Role of i-Pulse, a Polyherbal health drink in the management of Generalized weakness and Post-Operative Convalescence: A Randomized, Double blind and Comparative Clinical study

DR. CHITTA RANJAN DAS[1], DR. BALU KOLAR[2], SUJATA MISHRA[3]
[1]Faculty of Ayurveda, Unit of Kanchi University, Enathur, Kanchipuram.
[2] Department of Product Development, R&D, Indusviva Health Sciences Pvt. Ltd, Bangalore.
[3] Psychologist

Abstract: *The association of nutrition along with traditional medicine brings the long-standing consumer acceptance. Although the concept of nutrition is gaining more popularity recently, its roots can be traced to the ancient Indian system of medicine, 'Ayurveda'. The texts of Ayurveda are filled with references of implication of food products including fruits in various disease entities. Processed foods impair absorption by coating the intestinal walls. They cause the endocrine system to be on constant roller coaster ride through adjusting blood sugar and hormones in the blood, all which leads to adrenal and kidney fatigue. Antioxidants are a group of substances that protects the body cells by damage caused by free radicals by interacting with them and stabilizing them. The potency of antioxidants is measured by its Oxygen radical absorbance capacity (ORAC) which specifically measures the antioxidant capability against the damage induced by free radicals. These free radicals are released in the body during metabolic processes and external factors like pollution, radiation, smoking and stress will lead to a condition called oxidative stress which is the main reason for ageing and degenerative changes in the body. Post-operative convalescence (POC) is the phase of gradual recovery of health, strength and stamina after a surgical process during which the body requires adequate antioxidants. i-Pulse, an Ayurvedic health promoter drink from Indusviva Health Sciences Pvt. Ltd., Bangalore, with its innate blend of fruits provides the essential antioxidants required by the human body to fight against the free radicals. i-Pulse is considered safe and effective while it helps in reducing the symptoms associated with POC like generalised weakness, pain, nausea, vomiting, giddiness and fatigue while it increases the activeness and promotes early recovery in subjects.*[1-3]

Key Words: *Ayurveda, Nutrition, Antioxidants, Free radicals, Oxidative stress, i-Pulse, Generalised weakness, Post-operative convalescence (POC).*

1. INTRODUCTION:

Oxidative stress plays a major part in the development of chronic and degenerative diseases such as cancer, arthritis, aging, autoimmune disorders, cardiovascular and neurodegenerative diseases. Free radicals are generated from immune cell activation, inflammation, mental stress, excessive exercise, ischemia, infection, cancer and aging. They also result from air and water pollution, cigarette smoking, alcohol, heavy metals, certain drugs, industrial solvents, cooking and radiation.[4-5] Oxidative stress is common for many types of cancer cells that are linked with altered redox regulation of cellular signalling pathways.[6] An Antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules. The potency of antioxidants is measured by its Oxygen radical absorbance capacity which specifically measures the antioxidant capability of the product against the damage induced by free radicals.[7]

Adequate levels of antioxidants are required by the human body during the post-operative convalescence (POC) period. Postoperative recovery can be divided into three phases: early, intermediate and late recovery.[8] From a holistic perspective, postoperative recovery is described as a process defined by improvement in functional status and the perception that one is recovering.[9] Nutritional health supplements with antioxidant fruits can deliver the necessary antioxidants during POC aiding faster recovery. Studies in hospital patients have shown that up to 20% of meals are missed while patients attend or are fasted for investigative or therapeutic interventions pre and post-surgery. This leads to delayed wound healing, impaired respiratory and immune function, muscle weakness, depression, increased frequency and duration of hospitalisation, and premature death.[10] Post-operative convalescence (POC) is mainly characterised by pain at the incision site, nausea and vomiting. Thus, early antioxidant nutrition is critical in reducing post traumatic infective complications and catabolism.[11] It also includes generalised weakness, giddiness, lethargy, ambulatory difficulties, delayed wound healing, impairments or variation in haematological, biochemical parameters and weight loss. It is also found that time for wound closure can be shortened by oral antioxidants containing supplements in trauma patients with disorders in wound healing.[12,13]

Such antioxidant natural health supplements may be broadly classified under '*Rasayana*' branch of Ayurveda. They help the physiology in overcoming such oxidative injury by enhancing the enzymatic defence mechanisms of body.[14] i-Pulse, an Ayurvedic health promoter drink is a unique combination of herbs and anti -oxidant fruit blend which effectively combats generalised weakness and post-operative convalescence (POC). The fruit ingredients in i-Pulse are naturally credited with *Rasayana* (Rejuvenating) properties which help in respiratory functions, assist in cardiovascular functioning by improving circulation and may reduce raised lipid levels. It helps regulate fat and carbohydrate metabolism, improve appetite, digestion and assimilation.

