ORIGINAL

Role of Areca Catechu (BETEL NUT) In The Treatment of Cerebrovascular Diseases

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Summary:

40 patients of cerebrovascular diseases (CVD) with various disabilities were studied to see the effect of Areca catechu (betel nut). The mean age of the patients was 51 ± 7 years. 22 (intervention) patients were given Areca catechu along with the conservative measures and 18 (control) patients were given conventional vasodilator drugs along with the conservative measures. 79% of the Areca catechu treated patients and 31% of the control patients recovered after 3 weeks of treatment (P .01). Consciousness (P .001) and bladder function (P .01) were recovered in intervention group earlier than the control group patients. The intervention patients were discharged after 19 ± 5 days and the control patients were discharged after 26 ± 7 days (P .01). So it may be concluded here that the Areca catechu may be effective in the treatment of CVD.

Introduction:

Traditional medicine has aroused a great enthusiasm all over the world. It is a valuable aid to mankind. At present about 80% of the world population depend on traditional

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medicine for treatment (1). Areca catechu (betel nut) is one of such aides. Though the chewing of areca nut singly or in combination with piper betel (betel leaf), lime, tobacco leaf and others is a habit, it has been accepted as a culture as a means of entertainment of guests. It is used as a traditional medicine in many countries of the eastern hemisphere viz. India, China, Bangladesh, Pakistan, Indonesia, Thailand for time immemorial. It is used as stimulant, vermifuge, aphrodisiac, astringent in Ayurvedic and other traditional medicines and Homopathic and is also mentioned in many modern pharmacopias (2, 3).

Bombelon in 1886 first extracted an alkaloid, arecaine from areca nut. Later on, arecaine (1%), arecholine (0.07-0.1%) & arecaidine, guvacholine, guvacine in traces were extracted (3). A high percentage of many amino acids viz. proline, tyrosine, phenylalanine have also been detected. Besides these, areca nut also contains 15% of tannin and 14% of fat (3). The alkaloid whose function is known is arecholine (4,5). It is a parasympathomimetic agent. Until recently, cerebral circulation was thought to be almost entirely regulated by the local chemical changes. But now it is believed that the parasympathetic nervous system has vasodilatory effect on cerebral circulation (6). As areca nut contains parasympathomimetic agent, this nut was used to help the patients of cerebrovascular disease (CVD) to improve their cerebral circulation and it is also used to encourage the dysarthric patients to help the movement of the tongue. The result of treatment with this procedure was encouraging.

A pilot trial with areca nut was started on CVD patients. This paper deals with the preliminary results of that clinical trial. The CVD is a major burden on the community as a third cause of death and one of the major causes of permanent disability (7, 8). The treatment of CVD is still unsatisfactory (9). Huge amount of money is being spent on vague vasodilators and the disease itself imposes a great loss on the economy of a country (10). This study with areca nut on CVD is the first of this kind in this field. Areca nut grows in Bangladesh and is cheap and easily available. Its use as medicine may open a new era in the treatment of CVD.

Material & Method:

This is an open, controlled, randomised, prospective clinical study. It was started in the Neurology department of the Institute of Post Graduate Medicine & Research, Dhaka, Bangladesh in November, 1983. The patients who have a history of sudden cerebral dysfunction, presumptively of vascular origin that lasts for more than 24 hours, are included in the

study. The patients of transient ischaemic attack are excluded from the study. There is no age or sex bar. The admitted patients and the patients who attend the Neurology out patients deptt (NOPD) are included. The NOPD and the inpatient were examined by the same person on the 1st day and every alternate day in admitted patients and on first and then after 5th to 7th day onward in NOPD patients. The base-line informations are recorded in a printed proforma for every patient. A 2-5 scale chart is used to follow the patients. It is a summary of the standard methods. The following investigations are done routinely in every patient. Hb%, total and differential blood count, lumbar puncture, fasting blood sugar, urea, static and dynamic brain scanning from nuclear medicine deptt. The scanning is repeated after 15 days to 1 month. Carotid angiography is carried out in selective patients.

Method of use of areca nut:

Unripe areca nut is used. The aqueous extract of the nut is received from the Institute of Food Science & Technology unit of Bangladesh Council for Scientific & Industrial Research, Dhaka. A random chart is used. The patients who are unconscious, aqueous areca nut extract equal to one medium size areca nut, in divided doses daily is given by Ryle's tube. After gaining consciousness and the patients who are conscious, are advised to chew the uncrushed areca nut in small fragments (one nut in four equal doses per day).

The control group is treated by the conservative measure and other conventional vasodilator drugs (xanthine nicotinate). Other general managements are similar in both group of patients. The graded physiotherapy is started from the very beginning. The depressed patients of both the groups are treated with imipramine Hcl. The indoor patients are discharged when they can respond to their natural calls, attain self care capabilities, independent or minimally assisted, or when the recovery rate has stopped to a point that shows no further improvement.

Due to lack of required number of physiotherapists, the attendants relatives of the patients are given training on the principles of physiotherapy and they are motivated in this task. These newly motivated relative-physiotherapists are also advised to continue physiotherapy at home after discharge of the patients from the hospital.

