands at 9% only [1].

Worldwide incidence and mortality rate of pancreatic cancer in both males and females increases with age, and almost 90% of all deaths occur after the age of 55 years [4]. Pancreatic cancer is very difficult to detect and is often very advanced at the time of detection, making it a deadly and frightening cancer. That's why finding pancreatic cancer as soon as possible is the most important point.

Tumor markers used to diagnose pancreatic cancer include CA 19 -9, CEA, Dupan -2, and Span -1. Some tumor markers are more likely to appear in certain organ cancers, but many are made in more than one organ. It can also be elevated in diseases other than cancer (false positive), so high tumor markers do not make a cancer diagnosis [5]. Also, tumor markers are often not elevated in early stage cancers and cannot be used for early diagnosis of pancreatic cancer.

Abdominal ultrasonography (so-called abdominal echo)" is a standard and most sensitive imaging examination that may detect pancreatic cancer [6]. Pancreatic cancer must be detected early, when the tumor is 2 centimeters or smaller, but data show that abdominal ultrasound has only a 0.003% chance of detecting pancreatic cancer early. That means it's very difficult to detect pancreatic cancer early in a standard physical examination. Therefore, there are currently no definite guidelines for effective screening for pancreatic cancer.

The miRNA diagnosis used in this study is epoch-making because it has high specificity and sensitivity and can detect early lesions as small as 0.1 mm^3. However, diagnosis of pancreatic cancer with such sensitivity is difficult because the neuroradiological system and sensitivity do not catch up, and there is no other way than to closely follow patients. If the ES of the miRNA diagnosis is high, even if it is not visible in the image, the risk can be reduced by the supplement we devised, and if the lifestyle is not disturbed, the reduction in risk lasts more than 8 months.

Meshimas are mainly composed of P-glucan obtained from mushroom hyphae. P-glucan is known to activate natural killer T cells, T cells, B cells, and macrophages several times [7]. Pterostilbene also increases the activity of inhibitory miRNAs and exhibits anticancer effects [8]. Meshimakobu (1 pack/day) and pterostilbene (2 tablets/day) were taken after meals and continued for 3 months. After taking the drug for 3 months, a blood sample is taken, and risk is determined by miRNA.

Based on scientific evidence it is suggested that quitting smoking, drinking moderately, eating a balanced diet, physical activity, proper weight, and infection prevention are effective in preventing cancer. Those items are [1] related to daily life habits. By practicing the five health habits, we can lower the chance of getting cancer by our own efforts.

In conclusion, the paradigm of preventive medicine in the future is to use miRNA diagnostics to identify disease risk and, if there is no visible cancer, to take our cancer-reducing supplement for 3 months. After confirming that the cancer risk has decreased, it may be important to observe the five lifestyle behaviors such as quitting smoking, drinking moderately, eating a balanced diet, physical activity, and keep proper weight, and to protect your body so that the cancer risk does not rise again. This is what preemptive medicine should be and is a goal.

5. Conclusion

For patients at high risk of pancreatic cancer (e. g., those with a high ES), we found it possible to efficiently reduce the ES by means of our newly designed supplies. The risk reduction effect lasted at least eight months. This treatment represents effective practice of preemptive medicine.

6. References

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