Homoeopathic Treatment as an Add-On for Minimizing After Effects of Conventionally Treated Cancer Patients: A Simple Randomized Pilot Study—Protocol from Northeast India Perspective

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Abstract

The north-eastern region of India accounts for a total of 37,448 cancer cases reported from 11 population-based cancer registries (PBCRs) from 2012 to 2014. Studies suggest that with the holistic approach adopted by homoeopathy, not only the symptoms like cancer pain are alleviated, but also the overall well-being of the patient. Homoeopathy can be beneficial to minimize the treatment-induced adverse effects like radiation-induced mucositis, skin reactions, postoperative seroma, bleeding, and complications associated with the use of surgery, chemotherapy, and radiation therapy. This study intends to provide homoeopathic services as an add-on to conventional treatment to the patients referred for homoeopathic treatment after their due consent. The primary objective is to study the usefulness of homoeopathic medicines for combating the suffering of cancer patients having complaints other than cancer. A sample size of 70 patients per group in two arms (Arm A: standard allopathic drug and Arm B: standard allopathic drug + homoeopathic treatment) will be recruited using simple random sampling without repetition. Cancer patients reporting complaints other than cancer itself and suffering from the after-effects of cancer treatment with chemotherapy and radiation therapy to any reputed cancer institute will be screened and will be recruited according to inclusion and exclusion criteria. After completion of the six months study duration, results will be able to predict the role of homoeopathic treatment as an add-on to conventionally treated cancer patients to minimize the suffering other than cancer and the after-effects of chemotherapy and radiation therapy. If found significant, this could prove to be a contribution in the health care system in handling cancer cases that are very difficult to treat. Further, the cost-effectiveness of homoeopathy will enable developing countries to manage such a disease effectively.

Keywords

- cancer
- side effect
- add-on
- chemotherapy
- homoeopathic treatment
- north-east India
- protocol

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Introduction

The Northeastern region of India comprises eight states, namely, Arunachal Pradesh, Assam, Manipur, Meghalaya, Mizoram, Nagaland, Sikkim, and Tripura. A total of 37,448 cancer cases are reported from 11 population-based cancer registries (PBCRs) of 8 states during 2012 to 2014. Of these, male cases outnumber females, except in Manipur state. The number of cases ranges from 334 in Pasighat, Arunachal Pradesh and 5,463 in Kamrup district of Assam alone to 6,330 in Tripura. The average risk that a person will develop cancer in their lifetime (0–74 years) is ~1 in 5 for both sexes in Kamrup urban district. Risk factors are tobacco, alcohol, obesity, and so forth. Among males, lung cancer shows statistical significance increase than cancer of hypopharynx and esophagus. Incidence rate of breast and gallbladder cancer in females increased significantly from the year 2003 to 2014. Case fatality ratio in males is 32.9% whereas in females is 21.9%. For both sexes the case fatality ratio is 21.8%.

Cancer affects not only the patient in terms of pain, suffering, and quality of life (QoL) but their families too who face emotional, physical, and financial hardship owing to this life-threatening illness. The potential of homoeopathic medicines in preclinical and clinical stages of cancer has not been vastly explored. However, some preclinical studies have demonstrated the anticancer properties of homoeopathic medicines on different cell lines.^{1–10} The Central Council for Research in Homoeopathy (CCRH) has also conducted preclinical studies with Bose Institute, Kolkata, wherein the antitumorigenic activity of *Calcarea carbonica*, *Thuja occidentalis*, and sulphur were identified and their molecular mechanism(s) of action underlying apoptosis and tumor regression were delineated.^{11–13} Studies indicate that cancer pain can be palliated with homoeopathic treatment.^{14,15} PBCR of 2012 to 2014 recommends radiotherapy and palliative care for the treatment of cancer. Palliative care prevents and relieves suffering through early identification, correct assessment, and treatment of pain and other problems, whether physical, psychosocial, or spiritual.¹⁶ So homoeopathy can play a key role in palliative care treatment as it is evidenced that homoeopathic treatment is safe and causes minimal to no adverse effects. This is the main reason for its popularity in the world¹⁷ and it can be successfully integrated in supportive care integrative oncology service.^{18–20} The overall well-being of a cancer patient can be achieved by homoeopathy; positive results for emotional, physical, psychological, and QoL have been reported, evaluated on the basis of different validated questionnaires.^{13–15,21,22} Complications associated with the use of chemotherapy and radiation therapy may decrease the effectiveness of treatment by the need to reduce the dose or increase of the interval between cycles.²³ In this sphere also, homoeopathy can be used to minimize the treatment-induced adverse effects. Homoeopathic remedies can alleviate chemotherapy and radiation therapy side effects such as nausea, vomiting, fatigue, loss of appetite, depression, radiation-induced mucositis, and skin complaints^{24–27} without antidoting the positive effects. A prospective observational study of two

independent cohorts showed an improvement of QoL as well as a tendency of fatigue symptoms to decrease in cancer patients under complementary homeopathic treatment in comparison to conventionally treated cancer patients.²⁸