2. AIM:

Randomized, double blind, comparative, parallel group study of i-Pulse, an Ayurvedic health promoter formulation in the management of generalised weakness and post-operative convalescence.

3. MATERIALS AND METHODS:

Local ethical committee approval was obtained before initiation of the study. Those who opted for treatment were informed of voluntary nature of trial and written consent was obtained from the parent or guardian. They were free from withdrawal of the study.

3.1 INFORMED CONSENT PROCESS

All subjects who were willing to participate in the study were given detailed description about the investigational product, nature and duration of the study. Also, subject's responsibilities after entering, the study were explained. Subjects were pre-screened by the investigators for the inclusion criteria. Only subjects who met the requirements of this section, signed an informed consent form, subjects who were willing to follow instructions given by the investigator and have an updated medical history on file with the investigator were entered in the study. A written informed consent by subject using an 'informed consent form' was obtained from each study subject. The subjects of each study subject were informed about the study verbally as well as using a patient information sheet, in an easy-to understand language.

3.2 STUDY DESIGN

Randomized, double blind, comparative, parallel group study of i-Pulse, an Ayurvedic health promoter formulation in the management of Generalised weakness and Post-operative convalescence.

A baseline history was obtained in order to determine the patient's eligibility for enrolment in the study. The baseline assessment included personal data, a description of symptoms and details of past medical history, history of possible exacerbating factors, etc. All the patients were advised to consume the product for a period of 4 weeks.

The subjective improvement evaluation will be done by a predefined global grading system, which includes following gradations:

- No improvement
- Fair improvement
- Remarkable improvement
- Very good improvement
- Excellent improvement

30 ml of i-Pulse was given twice a day along with warm milk or warm water for a period of 4 weeks for group A, and 30 ml of commercial fruit based health drink twice day along with warm milk or warm water for group B. Every day the subjects recorded the actual time when the product is consumed.

3.3 NOTE OF ADVERSE EVENT (AE):

An adverse event is the development of an undesirable medical condition - e.g. symptoms or abnormal results of an investigation - or the deterioration of a pre-existing medical condition (not relevant in this study). AE's were be collected by means of a standard question: "Have you had any health problems since the previous visit?"

AE's were recorded at every visit. Spontaneously reported AE's and/or observed AE's and the subject's response to this question were recorded on the AE form with information about seriousness, action taken, date of onset and recovery, maximum intensity and outcome.

The subjects were asked to assess the intensity of the reported Adverse Event according to the following scale: Mild = awareness of sign or symptom, but easily tolerated
Moderate = discomfort sufficient to cause interference with normal activities Severe = incapacitating, with inability to perform normal activities.

Relation of adverse events to study medication was predefined as 'Unrelated' (a reaction that does not follow a reasonable temporal sequence from the administration of the drug), 'Possible' (follows a known response pattern to the suspected drug, but could have been produced by the subject's clinical state or other modes of therapy

administered to the subject), and 'Probable' (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the subject's clinical state).

3.4 INCLUSION CRITERIA

- Both male and female subjects aged more than 18 years.
- At least three days following surgery and ambulatory cases.
- Individuals who were already started with oral foods and who were willing to follow the study rules and responsibility.
- Generalized weakness.

3.5 EXCLUSION CRITERIA

- Postoperative subjects advised nil per oral.
- Subjects with intestinal obstruction, paralytic ileus, pulmonary embolism or any severe infection.
- Postoperative cases who are critical requiring observation in intensive care unit (ICU), patients with cardiac, hepatic or renal failure.
- Subjects regularly on any treatment.
- Those with a strong history of food or drug allergy.
- Subjects not willing to provide informed consent or abide by the requirements of the study.
- Pregnant and lactating mothers.
- Patients with features of other co-morbidity features like stroke, heart disease, insulin dependent Diabetes mellitus.
- Cancers.
- Asthma and psychosis.
- Depressive disorders.
- Patients with addiction of higher levels of alcohol and nicotine.

3.6 STATISTICS:

Descriptive statistics was used to describe variables and comparison with baseline. No statistical method will be used for determination of level of significance.

