Original Article

Management of chronic pain with *Jalaprakshalana* (water-wash) *Shodhita* (processed) *Bhanga* (*Cannabis sativa* L.) in cancer patients with deprived quality of life: An open-label single arm clinical trial

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Abstract

Introduction: Pain is a common and complex symptom of cancer having physical, social, spiritual and psychological aspects. Approximately 70%–80% of cancer patients experiences pain, as reported in India. Ayurveda recommends use of *Shodhita* (Processed) *Bhanga* (*Cannabis*) for the management of pain but no research yet carried out on its clinical effectiveness. **Objective:** To assess the analgesic potential of *Jala-Prakshalana* (Water-wash) processed *Cannabis sativa* L. leaves powder in cancer patients with deprived quality of life (QOL) through openlabel single arm clinical trial. **Materials and Methods:** Waterwash processed Cannabis leaves powder filled in capsule, was administered in 24 cancer patients with deprived QOL presenting complaints of pain, anxiety or depression; for a period of 4 weeks; in a dose of 250 mg thrice a day; along with 50 ml of cow's milk and 4 g of crystal sugar. Primary outcome i.e. pain was measured by Wong-Bakers FACES Pain Scale (FACES), Objective Pain Assessment (OPA) scale and Neuropathic Pain Scale (NPS). Secondary outcome namely anxiety was quantified by Hospital Anxiety and Depression Scale (HADS), QOL by FACT-G scale, performance score by Eastern Cooperative Oncology Group (ECOG) and Karnofsky score. **Results:** Significant reduction in pain was found on FACES Pain Scale ($P < 0.05$), OPA ($P < 0.05$), NPS ($P < 0.001$), HADS ($P < 0.001$), FACT-G scale ($P < 0.001$), performance status score like ECOG ($P < 0.05$) and Karnofsky score ($P < 0.01$). **Conclusion:** *Jalaprakshalana Shodhita Bhanga* powder in a dose of 250 mg thrice per day; relieves cancerinduced pain, anxiety and depression significantly and does not cause any major adverse effect and withdrawal symptoms during trial period.

Keywords: Anxiety, *Bhanga*, *Cannabis sativa*, cancer pain, depression, quality of life, *Shodhana*

Introduction

Despite all advancements in prevention, early detection, with newer and more effective treatment modalities, cancer remains one of the most debilitating and deadly diseases and is second leading cause of mortality.[1] Sheer potential of suffering from cancer can be a horrifying experience for anyone bearing this diagnosis, while 'pain' is probably one of the most frightening symptom of cancers which usually intensifies as the disease progresses in 50%–70% patients.[2] Less than half of patients get adequate relief of pain, which negatively impacts their quality of life (QOL).[3] Generally, pain is a subjective feeling that has not till date been easily and universally quantified.[4] Patients with similar cancer types may experience different intensities of pain. Current WHO ladder method consistently failed to provide sufficient relief to 10%–20% of advanced cancer patients with pain and reported side effects of analgesics are the reasons for concern over these symptoms.[5] *Bhanga*

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(Cannabis) is a potent analgesic reported by folklore, Ayurveda as well as modern medical science and researches.[6] If used in *Ashodhita* (Unprocessed) form, may cause *Madakari* (Intoxicant) effects hence, Ayurveda classics have advised *Shodhana* (Purifying process) of *Bhanga* before its therapeutic use.[7] *Cannabis* leaves processed with water-wash method has been advised for the management of pain.[8,9] As per 'The 1961 Convention', due to inclusion under narcotic category,[10] therapeutic as well as research use of Cannabis was stopped. In 19th century, again, the drug started gaining scientific attraction due to its significant therapeutic effects in palliative oncology care; as concurrent use of morphine is reported to causes many ill effects.[11] Various researches report positive results of *Cannabis* in managing symptoms cluster developed in cancer patients.

Objective

To assess the clinical effectiveness of water-wash processed *Cannabis* leaves powder in cancer patients having complaints of pain, anxiety, depression and deprived QOL.

Material

Preparation of trial drug (TD) by *Jalaprakshalana* (Water-wash) processing method

Leaves of female species of *Cannabis sativa* L. were tied in a muslin cloth; washed with water till greenish color stops oozing out from leaves, later shade dried,[12,13] finely powdered with mixer grinder and filled in red and white hard gelatine capsule of size "0" and dimension 21.04 ± 0.4 having capacity of 250 mg. Patients were selected by 'purposive sampling' (Non-random) method from outpatient department and in patient department section of Raja Ramdeo Anandilal Podar, Central Ayurveda Research Institute for Cancer (RRAP-CARIC), Worli, Mumbai; irrespective of specific region, religion country.