Background and Justification

Clinical trials are prospective research studies on human subjects, which clarify the new treatment modalities (novel vaccine, drugs, supplements, medical devices, etc.). Clinical trials provide guidance for further study or comparison with other modalities. Clinical trials are important to ensure the safety and efficacy of a drug. Modern system of medicine requires new medicine with the emergence of new diseases and hence the need of clinical trial is in evidence. Homoeopathic Pharmacopoeia of India (HPI) is the official book of standards of homeopathic medicine in terms of Schedule-II of the Drugs and Cosmetics Act, 1940, and Rules, 1945. Indian manufacturers are legally bound to manufacture homoeopathic medicine as per the standards and methodology given in the HPI. In this study we are using the drugs mentioned in the HPI which are proved on healthy human being. Homoeopathic drugs are tested in preclinical study setting.^{2,7,9–13,29–40} Further some studies show the effectiveness of the homeopathic drugs in malignant cases.^{14,41–45} But the objective of this study is to give supportive care to cancer patients using homoeopathic treatment as an add-on supportive therapy for minimizing the after effects and side effects of conventionally treated cancer patients. Clinical studies have found that homoeopathy is efficacious in the treatment of radiation-induced mucositis,²⁴ joint pain related to aromatase inhibitors,¹⁵ radiation-induced itching,²⁵ skin reactions during radiotherapy,²⁶ nausea, vomiting, fatigue, loss of appetite, depression, and so forth. Also, homoeopathy has a role in cancer treatment as supportive medicine,^{14,21,27} with better survival.²⁰ Cancer is not only a burden to the society but also causes distressing symptoms and a huge socioeconomic loss to the patient as well as to the country. Though the treatment comprises surgery, radiotherapy, and chemotherapy, the latter has been frequently advised to the patients as the mainline treatment until now. But chemotherapy is always accompanied with side effects that disrupt QoL of the patient. Chemotherapy, while destroying cancer cells, also damages healthy cells, whereas homoeopathic preparations are known for selectively targeting the cancer cells while sparing the healthy counterparts.⁴⁶ There are several studies which report that adding classical homoeopathy to conventional cancer care significantly improves the QoL and global health status.^{28,47} Studies have also reported positive effects of homoeopathy on fatigue symptoms in post chemotherapy patients.^{28,48} *Traumeel*, a homeopathic combination medicine, is known for reducing pain in cancer patients.⁴⁹ Preliminary data from a study suggested that there is some beneficial effect of homoeopathy in chemotherapy-induced stomatitis, but there is no convincing evidence for the efficacy of homeopathic remedies for other adverse effects in cancer treatments.⁵⁰ Few studies show the positive role of homoeopathy in controlling adverse effects of CT with

variable success including alleviating the most distressing symptoms as well as the QoL.^{48,51-53}

Objective

The primary objective is to study the usefulness of homoeopathic medicines for combating the suffering of cancer patients having complaint other than cancer using the Edmonton Symptom Assessment Scale revised version (ESAS-R), whereas secondary objectives are to assess the QoL using European Organization for Research and Treatment of Cancer–Quality of Life Questionnaire (EORTC QLQ-C30). Permission to use these scales should be taken from concerned scientific group.

The ESAS-R provides symptoms like pain, tiredness, drowsiness, nausea, lack of appetite, shortness of breath, depression, anxiety, and well-being, and any other complaint, if any. Each complaint has been graded 0 to 10 with best/no complaint to worst. The ESAS-R is intended to capture the *patient's perspective* on symptoms. However, in some situations it may be necessary to obtain the caregiver's perspective.

Health-related quality of life: The EORTC QLQ-C30 is an integrated system for assessing the QoL of cancer patients participating in clinical trials and other types of research in which patient-reported outcomes are collected. The EORTC QLQ-C30 is designed for use with a wide range of cancer patient populations. The EORTC QLQ-C30 incorporates nine multi-item scales—five functional scales (physical, role, cognitive, emotional, and social functioning); three symptom scales (fatigue, pain, and nausea/vomiting); and a global health status/QoL scale. Six single-item scales are also included (dyspnoea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties).