These patients are followed every fortnightly. The patients attend themselves or contact through letters. The follow up is carried out by the same group of doctors of the Neurology unit. The base line features include the physical and neurological findings, activity of daily

living, laboratory findings and any new development if any. These are recorded in a printed proforma. This paper discusses the follow up result of one month. The difference is compared by Student's T test.

Results:

52 patients have been registered so far upto August, 1984. 12 patients have been excluded from the study during assesment of the results because of their failure to attend the follow up programme and intolerance to areca catechu. This paper discusses the result of 40 patients of which 22 patients were in the intervention group and 18 patients were in the control group. The mean age group of these patients were 51 ± 9 yrs (intervention, 49 ± 10 yrs and control, 54 ± 7 yrs). 34 of these patients were males and only 6 of these patients were females (ratio 5.6:1). All of these patients had sudden cerebral dysfunction that persisted for more than 24 hrs. Radio-isotope scanning of these patients showed increased uptake somewhere in the brain suggesting CVD. The gross disabilities are shown in the table-1.

Table - I : shows the various gross disabilities in 40 patients on the first day of enrolment :

Disability	Intervention (n-22)	Control (n-18)
Unconsciousness	12	8
Hemiplegia	19	16
Aphasia	6	4
Bladder dysfunction	11	7

During treatment these patients started improving at different pace. Graph -1 shows the state of consciousness in 20 patients. As shown in the graph. 13 patients were in deep commatose state and 7 patients were in stuporous state. The patients in intervention group started gaining consciousness from 2nd day whereas the patients in control group started gaining consciousness later. The grade-0 patients of the control group did not show the sign of consciousness after 10 days whereas the grade-0 patients of the intervention group showed signs of consciousness earlier (p .001). After 10 days, 10 of the intervention and 3 of the control patients became fully conscious. None of the intervention and 2 of the control patients died during this period.

Graph - 2 shows the activity of daily living in 35 patients who had hemiplegia along with other incapacities as mentiond earlier. As shown in the graph, 7 patients of the inter-

vention group and 3 patients of the control group could do their activity of daily living without support at the end of 3rd week. 8 of the intervention group and 3 of the control group patients could work without support but slower than normal person.

6 of the 16 patients of the control group and none of the 19 patients of the intervention group remained in the stage of complete disability. The patients of the intervention group were discharged in 19 ± 5 days and the control group patients in 26 ± 7 days ($p < .01$). This shows that the rate of recovery (ADL) is quicker in areca nut treated group.

Graph - 3 shows the state of bladder function in 18 patients. After 7 days, 5 of the 11 patients in the intervention group and one in the control group were able to control the bladder function. At the end of 14 days, all the patients in the intervention group and one in the control group could control their bladder or could inform their attendants that they felt urge to evacuate their bladder. Three of this group died in 14 days. This shows that the areca nut helps to control the bladder function effectively and quickly.

The haemodynamic study of the patients of the intervention and the control group shows the changes in static and dynamic study before and after treatment. The result is encouraging in the intervention patients.

There was no significant change of blood pressure or pulse rate in the areca nut treated group ($p < .01$) during the treatment. One patient had loose motion who was given areca nut extract in larger doses. Another patient developed bronchospasm who had previous history of bronchial asthma. However, both the patients became normal after withdrawal of the areca nut. The first patient was again put on areca nut while the second one was not given it again. One of intervention and 2 of control group patients died in the hospital.

Depression was marked in control group patients while in the intervention group the problem was negligible and these patients improved faster with tricyclic antidepressant drugs.

Discussion:

The main approach of the management of CVD patients is rehabilitation which is aimed at diminishing the extent of incapacity and enabling the patients to regain maximum independence so that these patients can live a useful and dignified life inspite of their disabilities (11). This demands more than the management of acute situation. Intersectoral co-

operation is the most important aspect in the management of CVD patients (12). This aspect of treatment is unsatisfactory in the underdeveloped countries. Though there has been some improvement in the diagnosis of CVD with the advancement of medical science, still the results appear to be unchanged as shown in the following table (table - 3, 4). Generally 30% of the CVD patients die in the first month and among those who survive, one third will recover to be independent (13). The over all prognosis depends on several factors viz. age of the patients, site and extent of the lesion, mode of treatment (14, 15, 16).

In our series, result of treatment shows that the unconscious patients regained consciousness and the dysphasic patients start speaking normally much earlier than the control group of patients ($p < .001$). As shown in the successive graphs, the recovery in bladder control and improvement in the activity of the daily living were also earlier ($p < .01$). These patients were given physiotherapy by the attendants and relatives of the patients, which was satisfactory. This procedure of the physiotherapy is easier, cheaper and whole time available. This helps early recovery as observed by Garraway and other (17). In our series, the patients of the intervention group could be discharged in 19 ± 5 days with minimum disabilities whereas in control group the patients could be discharged after 26 ± 7 days. In other studies the mean hospital stay was 21 days to few months (18, 19).