3.6.1 EVALUATION OF SAFETY PARAMETERS

TABLE.1 EVALUATION OF i-PULSE ON SAFETY AND TOLERANCE PARAMETERS		
PARAMETERS	**Day 1**	**Day 90**
Erythema	**0**	**0**
Edema	**0**	**0**
Vomiting	**0**	**0**
Pruritus and Urticaria	**0**	**0**
Burning micturition	**0**	**0**
Hypopigmentation	**0**	**0**
Hyperpigmentation	**0**	**0**

All the scores are expressed as Nil- 0, mild-1, moderate-2 and severe-3.

Follow up visits and observation:

Subjects were assessed at entry, and at the end of 15 days and 30 days. At each visit, the subject was evaluated for parameters for time for ambulation, incision site or dressing inspection and weight gain, improvement in haemoglobin (Hb%), fever, bowel sounds, stool frequency, pain, nausea/vomiting, appetite weakness and lethargy. The grading of the other parameters was done as follows: Severe-3, Moderate-2, Mild-1, Disappearance of the symptoms-0. The overall clinical assessment was defined as cured, improved and unchanged.

3.6.2 EVALUATION OF EFFICACY PARAMETERS

TABLE 2. CHARACTERISTICS OF THE TREATMENT AND COMPARATIVE GROUPS IN HAEMATOLOGICAL PARAMETERS				
Details	**i- Pulse**		**Comparative**	
	Initial	**Final**	**Initial**	**Final**
Hb% (gm%)	12.50 ±0.60	13.50 ±0.50	12.59 ± 1.71	12.58 ± 1.51 (NS)
WBC count (% w. cm)	8654 ± 1085	8190 ± 595.8	8305 ± 1810	7425 ± 1203

TABLE 3. BIOCHEMICAL AND CLINICAL CHEMISTRY PARAMETERS				
Details	**i- Pulse**		**Comparative**	
	Initial	**Final**	**Initial**	**Final**
SGPT	31.80 ± 2.22	32.40 ± 2.63 (NS)	31.95 ± 3.58	32.15 ± 3.25 (NS)
Serum creatinine	0.77 ± 0.21	0.83 ± 0.14 (NS)	0.90 ±0.25	0.93 ± 0.14 (NS)

TABLE 4. WEIGHT PROFILE						
Details	**i-Pulse**			**Comparative**		
Days	Initial	Day 15	Day 30	Initial	Day 15	Day 30
Weight	55.10	55.11	55.08	56.00	57.50	58.25

TABLE 5. LETHARGY AND WELLBEING SCORE				
Details	**i-Pulse**		**Comparative**	
	Initial	Final	Initial	Final
Lethargy	9.0	7.0	9.2	9.1
Giddiness	8.0	7.5	8.5	8.3
Activeness	7.0	8.0	6.0	6.0

TABLE 6. PAIN AT THE INCISION SITE		
Details	**Pain**	
	Seen	Not seen
i-Pulse		
Day 0	30	0
Day 15	02	28
Day 30	0	30
Comparative		
Day 0	20	02
Day 15	02	18
Day 30	0	20

TABLE 7. RECOVERY PHASE		
Details	**i-Pulse**	**Comparative**
Ambulatory days	2.00	1.50
Recovery phase	8.00	12.00

4. RESULTS:

THE SAFETY AND TOLERABILITY OF I-PULSE ARE SHOWN IN TABLE.1: i-Pulse is seen to be safe and tolerable. None of the subjects complained about erythema, oedema, vomiting, pruritic, urticaria, burning micturition, hypopigmentation and hyperpigmentation. I-Pulse was observed to be safe from baseline till the end of the study.
CHARACTERISTICS OF TREATMENT IN BOTH TRIAL AND COMPARATIVE GROUPS WITH SPECIAL REFERENCE TO HAEMATOLOGICAL PARAMETERS ARE DESCRIBED IN TABLE.2: It is observed that the post-operative haematological parameters like Haemoglobin (Hb%) and WBC are well improved after i-Pulse consumption.

- **i-Pulse group**: Haemoglobin (Hb%) was recorded at 12.50±0.60 in the pre-treatment phase. Post treatment, the Haemoglobin (Hb%) was recorded at 13.50±0.50
- **Comparative group**: Haemoglobin (Hb%) was recorded at 12.59±1.71 in the pre-treatment phase. Post treatment, the Haemoglobin (Hb%) was recorded at 12.58±1.51

- **i-Pulse group**: White blood corpuscles (WBC) was recorded at 8654±1085 in the pre-treatment phase. Post treatment, the WBC was recorded at 8190±595.8

- **Comparative group**: White blood corpuscles (WBC) was recorded at 8305±1810 in the pre-treatment phase. Post treatment, the WBC was recorded at 7245±1203

BIOCHEMICAL AND CLINICAL CHEMISTRY PARAMETERS ARE DESCRIBED IN TABLE.3: It is observed that there is marked improvement in biochemical parameters in both treatment and comparative groups.