Study Design

Sample size was estimated to detect a difference of 1.2 points between two groups in pain intensity improvement based on recommendation of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) in the chronic pain trial. A sample size of 70 patients per group provided at least 80% power to detect the difference at a significance level of 0.05 using a two-tailed test.

- Sampling: simple random sampling without repetition will be used.
- Study group: two arms:
 - Arm A: standard allopathic drug.
 - Arm B: standard allopathic drug + homoeopathic treatment.

Statistical Methods

For this comparison, *t*-tests and analysis of variance (ANOVA) will be done for continuous variables and chi-square or Fisher exact tests will be performed for categorical variables. To achieve the objective a series of regression analyses were

performed to ascertain associations between variables. A 95% confidence interval (CI) along with *p*-value will be calculated to describe the association. A *p*-value < 0.05 was considered as statistically significant. IBM SPSS Statistics and GraphPad (Prism 5, Medcal, and Epi info software) will be used for all the statistical analysis.

Inclusion

The inclusion criteria are as follows:

- Patients willing to sign written informed consent.
- Patients with any stage of any type of cancer undergoing cancer treatment at a reputed cancer institute.
- Patient having any two of the following symptoms—
anorexia, nausea, vomiting, diarrhea, constipation, cough, shortness of breath, taste alterations, dry mouth, mucositis, dermatitis, conjunctivitis, lachrymation, hair loss, sensory neuropathy, flu-like symptoms, reduced blood count (but hemoglobin percentage [Hb%] not less than 6.5 mg/dL), cramping, urinary frequency, vaginal irritation, impotence, skin redness, fatigue, myalgia, anxiety, depression, and drowsiness.
- The patient should not be under homoeopathic treatment in the last 2 weeks.

Exclusion Criteria

The exclusion criteria are as follows:

- Patients who were not willing to volunteer for the study.
- Patients who developed serious complications like renal failure, idiosyncratic reactions, and severe medicinal aggravation.
- Patients requiring emergency surgical intervention like in the case of gastrointestinal obstruction.

Withdrawal

No serious risks are anticipated in this study due to homoeopathic intervention. In case the medicine does not give relief or aggravates the present condition and the disease progresses further, immediately care will be taken by providing the proper dose of medicine and/or rescue medicine (clinical homoeopathic treatment) where indicated. If any adverse event occurs, the participant will be withdrawn from the study.

Subject Recruitment and Screening

Patients reporting with complaints other than cancer itself and suffering from the after effects of cancer treatment with chemotherapy and radiation therapy to any reputed cancer institute will be screened for treatment.

Administration and Compliance

The first dose of the study drug will be administered under direct observation of the study physician in the hospital. Patients will be advised to take rest of the medication as per the study protocol and their compliance will be monitored in 15-day intervals or as per requirement.

Time Allocation for Study

Time allocation for the study is as follows:

- Screening and enrollment for 2 months.
- Treatment for 3 months from the date of screening.
- Data analysis for 1 month.

Homoeopathic Intervention

Procurement and Dispensing of Medicine

Procurement and dispensing of medicine will be done as follows:

- Homoeopathic medicines in dilutions of centesimal potency (6C, 30C, 200C, and 1M) for the study will be procured from any of the approved good manufacturing practices (GMP) firms.
- Globules/pills of size 30 will be used for medicating dilutions and dispensing alcohol will be used for preparing placebo resembling the medicine. These globules will be procured from same firms. One dose will constitute 4 globules moistened with the medicine or placebo.
- Investigator/pharmacist will dispense the homoeopathic medicine/placebo to the patients as per protocol.

Method of Selection of Individualized Homoeopathy Medicines

- Selection of the medicine will be done after case-taking on the basis of totality of symptoms.
- Repertorization shall be done using Homopath software.

Only one medicine whose portrait confirms in the *Materia Medica* will be selected as the first prescription with justification for the respective patient.

Follow-up treatment: Each patient will be followed-up (if necessary telephonically) at entry and on every third day or as per requirement.

- ESAS-R and EORTC QLQ-C30 will be filled at entry and on every third day till 3 months.
- Complete hemogram is to be done at entry and on every month till 3 months.
- Final assessment will be done after 3 months. It will include the filling of ESAS-R and EORTC QLQ-C30 questionnaires. Final analysis will be done by the statistician as per the directions given in the module of the scales.
- If the patient does not report on a fixed date effort will be made to contact him/her in any way. The data will be maintained in an Excel sheet so that it can be procured every month and when necessary for interim analysis.