Selection of patients

Inclusion criteria

Clinically diagnosed patients of all type of cancer; irrespective of their gender; between age 18 to 70 years; who were receiving possible available treatment(s) for the management of cancer or terminally ill patients with any Eastern Cooperative Oncology Group (ECOG) score; presenting 'pain' as a chief symptom and willing to participate in clinical trial after getting information about drug and treatment protocol were included.

Exclusion criteria

Patients suffering from systemic diseases such as uncontrolled hypertension/diabetes, cardiac/pulmonary/hepatic or renal dysfunctions, HIV/VDRL, pregnant or breast-feeding women, patients with inability to comprehend and complete proposed course of intervention were excluded.

Ethical and legal approval

The study was approved by the Institutional Ethics Committee of IPGT and RA, Gujarat Ayurved University, Jamnagar (PGT/7/-A/ethics/2015-16/2625) and RRAP, CARIC, CCRAS, Worli, Mumbai (CARIC/Ref. No. 03/16-17). 'Clinical Research Proforma' (CRP) was designed exclusively for cancer palliative care focusing on patient's symptoms and related details. 'Patient's consent form' (according to the guidelines of the CCRAS) and 'drug compliance form' was developed which was presented and approved through IEC-CARIC and Departmental Research Committee meeting at IPGT and RA, Jamnagar. Trial drug was procured through the pharmacy of Gujarat Ayurved University, Jamnagar after taking due approval of the state excise authority. Records were maintained as per the present rules and regulations.

Trial registration

Study was registered in Clinical Trials Registry of India. (CTRI/2016/02/006658).

Methods

Study design

An open labelled single arm clinical trial of sample size 40 (Dropout rate of 25%) was conducted at RRA Podar CARIC, CCRAS, Worli, Mumbai, of duration 1 month with four follow-up at interval of a week and last one follow-up for assessment of withdrawal symptoms after trial drug was stopped. Before treatment (BT) and after treatment (AT), laboratory investigations namely complete blood count, urine test, biochemistry parameters such as total- direct- indirect bilurubin, albumin: globulin ratio, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, triglycerides, total cholesterol (TC), high-density lipoproteins (HDL), low-density lipoproteins (LDL), very LDL, TC: HDL ratio, serum urea, serum uric acid, serum creatinine, fasting and post prandial blood sugar level and ECG were done to check the safety aspects after 1 month of administration of trial drug and to check any biochemical parameter disturbance after TD administration. Recommended dose of water- wash processed cannabis leaves as per Ayurvedic pharmacopoeia of India is 250 mg[14] which was given to patients thrice a day (9 am, 3 pm and 9 pm) orally with 50 ml of cow's milk mixed with 4 g of crystal sugar as an adjuvant; for the period of 4 weeks. Patients were asked to discontinue any type of analgesic drug during trial period. However if patient had intolerable pain, then they were advised to inform and report trial center or nearby clinic and rescue medicine advice was kept in protocol. Patients were given 'drug compliance form' to fill the details of consumption of medicine capsules.

Telephonic follow-up was maintained with patients who failed to attend follow-up every week due to continuation of their chemotherapy or radiation cycles or due to long distance as some patients in trial were from other states.

Case report form

Data filled in 'Case Report Form' (CRF) was also entered in electronic format designed in Microsoft Excel. After trial completion, CRFs along with laboratory investigations reports were submitted to IEC for evaluation.

Outcome measures

For assessment of pain, Wong -Baker FACES Pain Rating Scale for pain (FACES),[15] Objective Pain Assessment (OPA)[16] and Neuropathic Pain Scale (NPS) were used.[17] Anxiety and depression were assessed by Hospital Anxiety and Depression Scale (HADS).[18] Associated complaint"s scoring was evaluated by WHO-DFC project guidelines for developing clinical research methodology in Ayurveda.[19] For estimation of QOL in cancer patients, FACT-G scale was adopted.[20] Performance status of a cancer patient was evaluated by ECOG and Karnofsky score.[21] All the above parameters scorings were recorded at baseline and after every week of assessment. 'Post withdrawal effects assessment scale'[22] and 'adverse drug reaction (ADR) reporting forms' were noted at the end of 5th week.

