John R Saunders, Jr, MD Research Award Proposal

Complementary medical therapy (acupuncture) to improve the control of head & neck cancer patient symptoms of disease and treatment side effects

Investigators

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Abstract

Complementary medical therapies such as acupuncture have independently been shown to be highly effective in controlling symptoms of disease without unpleasant side effects of traditional therapy. We propose to test the hypothesis that in a population of Head & Neck cancer patients acupuncture can reduce symptoms of disease while preserving the delivery of anti-neoplastic oncologic treatments such as chemotherapy or radiation therapy. Moreover, we will be able to calculate the cost-effectiveness of acupuncture to determine the value of complementary therapy in caring for Head & Neck cancer patients.

Background

Head and neck cancer patients experience an array of unpleasant symptoms due both to their disease and from the side effects of conventional treatments used to treat those diseases (surgery, chemotherapy or radiation therapy). Pharmacological interventions used to treat both ancillary symptoms of disease and side effects of treatment are sometimes ineffective or not very well tolerated by patients.

Complementary medical therapies such as acupuncture have shown the ability to provide relief of these symptoms of disease without unpleasant side effects of traditional therapy or reduction in efficacy of anti-neoplastic oncologic treatments such as chemotherapy or radiation therapy (1-4). Moreover, acupuncture has been shown to boost red blood cell counts, and enhance lymphocyte and natural killer (NK) cell activity (5-8).

In general, acupuncture has proven to be clinically highly effective in the treatment of nausea, xerostomia and pain syndromes (9-14) which are the most common symptoms and side effects experienced by head and neck cancer patients. We propose to investigate the impact of complementary health therapies such as

acupuncture as an adjunct therapy in conjunction with conventional medical treatment, hospice and rehabilitation protocols to manage these symptoms.

There is considerable literature supporting acupuncture treatment of chemotherapy induced nausea and vomiting (15). For pain management of various origins there is also considerable literature to show efficacy of acupuncture (16-18). Furthermore, there is also research demonstrating the efficacy of acupuncture for treating xerostomia (19-22). Review of the literature reveals that there has never been a direct head to head measurement - in the same patient population (specific cancer patients) at the same time - of traditional vs traditional plus complimentary therapies in the management of cancer patients' symptoms.

Healthcare in the U.S. is on the threshold of fundamental change. Powered by advances in federal policy, the underlying way in which we pay for healthcare is moving from traditional fee-for-service, pay-for-volume historic approach to one that pays for demonstrated value. The way in which value is measured is still evolving, but risk-sharing, measuring the health status of populations and coordinating care in order to improve effectiveness and reduce total cost of care are the planks upon which this new environment is being built. Since current healthcare delivery is so fragmented, it is unclear how much is typically spent on therapy for head and neck cancer patients. Specifically, it is not known what the relative contributions to the cost of care are made

up by cytotoxic tumorocidal therapy and/or therapy directed toward rehabilitative and palliative care to control undesired symptoms.

Methods

We propose to measure traditional variables associated with both intra-therapy and post-therapy recovery to ascertain whether acupuncture has any effect. Utilizing a validated head & neck cancer specific psychological, quality of life and satisfaction tool we will measure whether acupuncture has an effect on those important parameters of care reflective of recovery and return to normal activity post-therapy. Specifically, we intend to collect metrics of patient adherence, compliance, tolerance of prescribed treatments and the ability to complete all prescribed therapy to ascertain whether acupuncture has an effect on those important clinical outcomes.

We intend to employ new business intelligence tools to query all aspects of the healthcare system for both historical data and then measure data prospectively once patients are enrolled in the trial. Specifically, we propose to leverage the Crimson suite of business intelligence tools (Crimson Clinical Advantage, Crimson Continuum of Care, Crimson Market Advantage and Crimson Population Risk Management) to track care delivery and cost (charges) of care delivery across the continuum of care to advance quality goals and identify opportunities for efficiency and cost savings. Since acupuncture typically occurs outside the framework of the medical healthcare system, it is unknown how much is spent on patients who receive acupuncture throughout their course of treatment. We intend to employ the same business intelligence tools to measure that component of care as well. Having unique access to these two

metadata sets, will allow us to begin to calculate value propositions in the care of this specific group of cancer patients. Beginning with this study which will compare one facet of care (acupuncture), we will be able to elaborate a model for future measurement of the value of complementary therapeutic interventions in other patient populations.

