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Boerhavia diffusaL MAY HAVE PROMISING POTENTIAL TO ALLEVIATE HYPERKALEMIA

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ABSTRACT:

To study efficacy of ***Boerhavia diffusa*** L. extract (***Punarnava*** capsule) to treat hyperkalemia , 30 patients were selected and categorized in 3 groups according to mild ,moderate and severe hyperkalemia status with 10 patients in each group . ***Punarnava*** capsule containing 250 mg of ***Boerhavia diffusa*** L. extract from Himalaya drugs were prescribed to treat hyperkalemia . Mild patients were treated for total 30 days and serum potassium level were measured for first time after 7 days and second time after 15 days of treatment . Moderate hyperkalemic patients were treated for 45 days(30 days up to normokalemia and next 15days follow up treatment) and serum potassium level were assessed after 15 days and 30 days of treatment. Severe hyperkalemic patients were provided with ***Punarnava*** capsule and treated for 60 days with 2 capsule twice a day for 1st 30 days and last 30 days with 1 capsule twice a day for last 1 month . Serum potassium level were assessed after 30 days and 60 days of treatment . All the patients after scheduled period of treatment able to be achieved normokalemia status after ***Boerhavia diffusa*** **L**. extract capsule administration . Patients were free from symptoms e.g. Vertigo, nausea , tremor and weakness in muscles ,myalgia or paresthesia etc. From the above study it was conclude that ***Boerhavia diffusa*** L. extract may be a potential drug to treat hyperkalemia .

Key Words: Hyperkalemia ,Normokalemia , ***Boerhavia diffusa*** L ,***Punarnava***.

INTRODUCTION: Hyperkalemia is a condition in which the concentration of the electrolyte potassium (K+) in the blood is elevated . Hyperkalemia (hyperkalaemia in British English, hyper- high; kalium, potassium; -emia, "in the blood") . Normal serum potassium levels are between 3.5 and 5.0 mEq/L[1]

Symptoms: Symptoms are elevated serum potassium in blood, malaise, palpitations and muscle weakness; mild hyperventilation may indicate a compensatory response to metabolic acidosis, cardiac arrhythmia and sometimes rhabdomyolysis(The destruction of striated muscle cells), tingling, numbness, or other unusual sensations, paralysis, difficulty breathing, nausea and vomiting[2]

Diagnosis of Hyperkalemia

Hyperkalemia can be classified according to serum potassium into mild (5.5–6.5 mmol/l), moderate (6.5–7.5 mmol/l) and severe (>7.5 mmol/l) hyperkalemia.

Hyperkalemia is rarely associated with symptoms, occasionally patients complain of palpitations, nausea, muscle pain, or paresthesia. However, moderate and especially severe hyperkalemia can lead to disturbances of cardiac rhythm, which can be fatal[3],[4]. Electrocardiography (ECG) monitoring is mandatory in patients with

serum potassium >6.5 mmol/l. ECG changes may present as non-specific repolarization abnormalities, "peaked" T-waves, and QRS widening as well as depression of ST-segment[5] .

Examination and investigations should be systematic and always include assessment of cardiac function, kidneys, and urinary tract as well as hydration status and neurological evaluation[5].

Punarnava* capsule**:Punarnava*** Capsules(**Himalaya Drugs India**) have been made from 250mg of extract of ***Boerhavia diffusa*** L. (***Punarnava***), a herb which has been recognized for its diuretic properties. ***Punarnava*** capsule from Himalaya drugs usually prescribed by the Ayurvedic physicians throughout India ,for Urinary tract infections, Edema (swelling) and also as an adjuvant for efficient kidney function, with its diuretic, antispasmodic and anti-inflammatory action.

MATERIALS AND METHOD –

Inclusion criteria for the patients

The patients for this study have been selected randomly irrespective of their age, sex, religion, caste

Patients with clinical positive history of elevated potassium are selected for the present study.

Diagnosis- The most reliable method is to blood test for serum potassium level .The normal serum level of potassium is 3.5 to 5 mEq/L. In this study the The serum potassium level was measured through Kinetic method using KM-5V2 Transasia Semi Auto analyzer .

Statistical test method used – Two tailed paired t-test .

QUALITATIVE AND QUANTITATIVE ANALYSIS OF *PUNARNAVA* CAPSULE-

Instrument used- HPLC Agilent-1100series - Chromatographic separation was carried out on an Inertsil ODS-3 column by using gradient mobile phase containing 0.1% v/v orthophosphoric acid in water and Acetonitrile. The detection was carried out at 276 nm. The method was validated for specificity, precision, accuracy and robustness. The linearity (r(2) = 0.9989 and 0.9991) was found to be in the range of 7.26-35.75 µg mL(-1) and 2.20-11.00 µg mL(-1) for boeravinone E and B, respectively. This qualitative analysis confirms the capsules from Himalaya Drugs India, as pure grade ***Boerhavia diffusa*** L. (***Punarnava***) extract with presence of marker compound active ingredients content in the extract powder analyzed by HPLC method .