Statistical analysis

Obtained data were analyzed statistically using SigmaStat 3.5 version for Windows (Systat Software, Inc., 501 Canal Blvd., Suite E, Point Richmond, California). Statistical analysis was done by applying 'paired t-test' to BT and AT assessment scores. $P < 0.05$ was considered statistically significant.[23] Percentage difference of change in relief of each symptom at every week period to achieve 50% relief in respective symptom was calculated. Overall improvement in signs and symptoms. Percentage improvement of every symptom per week for each patient was calculated by the formula (Before Treatment value -After Treatment value)/Before Treatment value ×100. Average of the percentage improvement was calculated. of the percentage improvement was calculated. Obtained results were measured according to the grades as cure/complete remission 75% ≥100%, marked Improvement 51% ≥74%, moderate improvement 26%–50%, mild Improvement 1% ≥25% and unchanged 0%.

Observations and Results

Status of enrolled patients

Total 37 (100%) patients were enrolled in trial out of which 24 (64.86%) have completed treatment while 13 (35.14%) patients dropped out due to reasons such as conventional therapy settings and inconvenience in long distance travelling to reach trial center.

Demographic profile

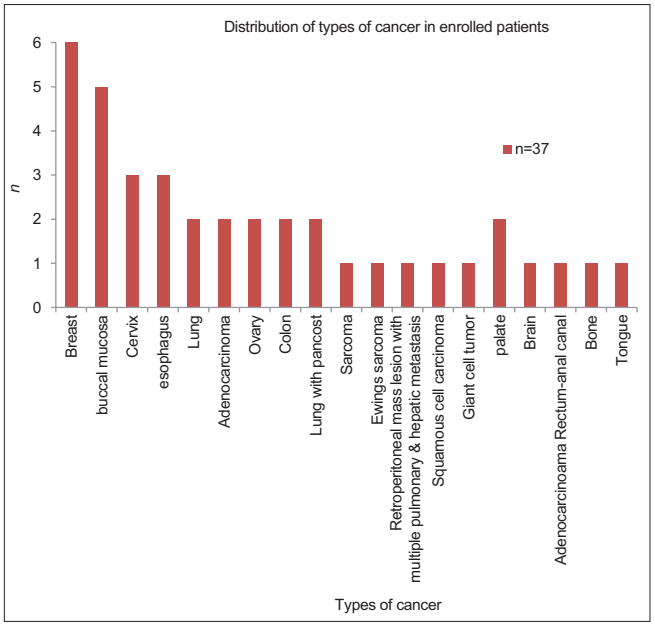
Demographic data of enrolled patients ($n = 37$) viz. distribution of patients according to age, gender, marital status, educational status, past and present occupation, habitat and religion are depicted in Table 1.

Treatment modalities opted by patients for symptoms management

Conventional treatment like chemotherapy and radiation therapy were received (ing) by 40.54% and 18.92% patients respectively whereas 37.83% patients were undergoing treatment from Complementary and Alternative Medicine pathies and 40.54% patients were found suffering from various side effects of conventional treatment for cancer.

Table 1: Demographic profile of enrolled patients

Data	Criteria	*n* (*n*=37)	Percentage
Age	18-70	37	100
Gender	Male	15	40.54
	Female	22	59.46
Marrital status	Married	22	59.46
	Unmarried	7	18.92
	Widow/r	8	21.62
	Divorcee	0	0
Educational status	Illiterate	7	18.92
	Read/write/educated	30	81.08
Past occupation	Desk	12	32.43
	Field	0	0
	Field + labour	6	16.22
	Housewife	12	32.43
	Business	5	13.51
	Student	1	2.70
	Other	1	2.70
Present occupation	Desk	7	18.92
	Field	0	0
	Labour	0	0
	Housewife	18	48.65
	Business	5	13.51
	Student	1	2.7
	Other	6	16.22
Habitat	Urban	22	59.46
	Semi-urban	11	29.73
	Rural	4	10.81
Religion	Hindu	36	97.30
	Christian	1	2.70



Graph 1: Cancer of: breast (16.21%), buccal mucosa (13.51%), cervix (8.10%) and oesophagus, lung, adenocarcinoma, ovary, colon, lung with pancost, sarcoma, ewings sarcoma, retroperitoneal mass lesion with multiple pulmonary and hepatic metastasis, squamous cell carcinoma, giant cell tumor, palate, brain, adenocarcinoama, rectum-anal canal, bone, tongue (In sequence)

Distribution of patients according to types of cancer

Patients presenting 'pain' as chief complaint having various nineteen different types of cancer are depicted in Graph 1, out of which cancer of breast (16.21%), buccal mucosa (13.51%), cervix (8.10%) and esophagus (8.10%) were found in most patients.