Innovation

The value of complementary therapies in traditional healthcare practice in general and in cancer care specifically is difficult to measure. Typically, complementary therapy is administered in an *ad hoc* fashion, usually outside the confines of traditional care delivery. We propose to integrate complementary therapy into the same care pathway and to collect the cost of care and outcomes of care using the same metrics and quality of life and business intelligence tools. This will allow the aggregation of disparate data from sources not typically aligned and interoperable, thereby allowing direct measurement of the global impact of complementary therapy on the total care delivery system.

Specific Aims

Primary Aim:

Can acupuncture treatments improve quality of life for head and neck cancer patients during and 6 months after treatment (surgery, chemotherapy and/or radiation therapy) by alleviating side effects of disease and conventional medical treatments?

Secondary Aims:

(1) can complementary therapy (acupuncture) provide symptom relief and mitigate specific side effects (*e.g.* pain, xerostomia, dysphagia, odynophagia) in patients with head & neck cancer undergoing therapy or in hospice care?

(2) are complementary therapies such as acupuncture cost effective?

Design

Interventional Clinical Trial: Compare head & neck cancer patients undergoing anti-neoplastic treatment receiving conventional therapy only to control symptoms of disease and mitigate side effects of therapy with a group of identical patients receiving acupuncture therapy in addition to conventional therapy.

Subject Selection

Male and female adult head and neck cancer patients currently undergoing active anti-neoplastic treatment (including hospice and social and psychological support) at GBMC.

Inclusion Criteria:

Each patient must meet the following criteria to be enrolled in the study.

1) Age greater than ≥ 21 years.
2) Ability to comprehend and willingness to provide written informed consent in accordance with institutional and regulatory guidelines.
3) Willing and able to comply with the investigational nature of the study and cooperate with study investigators.
4) Patients undergoing

a. Primary radiation with or without chemotherapy, or
b. Surgery followed by radiation with or without chemotherapy, or
c. Induction chemotherapy followed by radiation and chemotherapy

5) Biopsy proven carcinoma of the head and neck.

Exclusion Criteria:

Patients who meet any of the following criteria will be excluded from the study.

1) Patients who do not speak or are not fluent in English (written and spoken language).
2) Inability to demonstrate understanding of the scale used to rate quality of life.
3) Palliative care patients with expected life expectancy of < 6 months.

Recruitment: Educate internal and external physicians on the experimental protocol, inclusion and exclusion criteria and processes to identify potential study candidates. We will focus on oncology physicians (Medical Oncology, Radiation Oncology, Head & Neck Surgery, Otolaryngology, Thoracic Surgery, Hospice & Palliative Care) at GBMC

and active patients at The Sandra & Malcolm Berman Cancer Institute at GBMC, the Milton J Dance, Jr., Head & Neck Center and Gilchrist Hospice at GBMC.

Sample size: Using a validated cancer specific quality of life survey tool that measures both satisfaction and weighting of various metrics associated with the impact of disease and side effects we will be able to generate an impact score of the degree of disruption of patient's lives by their disease and treatment. Serial administration of the survey tool over the time frame of the study will allow us to measure the impact of therapeutic measures on the impact score of the degree of disruption of patient's lives.

A sample size of 30 in each group can achieve 81% power to detect a difference of 15 in score between the two groups when the FACT-HN score in the control group is 105 and the standard deviation is 20, with a significance level (alpha) of 0.05 using a two-sided two-sample equal-variance t-test.

The total sample size of 60 participants is considered very achievable within the timeframe of this study. The total annual caseload of Head & Neck Cancer patients makes it feasible and reasonable to conduct this study based on the estimated recruitment target numbers (368 new patients were presented to tumor board in FY15). The Sandra and Malcom Berman Cancer Institute at GBMC sees 2000 patients each

week. Head and neck oncology statistics at GBMC confirm that a significant number of patients would be eligible for participation in this protocol.

Analysis plan: The quality of life will be summarized in scores and the difference at 6 months will be compared with two-sided two-sample t-test. The average difference of quality of life between the two groups at all follow-up visits will be estimated with a GEE model. The side effects symptoms will be presented with categorical variables and compared between the two groups with chi-square test. The cost of the complimentary therapies group will be compared with the conventional therapy groups with two-sample t-test.