PLAN OF THE TREATMENT

The patients have been treated in OPD as well as in IPD depending on the severity and the circumstances.

All the patients have been treated with ***Punarnava***.

Total 30 patients have been taken for the study presently.

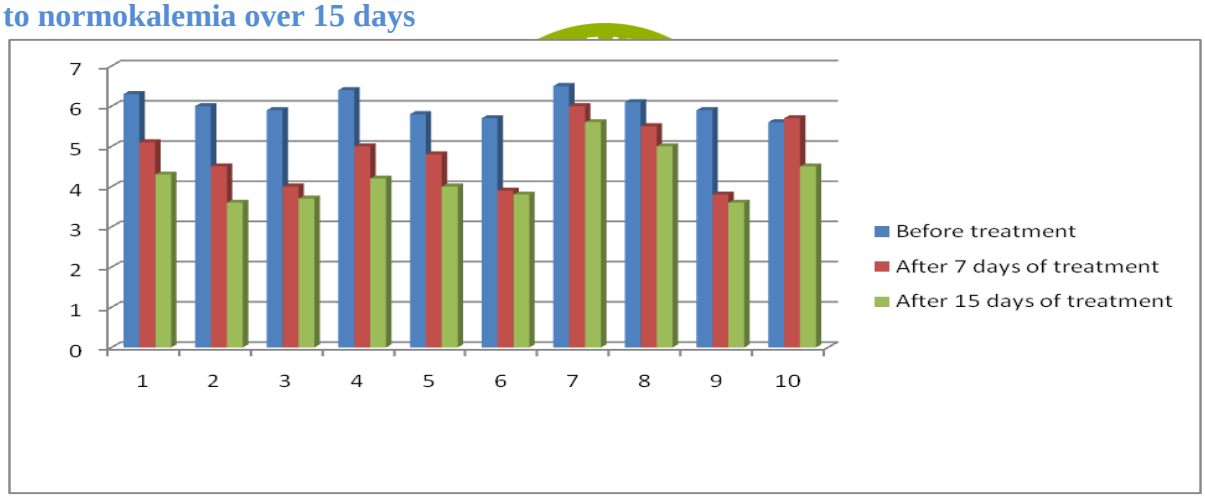
30 patients from the department of Kayachikitsa Govt. Ayurveda medical college Balangir Odisha were supplied with ***Punarnava*** capsule to treat their hyperkalemic condition . The patients were of common complain of nausea, vertigo, apathy ,malaise , fatigue ,muscular pain trembling with pedal edema in some cases of patients . When a blood test for serum potassium level were asked for investigation ,elevated level of serum potassium were observed .

Various associated symptoms of the patients e.g. vertigo ,nausea ,tremor ,weakness in muscles and pedal edema, in case of severe and moderate hyperkalemic patients were also

Table-1 For Mild hyperkalemia dose schedule (Total 30 days of treatment)

Patient Serial No	AGE	SEX	Serum K Level Prior to treatment	After 7 days with 2Caps BD Dose	After 15 days 1caps BD for next 8 days	Follow up dose for last 15 days
1	41	M	6.3	5.1	4.3	1 caps BD
2	33	Male	6	4.5	3.6	1caps BD
3	61	Male	5.9	4	3.7	1caps BD
4	56	M	6.4	5	4.2	1caps BD
5	52	M	5.8	4.8	4	1caps BD
6	45	M	5.7	3.9	3.8	1capsBD
7	48	M	6.5	6	5.6	2capsBD
8	43	F	6.1	5.5	5	1caps BD
9	46	M	5.9	3.8	3.6	1capsBD
10	35	F	5.6	5.7	4.5	1caps BD

Table-2 Showing the graphical figure in gradual improvement from hyperkalemia state to normokalemia over 15 days