Chief and associated complaints (n = 24)

Pain (100%) was the chief complaint presented by all patients followed by anxiety (79.17%), depression (83.33%), fatigue (70.83%), exhaustion (62.5%), loss of appetite (54.17%), insomnia (45.83%), tastelessness (45.83%), dryness of skin (29.17%), fever (16.67%), dyspnea (16.67%), constipation (8.33%), hair loss (8.33%) and diarrhea (4.16%). Score-wise distribution of enrolled patients complaining pain on Wong-Baker FACES Pain Rating Scale score between '6' and '8' BT while after treatment (AT) no patients had score above '6' [Tables 2-4].

Before treatment, OPA score of 87.5% and 12.5% patient's was '3' and '2' respectively while AT 95.83% patients had OPA score '1' [Table 5].

On NPS, BT assessment, patients showed 'pain score >5' on parameters like intensity (91.68%), sharpness (70.84%), hot (20.84%), dull (79.17%), cold (4.17%), sensitive (91.66%), itchy (20.84%), unpleasant (95.83%), deep (87.49%) and surface (50%) types of pain which was reduced below '5' in AT assessment in 100% patients [Table 6].

On HADS, at BT, in anxiety assessment; borderline abnormal and abnormal score was shown by 16.67% and 62.5% patients respectively which reduced up to 16.67% and 4.17% respectively AT. Borderline abnormal score of depression was reflected in 33.33% patients and abnormal score was detected in 50% patients which was reduced to 25% and 16.67% AT respectively [Table 3].

Table 2: Effect of *Shodhita Bhanga* therapy on Wong-Baker FACES Pain Rating Scale

Scale	Time of assessment	Score (% of patients), n=24					
		0	2	4	6	8	10
Wong-Baker FACES Pain Rating Scale	BT	0	0	4.17	20.83	62.5	12.5
	AT	41.67	54.17	4.17	0	0	0

BT: Before treatment, AT: After treatment

Table 3: Effect of *Shodhita Bhanga* therapy on Hospital Anxiety and Depression Scale

Parameter	Time of assessment	Normal (0-7) (%)	Borderline abnormal (8-11) (%)	Abnormal (12-21) (%)
Anxiety (n=19)	BT	20.83	16.67	62.5
	AT	79.17	16.67	4.17
Depression (n=20)	BT	16.67	33.33	50
	AT	45.83	25	16.67

BT: Before treatment, AT: After treatment

Before treatment, patient's showed scoring of severity of associated symptoms like *Agnimandya* (Loss of appetite) (41.67%; '3'), *Hrillasa* (Nausea) (20.83%; '2'), *Aruchi* (Tastelessness) (45.83%; '4'), *Atisara* (diarrhoea) (4.17%; '3'), *Vibandha* (Constipation) (8.33%; '1'),), *Daurbalya* (weakness) (29.17; '1' and '3'), *Twakrukshata* (Dryness of skin) (28.57% '2', 71.43% '1'), *Keshapatana* (Hair fall) (8.33%; '2'), *Jwara* (Fever) (16.67%; '1'), *Shrama* (Exhaustion) (29.17%; '1,' 16.67% '2' and 16.67% '3') and *Shwasa* (Dyspnea) (16.67% '1'). AT the scoring changes were found as loss of appetite (8.33; '1'), *Hrillasa* (Nausea) (20.83%; '0'), *Aruchi* (Tastelessness) (41.67%; "0'), *Atisara* (diarrhoea) (4.17; '1'), *Daurbalya* (weakness) (37.5; '1'), *Twakrukshata* (Dryness of skin) (71.43; '0'), *Keshapatana* (Hair fall) (4.17; '1'), *Jwara* (Fever) (16.67%; '0'), *Shrama* (Exhaustion) (37.5%; '1') and *Shwasa* (Dyspnea) (8.33%; '0') [Table 4].

Performance status

Before treatment, scorings of ECOG scale were found in 4.17% (4), 4.17% (3), 20.83% (2), 54.17% (1) and 16.67% (0). AT, ECOG score of patients was reflected as 4.17% (4), 4.17% (2), 75% (1) and 16.67% (0) [Table 7]. BT, Karnofsky score was found as 25% (90), 37.5% (80), 8.33% (70), 12.5% (60), 8.33% (50) and 8.33% (40). AT, it was reflected as 66.67% (90), 20.83% (80), 4.17% (70), 4.17% (60), and 4.17% (40) [Table 8].

Drug compliance

Duly signed 'drug compliance form' showing records of per week consumption of total capsules by each patient was collected during follow-up.

