Research Article

Combining Precision Treatment with Precision Prevention Based on Integration of Western and Chinese Medicine: A Protocol for A Novel Precision Medicine in Colorectal Cancer

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#Equally contribution

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Abstract

Colorectal Cancer (CRC) incidence and mortality had been steadily increasing over time in the past decades. To reduce CRC incidence and mortality, precision medicine in CRC needs to be extensively studied and highly developed. We proposed a novel precision medicine in CRC that should combine precision treatment with precision prevention in CRC based on integration of western and traditional Chinese medicine, which is theoretically much more precise, comprehensive, and have better efficacy than current routine treatment in CRC. In this protocol, we planned to conduct a randomized clinical trial. The expected survival indexes including the survival time, life quality and one-year or two-year survival rate in the proposed precision medicine group shall be significantly better than that in the control group. This novel precision medicine in CRC shall help reduce CRC incidence and mortality eventually.

Keywords: Colorectal cancer, Precision medicine, Combination of precision prevention and precision treatment, Integration of western and Chinese medicine

Introduction

Colorectal Cancer (CRC) has become a common malignant cancer worldwide [1-6]. There were 1800,977 newly diagnosed CRC cases and 861,663 deaths worldwide in 2018, and its age-standardized incidence rate was averagely 19.7/100,000 people, ranking in the third among 36 cancers, and its age-standardized mortality rate was 8.9/100,000 people, ranking in the second among 36 cancers [3,4]. Both CRC incidence and mortality in China were linearly increasing over time in the past 10 years [2-4]. There were 521,490 newly diagnosed CRC cases and 247,563 deaths in China in 2018, and its age-standardized incidence rate was 23.7/100,000, ranking in the second among 36 cancers, and its age-standardized mortality rate was 10.9/100,000 people, ranking in the second among 36 cancers [3,4]

The increasing trend in CRC incidence in China is mainly related to the economic development which index is named human development index in the past decades [3]. The risk factors associated with CRC incidence include smoking (cigarette smoke), drinking (alcohol consumption), lack or too little vegetables and fruit consumption, too much red/processed meat consumption, being obese, physical inactivity, being not periodically participating in screening tests (which helps remove polyps or other precancer conditions to prevent CRC), and other factors [2]. And the main factors related to CRC mortality have being diagnosed at the late stage, being not participating in screening tests, lack effective therapy, ineffective therapy to cause CRC recurrence, lack appropriate health education to prevent CRC recurrence, and others [2,7].

In order to reduce the CRC incidence and mortality, a lot of attention has been paid to precision diagnosis (focusing on individual CRC diagnosis) and precision treatment [5,6,8], but not much to the individual CRC prevention-precision prevention. Both precision diagnosis and precision treatment mainly depend on individual genetic mutations of the tumors obtained through biopsy which have not really helped improve the CRC prognosis in the population at all (as known the CRC mortality in China has been going up over time in the past 10 years). In addition, due to the colorectal special structure and functions and its residue after the surgery (it is impossible to remove the whole colon and rectum parts when the first primary CRC diagnosed), CRC have a good chance to get recurrent. Therefore, we proposed to combine treatment with precision prevention together during the CRC treatment.

Precision treatment in CRC based on western and traditional Chinese medicine tends to be more effective [9]. We believe adding precision prevention to precision medicine in CRC based on integration of western medicine and traditional Chinese medicine shall be much more effective. Therefore, we proposed an innovative precision medicine which combines treatment with precision prevention based on integration of western medicine and traditional Chinese medicine.

Precision prevention and treatment requires advanced technology and skills in medicine for CRC prevention, diagnosis, and treatment. Considering the facts that current medicine, molecular biology, environmental health science, genomics and many other related sciences and technologies have been getting advanced and matured enough, it is possible for precision prevention and treatment in CRC to come true.

With the current advanced science and technology, our protocol of precision treatment and prevention in CRC can be feasible theoretically and practically. Based on literature search through the databases of www.medbooks.com.cn, Medline, and PubMed, there was no similar report to our protocol, which indicated our proposed precision medicine in CRC is innovative.

Methods

Study Design and Patients

We designed a double blinded randomized clinical trial to test the efficacy of our proposed precision medicine in CRC. All patients shall be invited and provided with a consent form. Once patients agree and sign the consent form, they shall be randomized into two groups, one treated with individually personalized therapy based on proposed precision medicine as an experimental group and the other with routine treatment as a control group. This individually personalized therapy shall change with the CRC situation and other related information during the follow-up. This protocol was approved by the Ethics Committee of the Quzhou Hospital of Traditional Chinese Medicine (TCM) before and after obtaining the grant supported by the Zhejiang Chinese Medical University Affiliated Hospital Specific Scientific Research Fund (Grant #: 2021FSYYZZ11 to Dr. Hong-Hong Zhu).

Study patients shall be those diagnosed with primary CRC in Quzhou city.

A.   Inclusion Criteria are

a)   newly (defined as within three months) diagnosed with primary CRC patients and

b)   age ranging from 18 to 75 years old.