Setting

(1) Milton J Dance, Jr., Head and Neck Center at GBMC

The Milton J. Dance, Jr. Head and Neck Center provides comprehensive care to patients with disorders of the head and neck and their families. The Center includes head and neck surgery, multidisciplinary head and neck rehabilitation services, a full range of speech-language pathology services and a highly specialized voice center. The Milton J. Dance Jr. Head and Neck Center also provides a wide range of programs and services to improve our patients' quality of life. Patients and family members receive exceptional care through counseling and education, discharge planning, home health care coordination, support groups, professional voice care, head and neck cancer care, interdisciplinary patient care conferences, and more. Every step of the way, our patients experience compassion from people who care in a healing, supportive environment.

(2) Sandra & Malcolm Berman Cancer Institute at GBMC

The Sandra & Malcolm Berman Cancer Institute's comprehensive, multidisciplinary cancer program meets the rigorous standards that earn full accreditation by the American College of Surgeons Commission on Cancer. GBMC maintains our Commission on Cancer accreditation by going through a comprehensive facilities evaluation every three years. Approval is given only to those facilities that voluntarily commit to providing the highest level of quality cancer care and undergo a rigorous evaluation process and performance review.

In addition, we have been nationally and locally honored for outstanding care, service and innovation by a wide range of institutions and publications:

- Chosen as one of only two cancer programs in Maryland, and the only one in the Baltimore region, to receive the prestigious Outstanding Achievement Award for quality oncology care by the American College of Surgeons Commission on Cancer.
- Offers more than 60 research and treatment clinical trials annually through our affiliation with several national cancer research organizations, and our partnership with the Johns Hopkins Clinical Research Network. Approximately 150-200 patients are enrolled in research trials annually.

(3) Integrative Health Centers

The Integrative Cancer Program at IHC aspires to aid patients in their cancer journey. The integrative treatments are meant to be used in addition to traditional Western medical care to lessen the side effects of treatment and improve patients' quality of life. This program is not a replacement for chemotherapy and radiation; rather, it complements those treatments to help patients heal and recover. IHC practitioners cooperate fully and coordinate with patients' surgeons, medical oncologists, and radiation oncologists to ensure the delivery of optimum care. Customized treatment plans are created to meet patient's individual needs. Over the past 11 years IHC has treated over 7000 patients and IHC practitioners have developed relationships with dozens of physicians, physician groups and hospitals creating a unique integrative medical experience for our patients. IHC is a caring, peaceful environment with skilled practitioners who focus on supporting and empowering patients.

Protocol

Head and neck cancer patients undergoing standard anti-neoplastic therapy (surgery, chemotherapy or radiation therapy) or who have enrolled in hospice care will be offered the opportunity to participate in the study. Patients who demonstrate a willingness to participate will be educated about the 2 arms of the trial to control symptoms of disease and side effects of therapy – conventional pharmaceutical management or both conventional and complementary therapy (acupuncture) therapy.

Patients who agree to participate in the trial will be randomized to one of the two arms for adjunctive treatment of symptoms and side effects. Patients undergoing palliative care only will be so identified to allow for *post-hoc* analysis of this potentially confounding variable.

Cost of treatment (charges) of disease symptoms and side effects of therapy - but not anti-neoplastic therapy (surgery, chemotherapy or radiation therapy) – will be collected concurrently during the course of the trial. Because each patient is uniquely identified in the healthcare system, charges for treatment can be collected in parallel when they are generated. The cost of acupuncture treatments will be simulated by using standard charges for acupuncture treatments outside the context of this trial. All other charges for care will be collected as billed.

The ability of each arm of therapy to control symptoms of disease and side effects of anti-neoplastic therapy will be measured with a validate head & neck cancer specific quality of life tool (appendix I: FACT-H&N (Version4) questionnaire).

Patients who consent to participate in this study and are randomized to receive both traditional and complementary therapy (acupuncture) will receive acupuncture therapy before and after radiation treatments or chemotherapy infusion treatments at GBMC. Patients enrolled in hospice care will receive complementary therapy as dictated to control symptoms.