Table - 2 shows the summary of the results of treatment for one month. It is evident by comparing the results in the table 3 & 4 that the improvement in our patients treated with areca nut is far better whereas the improvement in the control group is similar to previous studies though the general management is similar to both groups of patients.

How areca nut does work in the treatment of CVD patients needs further study. The probable mode of action of areca nut on CVD patient may be presumed as follows: —

1. by improving circulation of the brain;
2. by direct stimulation of the brain cell;
3. by improving metabolism and nutrition of the brain cell;
4. by combination of the above mechanism.

The improvement of the circulation of the brain were shown by the various indices and tracings of the haemodynamic study. As mentioned earlier, arecholine, which is a known parasympathomimetic agent, might have improved circulation of the brain by dilating cerebral

blood vessels thereby blood flow. Some other studies have shown that the areca nut extract constricts the peripheral blood vessels of the experimental animals (20). This may further explain the improved circulation of the brain by redirecting the blood flow to the brain. Generally the common vasodilators dilate the blood vessels of the systemic circulation along with the normal parts of the brain. This causes the affected parts of the brain to suffer more which is known as reverse steal phenomenon. But in case of areca nut, the systemic blood vessels constricts and the cerebral blood vessels dilate resulting in the improvement of total blood flow of the brain. This total improvement in circulation may be due to some factors other than arecholine.

The patients treated with areca nut regained consciousness earlier. This may be due to direct stimulation of the CNS by some elements if not arecholine in the areca nut. This early improvement in mental function helped the patients to control their bladder function. This improved consciousness further increased the urge of the patient to be cured and rehabilitated which made the early recovery easier. Generally the patients of CVD become emotionally labile. In most of the times, the patients are depressed. This is one of major causes of delayed recovery. These patients are reluctant to move or to be moved and object physiotherapy. They complain of tenderness in the paralysed limbs. These findings were very common in control group of our patients but the problem was less acute in the patients treated with areca nut. In case of depression, tricyclic antidepressant helped in both groups of patients but in intervention group, it worked quicker. This aspect of the result may be explained by the fact that the areca nut perhaps directly stimulates the CNS.

The areca nut was useful in the patients of chronic CVD due to atherosclerosis. It is documented that vasodilators have little effect on atherosclerosis (6). The cerebral circulation of these patients was unchanged as evidenced from haemodynamic study. Still these patients improved clinically. The cause of improvement is something other than improved circulation. It may be presumed here that the improvement is due to improved metabolism of the CNS. Areca nut contains many essential aminoacids and other essential nutrients or some unidentified factors and they improve the metabolism of the brain.

The mode of action may be the combined effects of the factors discussed earlier. Arecholine may not be the only factor because, side effect of the arecholine was not detected regularly. The BP and pulse rate were unchanged. Only two patients showed side effects those could be incriminated to arecholine. But these side effects were due to over dose and the side effects were abolished when the areca nut was withdrawn. No other toxicity other than these two were seen during the treatment or follow up period.

Table - II : shows the results of treatment of 40 patients after one month's observation :

Group	No	% Recovered completely	% Recovered partialy	% Death
Intervention	22	78.9	15.7	4.5
Control	18	31.2	12.5	11.1

Table - III : Result of untreated patients in other studies :

	No	Recovd / Impvd %	Not Impvd %	Died %	Period (Mon)
Harris & Levine (41)	48	48	19	33	3
Hughes & Lecomte ('57)	18	50	5	45	3
Keen & Levaus ('58)	34	64	15	21	3
Canter ('57)	34	31	15	54	12
Well ('59)	53	32	38	30	2

Table - IV : Result of treatment in other studies :

	% Recovered	% Not improved	% Died
Canter (1965)	45	18	20
Garraway (1980)	50	31	19
MJA (1980)	44	36	18
Smith (1981)	20	30	33

Graph II

The result of treatment with Areca catechu and conservative methods for motor weakness of 35 out of 40 CVD pts. in a follow-up study of 21 days.

Graph III

The result of treatment with Areca catechu and conservative methods for Bladder dysfunction of 18 out of 40 CVD pts. in a follow-up study for 14 days.

○ - Control (16)
● - Intervention (19)

Grade - 0 = Totally dependent
Grade - 1 = Partially assisted,
Grade - 2 = Independent but slower than normal,
Grade - 3 = Normal
(N. B. 3 of the study pts. died during this period)

○ - Control (n=7)
● - Intervention (n=11)

Grade - 0 — Incontinence
Grade - 1 — Normal bladder function
(N. B. 3 of the studied pts. died during this period)

Graph I

The results of treatment with Areca catechu and conservative methods on mental state of 20 out of 40 CVD Pts in a follow-up study for 10 days.

● - Control (8)

○ - Intervention (12)

Grade-0=no response to any stimulus Grade-1=non-purposive movement Grade-2 = Purposive movement
 Grade-3=Response to verbal command
 Grade-4 =Normal Consciousness
 (NB: 2 of the study pts. died during this period)

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