- **i-Pulse group**: SGPT was recorded at 31.80±2.22 in the pre-treatment phase. Post treatment, the SGPT was recorded at 32.40±2.63 (NS).

- **Comparative group**: SGPT was recorded at 31.95±3.58 in the pre-treatment phase. Post treatment, the SGPT was recorded at 32.15±3.25(NS).

- **i-Pulse group**: Serum creatinine was recorded at 0.77±0.21 in the pre-treatment phase. Post treatment, the SGPT was recorded at 0.83±0.14(NS).

- **Comparative group**: Serum creatinine was recorded at 0.90±0.25 in the pre-treatment phase. Post treatment, the Serum creatinine was recorded at 0.93±0.14(NS).

WEIGHT PROFILE IS DESCRIBED IN TABLE.4

- **i-Pulse group**: Weight of the subjects at the baseline was recorded at 55.10. The weight at 15 days post treatment was recorded at 55.11 and the weight at the end of treatment was recorded at 55.08 (30 days)

- **Comparative group**: Weight of the subjects at the baseline was recorded at 56.00. The weight at 15 days post treatment was recorded at 57.50 and the weight at the end of treatment was recorded at 58.25 (30 days)

LETHARGY AND WELLBEING SCORE IS DESCRIBED IN TABLE.5

- **i-Pulse group**: Lethargy levels of subjects in the pre-treatment phase were recorded at 9.0 and post -treatment it was reduced to 7.0. Giddiness was recorded at 8.0 in the pre-treatment phase and post-treatment, it was reduced to 7.5. Activeness was recorded at 7.0 in the pre-treatment phase and post-treatment, it was increased to 8.0.

- **Comparative group**: Lethargy levels of subjects in the pre-treatment phase were recorded at 9.2 and post -treatment it was reduced to 9.1. Giddiness was recorded at 8.5 in the pre-treatment phase and post-treatment it was reduced to 8.3. Activeness was recorded at 6.0 in the pre-treatment phase and post-treatment it was recorded at 6.0.

PAIN AT THE INCISION SITE POST-SURGERY IS DESCRIBED IN TABLE.6

- **i-Pulse group**: Pain was observed in 30 subjects during the baseline (Day 0). Only 2 subjects complained of pain 15 days post-treatment. It was observed that none of the subjects complained pain after 1 month of treatment. (4 weeks)

- **Comparative group**: Pain was observed in 20 subjects during the baseline (Day 0). Only 2 subjects complained of pain 15 days post-treatment. It was observed that none of the subjects complained pain after 1 month of treatment. (4 weeks). This shows i-Pulse has very significant effect on reducing the pain at incision site post-surgery.

The present study reveals the effectiveness of i-pulse during the stress, convalescence, and improving the recovery phase. Study shows that i-Pulse is effective in accelerating postoperative recovery. The improvement in the postoperative parameters like Hb%, WBC count and time taken for complete recovery, significant weight gain was much quicker and significant in i-pulse group than with the comparator health drink. It had comparable results with respect to recovery from pain in the incision site and time taken for patient ambulation including fever, nausea and vomiting, infection at the incision site, appetite.

5. DISCUSSION:

The response to surgery is not purely physiological, but also behavioural and subjective: feelings of malaise and reluctance to mobilize commonly continue for weeks postoperatively. These behavioural and subjective changes are clinically important: muscle function is impaired by immobilization and patients' assessment of their own recovery

will reflect their subjective state and perceived ability to resume normal exertion.[15,16] Oral polyherbal and fruit based products are very well suited to manage generalised weakness and almost all the symptoms which prevail during the convalescence period post-surgery. They are beneficial with regard to morbidity and length of hospital stay.[17] The use of such immune-modulating diets over an extended period in patients with advanced liver disease may also ameliorate the malnutrition-induced immune suppression and hyperinflammatory state characteristic of these patients with subsequent survival benefit.[18-21.]

i-Pulse is an antioxidant rich juice powered by innate Ayurvedic principles which is composed of unique, innovative and scientifically validated combination of antioxidants, essential carbohydrates, health promoting proteins & lipids, trace minerals and micronutrients present within its composition.