Follow-up and second prescription: Follow-up of each case for the second prescription will be done in comparison to the symptoms at baseline. Subjective and objective amelioration and aggravation; new symptoms, if any; or no change with symptoms persisting will be noted down according to the proforma (►Table 1).

Degree of Improvement

The various degrees of improvement are listed as follows:

- **Marked**—more than 75% improvement in symptom score from baseline score.
- **Moderate**—50% to less than 75% improvement in symptom score from baseline score.
- **Mild**—25% to less than 50% improvement in symptom score from baseline score.
- **Not significant**—less than 25% improvement in symptom score from baseline score.
- **Not improved**—no change in symptom score from baseline score after sufficient trial of best-indicated drug has been done.
- **Worse**—increase of symptom score from baseline score.
- **Status quo**—no change of score from baseline score.
- **Referred**—referred for other therapy in the eventuality of any adverse event.
- **Withdrawal**—patient withdraws consent or refuses further treatment.
- **Drop out**—patient does not fulfill conditions as per the protocol.

The concept of this research is reflected in ►Fig. 1.

Safety and Adverse Events

At each contact with the subject, the investigator must seek information on adverse events by specific questioning as per “Reporting form for suspected adverse reactions–National Pharmacovigilance Programme for ASU & H Drugs” and reported immediately to Pharmacovigilance Centre.

Data Handling and Record Keeping

The patients will be informed by the investigator that all trial results recorded will be treated in strict confidence. During documentation and analysis of the trial, the individual patients will only be identified by their patient number, whereas the name of the patient and any personal data are subject to the data protection regulations. The investigator will be responsible for the completeness and accuracy of the study materials.

Study Monitoring, Auditing, and Inspecting

The study conducted in any suitable study site will be monitored according to the strict principles. The investigator will allocate adequate time for such monitoring activities. The investigator will permit study-related monitoring, audits, and inspections by the ethical committee, institutional review board, or government regulatory bodies of all study-related documents (source documents, regulatory documents, data collection instruments, study data, etc.).

Ethical Considerations

This study is to be conducted according to standards of good clinical practice. This trial will be conducted in accordance with the requirements of the Declaration of Helsinki. This consent form will be submitted with the protocol for review and approval by the ethics committee (EC) for the study.

Table 1 Follow-up and second prescription

Symptoms at baseline	Amelioration	Aggravation (indicate which type of aggravation)	New symptoms, if any	No change with symptoms persisting	Prescription with justification
	Not to disturb the action of the medicine (ref. Kent's 4th observation)	A prolonged aggravation without amelioration: reassess the case and observe the changes. If the same medicine is indicated, prescribe in suitable potency (ref. Kent's 1st observation). If another medicine is indicated, prescribe in lower potency. Long aggravation, but slow and final improvement: prescribe placebo, till the action of medicine is complete (ref. Kent's 2nd observation). Aggravation is quick, short, and strong with rapid improvement of the patient (homoeopathic aggravation): discontinue the medicine and prescribe placebo (ref. Kent's 3rd observation). Amelioration comes first and the aggravation comes afterwards: reassess the case and prescribe the indicated medicine in suitable potency (ref. Kent's 5th observation).	If the symptoms are not of a serious nature, wait till the new symptoms pass off. Then select another indicated medicine after reassessing the case. If the symptoms are of serious nature, reassess the case and prescribe the indicated remedy (ref. Kent's 10th observation). In case new symptoms keep on adding and patient's condition deteriorates further, the case may be referred for appropriate medical care.	In case there is no perceptible change (neither worse nor better) for a considerable time after administration of the medicine, same medicine to be repeated in the next higher potency. In case there is no perceptible improvement after adequate repetition of medicine in different potencies, the investigator must look for any obstacle(s) to cure and steps may be initiated to remove them. A record of such advice given to and/or followed by the patient is to be kept in the case follow-up forms. In case no such obstacle(s) is found, change of medicine is to be considered.	

Protocol Amendment

Protocol amendments will be possible only in exceptional cases (e.g., where the health or well-being of the patient is affected) and only after authorization by the authority. Every amendment must be justified in writing and signed by all those concerned.

Expected Outcomes

The results of the study will be able to predict the role of homoeopathic treatment as an add-on to conventionally treated cancer patients to minimize the suffering other than cancer and the after effects of chemotherapy and radiation therapy.