Effect of therapy

Assessment of percentage difference in relief per week

Pain

Fifty percent relief was observed between 2nd and 3rd weeks of trial period on FACES scale and NPS while between 3rd and 4th weeks on OPA scale. After completion of trial, 84.10% relief was found on FACES scale and OPA scale. 100% relief was found in cold pain while 92.02%, 74.79%, 79.3%, 78.38% and 66.64% relief was observed in itchy, intensity, unpleasant, deep and hot type of pain respectively as compared to initial status of pain score. TD relieved pain in 8.33%, 16.67% and 33.33% of patients at the end of first, second and third week respectively thus in to 58.33% of patients were relieved from pain while 46.67% patients still complained pain but of reduced intensity [Table 9].

Associated symptoms

Patients suffering from fever got relief during 2nd week. Fifty percent relief in symptoms such as loss of appetite, nausea and insomnia was achieved within a week while in tastelessness, diarrhea, dryness of skin, fatigue and dyspnea; relief was achieved within 2 to 3 weeks. AT, relief found in loss of appetite, tastelessness, insomnia and nausea was 94.87%, 90.91%, 90.91% and 78.57% respectively. More than 75% relief was found in diarrhea and fatigue while 50% relief was found in

Table 4: Effect of *Shodhita Bhanga* therapy on associated complaints

Associated symptom	*n*	Score	Time of assessment	
			Before treatment	After treatment
Daurbalya (Fatigue)	17	0	0	29.17
		1	29.17	37.5
		2	8.33	4.17
		3	29.17	0
		4	4.17	4.17
Shrama (Exhaustion)	15	0	0	20.83
		1	29.17	37.5
		2	16.67	20.84
		3	16.67	4.17
Agnimandya (Loss of appetite)	13	0	0	0
		1	0	8.33
		2	12.5	0
		3	41.67	0
Nidralpata (Insomnia)	11	0	0	45.84
		1	0	0
		2	0	0
		3	45.84	0
Aruchi (Tastelessness)	11	0	0	41.67
		1	0	0
		2	0	0
		3	0	0
		4	45.83	4.17
Hrillasa (Nausea)	7	0	0	20.83
		1	8.33	4.67
		2	20.83	0
		3	0	0
		4	0	0
		5	0	0
Twakrukshata (Dryness of skin)	7	0	0	71.43
		1	71.43	28.57
		2	28.57	0
		3	0	0
		4	0	0
Jwara (Fever)	4	0	0	16.67
		1	16.67	0
		2	0	0
		3	0	16.67
Shwasa (Dyspnea)	4	0	8.33	8.33
		1	16.67	4.17
		2	0	0
		3	0	0
Vibandha (Constipation)	2	0	0	0
		1	8.33	0
		2	0	0
		3	0	0
		4	0	0
Keshapatana (Hair fall)	2	0	0	0
		1	0	4.17
		2	8.33	4.17
		3	0	0
		4	0	0
		5	0	0
Atisara (Diarrhoea)	1	0	0	0
		1	0	4.17
		2	0	0
		3	4.17	0
		4	0	0

n: Number of patients suffering

Table 5: Effect of *Shodhita Bhanga* therapy on Objective Pain Assessment scale

Time of assessment	Score		
	1	2	3
Before treatment (%)	0	12.5	87.5
After treatment (%)	95.83	4.17	0

general debility after the completion of trial [Table 10].

Statistical significance and overall effect of therapy

Pain

Statistically reduction in pain was analyzed on FACES pain scale ($P < 0.05$), OPA scale ($P < 0.05$) and NPS. ($P < 0.001$) [Table 9] during and AT with TD except in two patient's where analgesic was used as a rescue medicine. 'Complete remission' was found in 41.67% patients while 'marked improvement' was found in 54.17% patients and 'moderate improvement' was found in 4.17% patient on cancer pain.

Pain and associated complaints

Statistically significant result was obtained in loss of appetite, nausea, tastelessness, general debility, dryness of skin, fever, fatigue and insomnia [Table 10]. No significant relief was found in diarrhea and hair loss. Diarrhea was presented due to metastatic carcinoma of rectum and hair loss was due to side effect of chemotherapy. However, TD has not created any negative impact on respective symptoms.

'Complete remission' was found in 66.67% of patients while 'marked improvement' was observed in 33.33% of patients when pain and associated symptoms were assessed together.

Anxiety and depression

Statistically significant reduction in anxiety and depression was found AT on HADS assessment ($P < 0.001$) [Table 11].

Quality of life

Statistically significant improvement was found on FACT-G scale except on social well-being parameter.[Table 11]. Social well-being parameter consists questionnaire of personalized relationship aspects influencing patients mind and eventually health. TD reported for creating positive impact on patient's psyche,[6] but during this trial period, score of social well-being parameter was unchanged.