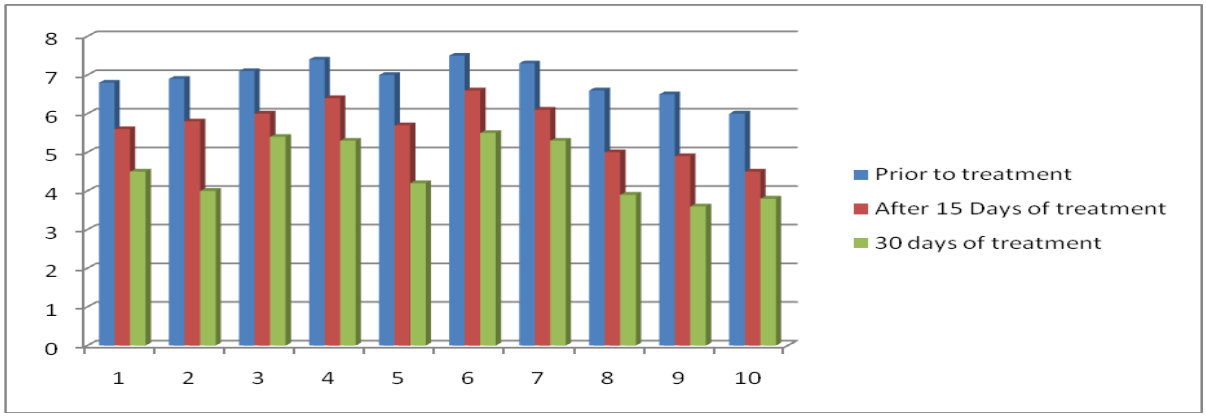
For moderate hyperkalemia 2 caps BD for 15 days and follow up treatment of 1 caps BD for last 15 days. The serum potassium level status were checked after 15 days and again after 30 days from the beginning of the treatment (Table-3 and 4).

Table-3 for Moderate hyperkalemia dose schedule (Total 1month treatment) follow up treatment for next 15 days .

Patient Serial No.	AGE	SEX	Serum K Level Prior to T/T	After 15 dayswith 2Caps BD	After 30 days	Follow up dose for last 15 days
1	33	F	6.8	5.6	4.5	1caps BD*
2	47	M	6.9	5.8	4.0	1caps BD
3	51	M	7.1	6.0	5.4	1caps BD
4	55	M	7.4	6.4	5.3	1caps BD
5	29	M	7.0	5.7	4.2	1caps BD

6	39	M	7.5	6.6	5.5	2caps BD
7	28	F	7.3	6.1	5.3	1caps BD
8	65	F	6.6	5.0	3.9	1caps BD
9	36	M	6.5	4.9	3.6	1caps BD
10	44	M	6.0	4.5	3.8	1caps BD

Table-4 Showing the graphical figure in gradual improvement from hyperkalemia state to normokalemia over 30 days .

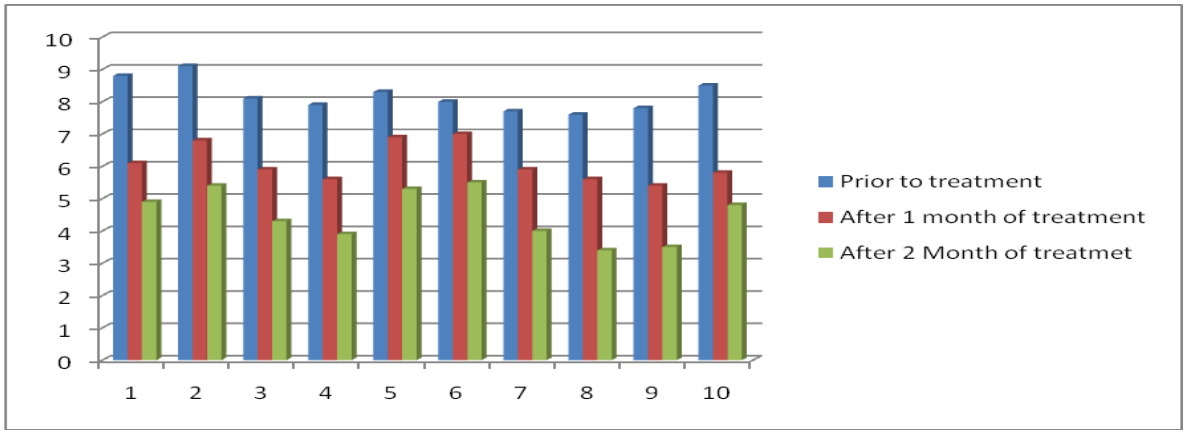


In severe hyperkalemia cases the dose of 2 caps BD extended for 1 month and for 1 caps BD for another one month with total of 60 days of treatment. The serum potassium level status were checked after 30 days and again after 60 days from the beginning of the treatment (Kindly refer to Table-5 and 6 and the statistical significance indicated).