We will arrange for space to be available either in the Thoracic Surgery offices (Physicians Pavilion West suite 400) or in the Milton J Dance, Jr Head & Neck Center (Physicians Pavilion West suite 401) so as to be convenient for patients coming to the Milton J Dance, Jr Head & Neck Center (Physicians Pavilion West suite 401) or the Sandra & Malcolm Berman Cancer Institute (Physicians Pavilion West suite 200 (Medical Oncology), or Greater Baltimore Medical Center (Radiation Oncology) for treatment.

Patients enrolled in rehabilitation or hospice/palliative care will receive treatment twice weekly on an outpatient basis either at GBMC or at Integrative Health Centers.

Acupuncture Therapy Protocol:

Patients will receive acupuncture therapy twice weekly for a period of 12 weeks. Progress will be evaluated following each visit with a more thorough evaluation of progress every 4 weeks. We will not use specific acupuncture points for every patient. The acupuncture point selection will be tailored to each individual's symptom presentation and adjusted each visit accordingly based on patient feedback.

Potential Risks:

There are rare serious complications associated with acupuncture. Reviewers point out that injuries relate directly to insufficient training (23-24). White (2004) surveyed 12 prospective studies of more than a million treatments reporting 'the risk of a serious adverse event with acupuncture is estimated to be 0.05 per 10,000 treatments, and 0.55 per 10,000 individual patients. The conclusion was that the risk of serious events occurring in association with acupuncture is very low, and below that of many common medical treatments.

Harms associated with acupuncture can be listed as risks of the following:

- Infection
- Lesions including organ, vascular, and nerve puncture injury
- Bleeding
- Broken and migrating needle

Negligence is involved in almost all cases of infection, organ or vascular puncture, bleeding and broken or migrating needle. Some infections and lesions are rare unexpected complications that might be avoided in the future.

Infection from negligent acupuncture has been associated with transmission of the following diseases:

- Hepatitis (in the U.S., Vietnam, Korea and China) (25-27)
- Tuberculosis (28)
- Mycobacterium (28)
- Methicillin-resistant Staphylococcus aureus (MRSA) infection

An MRSA infection related to acupuncture negligence caused a severe case of septic arthritis in Hong Kong and necrotizing aortitis with infected pseudoaneurysm in Korea (29). A medical practitioner in Perth, Western Australia who was colonized with MRSA was responsible for transmission to eight patients using acupuncture and joint injections.

Traumatic lesions include punctures of any of the following:

- Thoracic viscera (cardiac tamponade, endocarditis, pneumothorax)
- Abdominal or retroperitoneal viscera
- Peripheral nerves
- Central nervous system
- Blood vessels

While qualified acupuncture programs that lead to licensure have greatly reduced the incidence of traumatic lesions, “It is important to recognize that even one avoidable

adverse event is one too many...It should be emphasized that medical practitioners are not exempt from the need to study anatomy relevant to acupuncture, since they are unlikely to have needed this information in conventional medical practice" (30).

Patient quality of life outcomes will be measured with a validate cancer specific quality of life tool (appendix 1: FACT-H&N (Version4)) modified specifically for this study for general symptom relief, pain levels and quality of life metrics at baseline, 3 months, 6 months and 12 months of participation in the research protocol.

Timeline

Months 1-2 – Internal and external patient recruitment/education

Months 1-12 – Administer treatment(s) – collect data

Month 12 – Analyze data

Budget

Funds awarded through the John R Saunders, Jr, MD Research Award will be used to:

(1) Provide a stipend to the provider of acupuncture treatments (DT) on the GBMC campus ($15,000).

(2) Help cover the costs of having the Clinical Research Associates (CRAs) in the Milton J Dance, Jr Head & Neck Center and the Sandra & Malcolm Berman Cancer Institute administer the Quality of Life Surveys and collect survey data ($2500).

(3) Help pay for the costs of having a health information technology data analyst at GBMC create and run financial reports to collect and analyze the cost of care data ($2000).

(4) Create and disseminate tactical tools to advertise and promote the study and facilitate patient enrollment ($500).

Other sources of Research Support

None

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Appendix I – Quality of Life Assessment Tool

FACT-H&N (version4) – file attached.

Appendix II – Biographical Sketches and CVs of All Investigators

Investigator's CVs and Biosketches – files attached.