Table 6: Effect of *Shodhita Bhanga* therapy on Neuropathic Pain Scale

Symptom	TOA	Score (%)										
		0	1	2	3	4	5	6	7	8	9	10
Intensity	BT	0	0	0	4.17	4.17	0	4.17	4.17	41.67	37.5	4.17
	AT	4.17	37.5	25	25	8.33	0	0	0	0	0	0
Sharpness	BT	25	0	4.17	0	0	16.67	12.5	12.5	12.5	12.5	4.17
	AT	54.17	16.67	16.67	12.5	0	0	0	0	0	0	0
Hot	BT	66.67	0	0	8.33	0	8.33	4.17	4.17	4.17	0	0
	AT	83.33	4.17	4.17	0	8.33	0	0	0	0	0	0
Dull	BT	8.33	0	4.17	0	12.5	8.33	16.67	8.33	29.17	12.5	4.17
	AT	29.17	45.83	20.83	4.17	0	0	0	0	0	0	0
Cold	BT	91.67	4.17	0	0	0	0	0	0	4.17	0	0
	AT	95.83	4.17	0	0	0	0	0	0	0	0	0
Sensitive	BT	4.17	0	0	4.17	0	4.17	8.33	8.33	37.5	20.83	12.5
	AT	20.83	37.5	29.17	4.17	8.33	0	0	0	0	0	0
Itchy	BT	62.5	4.17	0	4.17	8.33	4.17	0	8.33	4.17	0	4.17
	AT	83.33	16.67	0	0	0	0	0	0	0	0	0
Unpleasant	BT	4.17	0	0	0	0	4.17	0	8.33	37.5	33.33	12.5
	AT	16.67	29.17	25	16.67	8.33	0	0	0	0	0	0
Deep	BT	0	0	0	0	12.5	8.33	8.33	20.83	25	25	0
	AT	16.67	45.8	16.67	16.67	4.17	0	0	0	0	0	0
Surface	BT	16.67	0	20.83	4.17	8.33	16.67	12.5	8.33	8.33	0	4.17
	AT	50	41.67	4.17	0	4.17	0	0	0	0	0	0

BT: Before treatment, AT: After treatment, TOA: Time of assessment

Table 7: Effect of *Shodhita Bhanga* therapy on eastern cooperative oncology group performance score

TOA	Score %					
	0	1	2	3	4	5
BT(%)	16.67	54.17	20.83	4.17	4.17	0
AT(%)	16.67	75	4.17	0	4.17	0

BT: Before treatment, AT: After treatment, TOA: Time of assessment

Table 8: Effect of *Shodhita Bhanga* therapy on Karnofsky score

TOA	Score (%)										
	0	10	20	30	40	50	60	70	80	90	100
BT(%)	0	0	0	0	8.33	8.33	12.5	8.33	37.5	25	0
AT(%)	0	0	0	0	4.17	0	4.17	4.17	20.83	66.67	0

BT: Before treatment, AT: After treatment, TOA: Time of assessment

Performance status

Significant improvement in ECOG ($P < 0.05$) and Karnofsky score ($P < 0.01$) was found. Thus, TD helps in improving performance status QOL in cancer patients [Table 10].

Adverse drug reaction and *Cannabis* withdrawal scale

No ADR were noted during the trial period. No withdrawal symptoms were noted after completion of trial. Precautions had been taken while prescribing TD for *Pitta* predominant *Prakriti* (constitution) patients and those who were reported to have chronic addiction(s) of any form. Patients (n=1) who reported burning sensation after TD administration were dropped out from trial.

Discussion

Prevalence of cancer and associated symptoms did not find parallel with any studied parameter of demographic data [Table 1].

Fifty percent relief was found on all the three scales used for assessment of pain within 2–3 weeks of trial period. Relief on pain scales was statistically significant when compared to baseline score [Table 9]. *Bhanga*; due to its *Ushna*[24] (Hot) *Veerya* (Potency) helps in reliving *Sheeta* (Cold) completely as excess *Sheeta Guna* (Property) alleviates *Vata* and hence increases pain.[25] Being *Vyavayi*[24] (Potent in action) and analgesic in nature, drug helps in instant pain reduction. Due to potency of creating pleasurable effects, it helps in achieving feeling of accomplishment of mind's objects by creating state of euphoria thus, helps in reducing unpleasant pain. Hot pain was relived less as compared to other parameters, may be due to hot potency and acidic nature of drug.[24] Recent researches reports significant analgesic activity of Cannabis in cancer pain is due to presence of phytoconstituents like tetra-hydrocannabinol (THC) and Cannabidiol (CBD).[26-29] Water-wash processed *Cannabis* contains 65% THC and low traces of CDB in comparison with unpurified one.[6]