B.   Exclusion Criteria are those

a)   having severe disease with kidneys or heart

b)   being allergic to Chinese herbs

c)   having mental illness and

d)   having severe contagious diseases.

Proposed Innovative Precision Medicine in CRC: Precision Treatment and Prevention in CRC Based on Integration of Western and Chinese Medicine

Table 1: Proposed novel precision medicine in Colorectal Cancer (CRC) named as Precision treatment and prevention in CRC: Combining precision treatment with precision prevention based on integration of western and Chinese medicine [2,5,7-12].

Precision Treatment and Prevention in CRC			
Precision Prevention in CRC		**Precision Treatment in CRC**	
Western Medicine	**Chinese Medicine**	**Western Medicine**	**Chinese Medicine**
1st Prevention: Exposure prevention	Treat before CRC onset: prevention prescription	Health education: No smoking, less drinking, healthy diet, appropriate exercise, keep a good mood, etc.	Herbal treatment Herbal extracts Chinese exercises Keep a good mood etc.
2nd Prevention: Acquisition prevention	Treat CRC at its early stage: prevention prescription	Health education & Screening for early stage: colonoscopy, FOBT, FS, surgery, etc.	Herbal treatment Ear point sticker Herbal extracts Chinese exercises Keep a good mood etc.
3rd Prevention: Progression prevention	Treat CRC to prevent its progression: prevention prescription	Health education for behavior & diet changes and treat to prevent progression:	Herbal treatment Acupuncture Point injection Ear point sticker Multiple-herb chemotherapy Modern herbal extracts Herbal coloclyster Chinese exercises Keep a good mood etc.
4th Prevention: Complication prevention	Treat CRC to prevent complications: prevention prescription	The same as 3rd stage but emphasize on health education for behavior & diet changes	The same as 3rd stage but the dose and combinations may be different
5th Prevention: Death/disability prevention	Treat CRC to prevent death/disability: prevention prescription	The same as 4th stage	The same as 4th stage but the dose and combinations may be different

We proposed an innovative precision medicine in CRC named as precision prevention and treatment in CRC in 2021, which combines precision treatment with precision prevention in CRC based on integration of western medicine and traditional Chinese medicine (Table 1) [2,5,7-12] to come up with individually personalized therapy for each CRC patients in the experiment group. For example, if a 55-years-old man with smoking and drinking habits is diagnosed with primary CRC at the stage II, then the individual personalized therapy for this patient shall be: health education for stopping smoking and drinking, to arrange a surgery to remove the tumor as soon as possible, to use acupuncture to help recover from the surgery, and then to start treatment (based on individual histopathological results and or genetic mutations, either chemotherapy based on western medicine or herb treatment based on tongue and pulse or acupuncture or their combination or sequential treatment when the patient has recovered from the surgery. This personalized therapy shall be changed with the change in disease situation during the follow-up.

Data Collection

Questionnaire data and clinical information shall be collected for each participant at the baseline and follow-ups. Questionnaire data including demographic information, lifestyle such as smoking and drinking, diet habit, and other related information shall be collected once the CRC is diagnosed. Clinical information includes CRC symptoms and signs and its stage, histopathologic results, and gene mutations such as KRAS, NRAS, BRAF, PI3KCA, and FGFR, serum biomarkers such as Carcinoembryonic Antigen (CEA), carbohydrate antigen 19-9 (CA-199), and pyruvate kinase isoenzyme M2 (M2-PK), clinical symptoms and signs based on Chinese medicine such as type of patients' tongue and pulse and others.

Statistical Analysis

STATA SE 15.1 shall be used to estimate the sample size for this pilot study. Set the type I error at 5%, type II error at 20% and expected survival rate ratio between the experiment and control group at 2, using Schoenfeld method for the log rank survival analysis, the minimum sample size needs 33 CRC patients per group. Considering the limit of the study time and effort and 20% lost to follow-up, we plan to recruit 50 CRC patients per group. Cox regression and log rank analysis will be used for data analysis.

Expected Results

After controlling for other risk factors, the survival time in the proposed precision medicine group shall be significantly longer than that in the control group; the life quality in the proposed precision medicine group shall be significantly higher than that in the control group; and the one-year or two-year survival rate in the proposed precision medicine group shall be significantly higher than that in the control group.

Discussion

Our proposed innovative precision medicine in CRC, i.e., precision treatment and prevention based on integration of western medicine and traditional Chinese medicine in CRC, shall have better efficacy than the current precision medicine in CRC based on the personal genome information in this pilot study based on the findings of the survival time, life quality and the one-year or two-year survival rate between the two groups. In theory, novel precision medicine combining precision treatment based on western medicine with

a) precision treatment based on traditional Chinese medicine

b) precision prevention based on western medicine and

c) precision prevention based on Chinese medicine together, either simultaneously or sequentially shall overall improve the CRC survival rate and time and their life quality.

In practically, the real situation of CRC, especially the metastatic CRC, however, is much more complicated than what we thought. We believe this innovative precision medicine in CRC shall help reduce CRC incidence and mortality in the long run.

Acknowledgment

Conflict of Interest

None.

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