Discussion

A global burden of disease (GBD) study published in The Lancet Oncology⁵⁴ reported that of the northeastern states of India (with a population of 45 million people), particularly the states of Mizoram, Meghalaya, Arunachal Pradesh, and Assam have the highest burden of cancer in terms of age-standardized incidence, mortality, and low survival rates. As per the GBD report the high disability-adjusted life years

(DALYs) shown in the GBD in the northeastern region states mainly are contributed by cancers of stomach, esophagus, hypopharynx, gallbladder, lung, and breast. According to the latest report of PBCR (2012–2014, PBCR, NCRP-ICMR), esophageal cancer was observed as the topmost common cancer in all northeastern states compared with mainland India. Cancer is a life-threatening illness which affects the patients and their surroundings in all aspects—physically, emotionally, and also financially. PBCR of 2012 to 2014 recommends radiotherapy and palliative care for the treatment of cancer. Palliative care is an approach that improves the QoL of patients (adults and children) and their families in which homoeopathy can play a key role, with minimum or no adverse effects. Homeopathy can be successfully integrated in supportive care integrative oncology service^{18–20} for palliative care, for better QoL, and to increase the chances of survival in cancer patients. Homoeopathic remedies can alleviate chemotherapy and radiation therapy side effects such as nausea, vomiting, fatigue, loss of appetite, depression, radiation-induced mucositis, and skin complaints.

The potential of homoeopathic medicines in preclinical and clinical stages of cancer has not been vastly explored. However, some preclinical studies have demonstrated the significant anticancer properties of homoeopathic medicines on different cell lines.^{1–10}

Fig. 1 Study methodology.

A review was conducted to determine the Cochrane reviewers' opinion if any evidence exists for the effects of conventional cancer therapies by homoeopathy. After exploring, the database revealed that 7 out of the total 8 controlled trials in this area of study were placebo controlled and 1 was against an active treatment. In the 8 controlled trials, outcomes of 664 people are covered who were suffering from the adverse effects of conventional cancer therapies like radiotherapy, chemotherapy, or breast cancer treatment. Two out of 8 trials had positive outcomes toward homoeopathy. One of these outcomes proved the superiority of homeopathic mother tincture of calendula for the prevention of dermatitis from radiotherapy, while comparing with the effects of topical corticosteroid.⁵⁰ In a study of 82 patients, randomly assigned Cobaltum 30C or Causticum 30C proved to be beneficial in significant reduction in the dermatological reactions to the radiotherapy when compared with placebo.²⁷ Twenty-five women were treated with individualized homeopathic medicines for radiotherapy-induced itching at the University of Vienna's Department of Radiotherapy and Radiobiology. After assessment for 27 days, homoeopathic treatment had been successful in 21 women enrolled in the study.²⁵

The preclinical research on homoeopathy has evaluated the beneficial effects of homeopathic medicines against radiation.⁵⁵ Ginseng 6X, 30X, and 200X and *Ruta graveolens* 30X and 200X were administered before and after exposure of 100 to 200 rad of X-ray (sublethal doses) to albino mice and then evaluated after 24, 48, and 72 hours. Mice given any of these homeopathic medicines experienced significantly less chromosomal or cellular damage as compared with the placebo as treatment. Ginseng 30X and 200X, in particular, had significant and substantial benefits.^{55,56} There are evidence of positive effects of homeopathic crude doses of Ginseng which finds that it repairs DNA after radiation exposure.⁵⁷

In another study, when albino guinea pigs were exposed to small doses of X-ray, it reddened the skin. Homeopathic medicine *Apis mellifica* 7C or 9C showed protective effect and an almost 50% restorative effect on X-ray-induced redness of the skin.⁵⁸ Also, postsurgical complication of cancer cases may be managed by homoeopathy. A study suggested that patients who underwent total mastectomy suffered from postoperative seroma and bleeding. *Arnica montana* reduced the seroma and bleeding in those cases.⁵⁹

Conclusion

These studies have reported the positive outcome of homoeopathy in cancer; however, the effectiveness in preclinical and clinical stages of cancer needs more exploration. The results of the present study will be able to predict the role of homoeopathic treatment as an add-on to conventionally treated cancer patients to minimize the suffering other than cancer and the after effects of chemotherapy and radiation therapy. If found significant, this could prove to be a contribution in health care system in handling cancer cases which are very difficult to treat. Further, the cost-effectiveness of

homoeopathy will enable developing countries in controlling such a disease effectively.

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Conflict of Interest

None declared.

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