Associated symptoms

Cancer patients often experience cluster of symptoms, which can independently predict changes in patient's function,

Table 9: Assessment of percentage difference in relief per week and statistical significance on pain

Interval	*n*	Percentage relief during treatment period			AT	Avg. 50% relief	Statistical significance (AT and BT)		
		BT-1 week	BT-2 weeks	BT-3 weeks	BT-AT	Week	Mean±SEM	*t*	*P*
Scale									
Wong-Baker FACES Pain Rating	24	26.39	48.54	74.10	84.10	2-3	6.42±0.32	20.176	<0.001
Objective Pain Assessment	24	26.39	48.54	74.10	84.10	2-3	1.83±0.08	23.592	<0.001
Neuropathic Pain Scale									
Intensity	24	26.37	42.79	62.54	74.79	2-3	6.00±0.36	16.849	<0.001
Hot	7	38.11	38.11	69.68	66.64	2-3	1.08±1.08	2.522	0.019
Dull	22	25.5	47.98	48.74	82.45	2-3	5.21±0.47	11.081	<0.001
Cold	2	50	50	100	100	At 2	0.33±0.34	0.984	<0.001
Sensitive	23	25.67	44.18	65.99	80.32	2-3	6.04±0.46	13.015	<0.001
Itchy	9	92.02	77.29	84.6	92.02	At 1	1.88±0.60	3.110	0.005
Unpleasant	9	23.48	43.95	75.28	79.3	2-3	6.58±0.35	18.780	<0.001
Deep	24	32.91	45.2	68.52	78.38	2-3	3.50±0.51	6.806	<0.001
Surface	20	33.33	59.83	66.34	85.98	At 2	3.46±0.50	6.918	<0.001

P<0.05, *P*<0.02, *P*<0.01, *P*<0.001 when compared with initial value (paired ttest).[18] SEM: Standard error of mean, BT: Before treatment, AT: After treatment

Table 10: Assessment of percentage difference in relief per week and statistical significance on associated symptoms

Symptoms	*n*	Percentage relief during treatment period				50% relief	Statistical significance (AT and BT)		
		BT-1 week	BT-2 weeks	BT-3 weeks	BT-AT	In week	Mean±SEM	*t*	*P*
Daurbalya (weakness)	17	18.63	25.49	42.16	50	4	0.83±0.21	3.890	<0.001
Shrama (Exhaustion)	15	22.22	37.79	55.56	65.56	2-3	0.63±0.15	4.307	<0.001
Agnimandya (Loss of appetite)	13	50	67.95	85.90	94.87	1	1.42±0.28	5.027	<0.001
Nidralpata (Insomnia)	11	53.03	83.33	90.91	90.91	1	0.17±0.08	2.145	0.043
Aruchi (Tastelessness)	11	0	34.09	84.09	90.91	2-3	0.42±0.16	2.632	0.015
Hrillasa (Nausea)	7	57.14	71.43	85.71	78.57	1	1.67±0.41	4.053	<0.001
Twakrukshata (Dryness of skin)	7	14.29	28.57	57.14	50	2-3	0.25±0.09	2.769	0.011
Jwara (Fever)	4	75	100	100	100	1	0.17±0.08	2.145	0.043
Shwasa (Dyspnea)	4	0	75	75	100	2	0.17±0.08	0.08	0.043
Vibandha (Constipation)	2	8.33	8.33	100	100	3	0.08±0.058	1.446	0.162
Keshapatana (Hair fall)	2	0	0	25	25	-	0.04±0.04	1.000	0.328
Atisara (diarrhoea)	1	33.33	33.33	66.67	66.67	2-3	0.08±0.08	1.000	0.328

P<0.05, *P*<0.02, *P*<0.01, *P*<0.001 when compared with initial value (paired ttest). SEM: Standard error of mean, BT: Before treatment, AT: After treatment, n: Number of patients suffering

treatment failures and post-therapeutic outcomes.[30] *Bhanga* being antipyretic[6] reduces fever effectively. Statistically significant effect was obtained in symptoms like loss of appetite, tastelessness, nausea, general debility, dryness of skin, fever, fatigue and dyspnea. More than 90% relief was found in loss of appetite, tastelessness and insomnia. After administration of TD, 50% relief was achieved within seven days in symptoms like loss of appetite, nausea, fever and insomnia while it took four weeks for improvement in fatigue symptom.