5.1 INGREDIENTS OF i-PULSE

TABLE8. COMPOSITION OF i-PULSE

Form	Sanskrit name	Botanical Name	Part used	Quantity
Liquids	Draksha	*Vitis vinifera*	Fruit	250 mg
	Bahunetra	*Ananas comosus*	Fruit	270 mg
	Seva	*Pyrus malus*	Fruit	280 mg
	Kadali	*Musa sapientum*	Fruit	520 mg
	Dadima	*Punica garantum*	Fruit	240 mg
	Kausumbham	*Citrus aurantium*	Fruit	380 mg
	Tanka	*Pyrus communis*	Fruit	200 mg

Draksha (*Vitis vinifera*) or Grapes are traditionally known to exert *Rasayana* (Rejuvenating) properties.[22] Grapes (*Vitis vinifera*) are rich in phenolic compounds existing in the skin and seeds. Among other beneficial effects, the active compounds in Grape are believed to have pharmacological activities such as anti-inflammatory, anticancer, antifungal, anti-bacterial and antioxidant.[23-29]

Bahunetra (*Ananas comosus*) or Pineapple fruit is traditionally used in the management of gastro intestinal disorders.[30] Pineapple fruits also exhibit high levels of other antioxidants such as phenolic compounds and vitamin C which have shown an effect in health protection, with not only antioxidant activity by scavenging free radicals, but also inhibition of hydrolytic and oxidative enzymes in human cells. [31,32]

Seva (*Pyrus malus*) or Apple fruit has a long history of use as a *Rasayana* (Rejuvenating) fruit. It is used as a bulk promoting agent.[33] Apple fruits are richest sources of antioxidants. It is important source of flavonoids and phenols. It is linked with the prevention of chronic diseases and with a lower incidence of cancer.[34]

Kadali (*Musa sapientum)* or Banana fruits are traditionally known for their bulk promoting properties. It is known for its constipating properties and is used in diseases like diarrhoea and dysentery.[35] Bananas are considered major antioxidants and an excellent source of potassium. A single banana provides potassium required on a daily basis. Potassium benefits the muscles as it helps maintain their proper working and prevents muscle spasms.[36]

Dadima (*Punica granatum*) or Pomegranate fruit juice relieves thirst and is useful in burning sensation and fevers. It is considered a potent appetizer and digestive.[37] Pomegranates are popularly consumed as antioxidant beverages, as food products and as extracts wherein they are used as botanical ingredients in herbal medicines and dietary supplements. The fruit is rich in tannins and other biochemicals, particularly phenolics, which have been reported to reduce disease risk.[38-40]

Kausumbham (*Citrus aurantium*) or Orange fruits are traditionally used in the management of fevers.[41] *Citrus aurantium* fruits are known to have high levels of phenolics which demonstrate strong antioxidant capability. Polyphenols comprise a wide range of components including flavanols, phenols, tannins, etc which are known for its potent antioxidant potential.[42,43]

Tanka (*Pyrus communis*) or Pear fruit is considered a good Rasayana (Rejuvenating) and an aphrodisiac.[44] Pear fruits are rich sources of Vitamin C, ascorbic acid and is a very good antioxidant. It is also a very important phytochemical against bacterial invasion and has shown significant activity as a wound healing agent.[45,46]

The efficacy of i-pulse can be attributed to the synergistic actions of the potent herbs and fruit based ingredients. The ingredients of I pulse provide balanced nutrition and promote overall health by their nutritive, energy boosting, digestive, antioxidant and immunomodulatory activities.

6. CONCLUSION:

This Clinical trial clearly demonstrates the preliminary safety and efficacy parameters related to i-Pulse. Major surgeries are common-ly followed by fatigue and convalescence. The aetiology and pathogenesis of postoperative fatigue can include sleep disturbances induced by cytokines and opioids in the period while the late fatigue and generalised weakness persisting for several weeks. The antioxidant capability of i-Pulse has shown significant results in the management of generalised weakness and its effectiveness in managing various conditions associated with post- operative convalescence (POC) is exemplary. i-Pulse, an Ayurvedic polyherbal health drink has shown remarkable results in accelerating post-operative recovery. It has shown significant results in improving the haematological parameters, weight, stabilizing the biochemical parameters, reducing giddiness & lethargy while increasing the activeness and ambulation time in the subjects. These results were significant in the i-Pulse group than the comparator health drink group. In addition to these parameters, i-Pulse has shown its effectiveness in reducing nausea, vomiting and pain at the incision site which substantiates the antioxidant potential of i-Pulse. Overall patient compliance was good and no adverse drug reactions were observed or reported with both trial and comparator health drink groups during the period of study. i-Pulse with its natural antioxidant fruit blend has further scope to be studied in various therapeutic areas.

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