Table-5 For severe hyperkalemia dose schedule (Total 2 month of treatment)

Patient Serial No.	AGE	SEX	Serum K Level Prior to treatment	After 1 month	After 2 months	Dose for 1st 1 month	Follow up dose for last 1month
1	78	Male	8.8	6.1	4.9	2capsBD	1capsBD
2	68	Male	9.1	6.8	5.4	2capsBD	1capsBD
3	40	Male	8.1	5.9	4.3	2capsBD	1capsBD
4	36	Male	7.9	5.6	3.9	2capsBD	1capsBD
5	53	Female	8.3	6.9	5.3	2capsBD	1capsBD
6	55	Male	8.0	7.0	5.5	2capsBD	1capsBD
7	44	Male	7.7	5.9	4.0	2capsBD	1capsBD
8	39	Female	7.6	5.6	3.4	2capsBD	1capsBD
9	41	Female	7.8	5.4	3.5	2capsBD	1capsBD
10	86	Male	8.5	5.8	4.8	2capsBD	1capsBD

Table-6 Showing the graphical figure in gradual improvement from hyperkalemia state to normokalemia over 2 months .



OBSERVATION- After the specific duration of ***Punarnava*** administration all the undesirable symptoms related to hyperkalemia were alleviated . In cases ; 3 out of 10 patients in severe hyperkalemia and 1 out of 10 in moderate hyperkalemia ,the pedal edema were also reduced after the completion of duration of medication . In this study however none of the patients were observed to be shown of hypokalemia . All the patients were able to achieve normokalemia status and confirmed after regular interval testing of the serum potassium level .

STATISTICAL ANALYSIS: All the three groups of patients (Mild, moderate and severe hyperkalemic) groups were statistically evaluated for effectiveness of therapy by paired-t test. In this method the patients' data before the treatment is taken as self control to compare with his/her readings after the treatment.(Table-7)

Table:7 . Overall normokalemic effect of *Punarnava* therapy in treatment for hyperkalemia in all the 3 groups

Group		**Treatment Duration**	**Readings**
Mild			
Hyperkalemia		B.T.	6.02±0.095
		A.T. 7days	4.83±0.245*
		A.T. 15days	4.23±0.207*
Moderate			
Hyperkalemia		B.T.	6.91±0.145
		A.T.15Days	5.789±0.191*
		A.T.30Days	4.633±0.248*
Severe			
Hyperkalemia		B.T.	8.18±0.155
		A.T.30Days	6.133±0.204
		A.T.60Days	4.467±0.275

Table-7 shows the improvement in hyperkalemia which has come in to the normal range after treatment in all the patients of 3 groups . There is highly significant reduction in serum potassium level to normal state with other symptoms related with hyperkalemia .

DISCUSSION - The serum K^+ and pedal edema lowering effect may be due to the known diuretic effect of Boerhavia diffusa . It is an established fact based on previous studies of evaluation of diuretic activity of alcoholic extracts of ***Boerhavia***

diffusa L in Rats,that it has significant urinary K^+ excretory effect[6] .

Apart from the K^+ lowering effect none of the patients in any of the above group has shown to be suffer from hypokalemia this balancing and homeostatic phenomenon may be due to the potassium nitrate containing properties . The vegetables have fairly adequate concentrations of sodium and calcium, equivalent concentrations of magnesium, but with low contents of potassium and iron [7].So with this low quantity of potassium it may favor an optimum normal range of serum potassium and thus may be preventing from being hypokalemia. All the other symptoms including muscle pain and fatigue .nausea ,dizziness etc. all were alleviated as convinced through routine physical examination of patients . ***Punarnava*** is regarded therapeutically highly efficacious for the treatment of renal inflammatory diseases and common clinical problems such as nephritic syndrome, oedema, and ascites developing at the early onset of the liver cirrhosis and chronic peritonitis [8].Punarnava has been in use to treat chronic nephritic syndrome which may be an important cause of hyperkalemia complication . As an adaptogen ***Boerhaavia diffusa (Punarnava)*** has the ability to support both adrenal over and under activation[9]. Adrenal gland which secrets aldosterone is responsible for excess K^+ ion excretion through urine and thus may be contributing for the K^+ homeostasis in blood . Another mechanism of hyperkalemia is increase in cortisol hormone transports potassium out of cells in exchange for an equal number of sodium ions which may trigger the hyperkalemia [10] .Cortisol is a steroid hormone, in the glucocorticoid class of hormones, and is produced in humans by the zona fasciculata of the adrenal cortex within the adrenal gland in response to stress.***Boerhaavia Diffusa*** has been found to decrease in serum cortisol when in elevated[11].

On the other hand, Boerhaavia diffusa has also demonstrated the ability to improve cortisol levels with end stage adrenal exhaustion [12] . Therefore the excess K^+ ion depleting effect may also be due to the decrease in the contributory factor serum cortisol.

CONCLUSION – The above small sample study indicates ***Punarnava*** Capsule(***Boerhavia diffusa*** L.) can be a potent drug for life threatening Hyperkalemia problem aroused due to multiple of etiology. This need more enhance clinical research to develop a potent anti hyperkalemic drug with promising results . Although a small sampled study observation ***Boerhavia diffusa*** L. (***Punarnava***) is a promising potential drug to deal with hyperkalemia complication .

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