Anti-pyretic action of *Bhanga* is due to its *Tikta* (Bitter) *Rasa* (Taste) and *Swedajanana* (hyperhidrosis) nature.[31]

Table 11: Statistical significance for anxiety, depression, quality of life and performance status on respective scales

Parameter/scale ($n=24$)	Mean±SEM	SD	*t*	*P*
Anxiety and depression (Hospital Anxiety and Depression Scale)				
Anxiety	7.167±0.996	4.878	7.197	<0.001
Depression	4.292±0.797	3.906	5.382	<0.001
QOL (FACT-G scale)				
Physical well being	8.208±0.849	4.160	9.667	<0.001
Social	0.0417±0.185	0.908	0.225	0.824
Emotional	3.458±1.077	5.275	3.212	0.004
Functional	3.250±0.615	3.011	5.288	<0.001
Performance status				
ECOG	0.250±0.109	0.532	2.304	0.031
Karnofsky	11.25±3.47	17.020	3.238	0.004

$P<0.05$, $P<0.02$, $P<0.01$, $P<0.001$ when compared with initial value (Paired t test). ECOG: Eastern Cooperative Oncology Group, QOL: Quality of life

Bhanga imparts *Deepana* (Appetizer), *Pachana* (Digestive) action thus improves loss of appetite, fever, nausea. Due to *Grahi* (Withholds secretions) action; it helps to reduce diarrheal frequency. Being *Balya* (tonic) in nature, it helps in replenishment of *Dhatu* (Body elements) and decreases fatigue.[6] According to Ayurveda, *Dhatuparinamana* (Formation of new body constituents/elements) is a sustainable process and takes time of whole month.[32,33] Thus, achieving 50% result in fatigue within a month; in patients suffering from cancer; can be considered satisfactory as in case of cancer; patients already gets deteriorated by the disease and its treatment modalities like chemotherapy and radiation.

Cannabis is well established medicine for chemotherapy induced nausea and vomiting,[34,35] loss appetite, weight loss, pain, depression[36] pain with depression, anxiety,[37] sleep disorders,[38-41] asthma[42]and diarrhea[43] due to its constituents like THC[44-46] and nabilone.[47-52]

Anxiety and depression

Anxiety and depression, commonly co-exist in cancer patients.[53] TD showed significant reduction in complaint of anxiety and depression. *Bhanga* creates pleasure and pleasantness, thus; calms patient. Being *Medhya* (memory enhancer) and *Uttejaka* (Stimulant) in nature helps to improve intellect[6,24] and alertness of mind respectively.[54]

Clinical researches report effectiveness of constituents of *Cannabis* such as nabilone[36,55,56] and cannabidiol[53,54] for the management of both anxiety and depression simultaneously.[36]

Quality of life

Statistically significant improvement in FACT-G scale's parameters confirms the processed herbal form of *Cannabis* possess role in improving QOL in cancer patients by combating multiple symptoms, similarly like its extract.[57,58] [Table 11]. Impact of TD on social behaviour is difficult to co-relate from this study. Clinical researches report, analgesic potential and improvement of QOL by Cannabis is due to its constituent nabilone.[59,60]

Performance status

Disease cancer has negative impact on all systems of body. TD has showed significant improvement in performance status, i.e., functioning status of a patient. *Cannabis* is well reported for aphrodisiac, adaptogenic and immune-modular actions.[61] It helps in nourishing and improvement of body tissue and immunity. Cannabis being appetizer, digestive, tonic, antipyretic, analgesic, aphrodisiac, adaptogen, quick acting, memory tonic etc., helps in skirmishing pain along with associated cluster of symptoms which eventually helps in improving QOL in patients.

Use of *Cannabis* helps to reduce consumption of opioids.[62] Clinically it is proved effective as adjunctive of morphine and found helpful in decreasing morphine induced side effects.[12] Still, when administered in unprocessed form Cannabis has risk of habit formation and other cognitive impairments.[63] The fundamental behind purification of *Cannabis* is to reduce its ill effects.[8] With consumption of processed *Cannabis* for a month, no withdrawal symptoms was noted, thus, proves a promising drug in the field of palliative oncology care cancer.

Conclusion

Administration of *Jalaprakshalana Shodhita Bhanga* (water-wash processed *Cannabis*) leaves powder in dose of 250 mg thrice a day with 50 ml of cow's milk and 4 g sugar as an adjuvant, for a period of 1 month; significantly relieves pain, anxiety and depression of cancer patients without creating any major side effects, dependency and withdrawal symptoms. Processed *Cannabis* is significantly effective for improvement in QOL of a cancer patient.

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Conflicts of interest

There are no conflicts of interest.

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