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Anti-Anxiety Effect of an Ayurvedic Compound Drug—A Cross Over Trial

K. Kuppurajan[1], C. Seshadri[2], V. Rajagopalan[3], Kanchana Srinivasan[4], R. Sitaraman[5], Janaki Indurthi[6] and S. Venkataraghavan[7]

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The results of a double blind study with a sequential cross-over design, comparing the efficacy of an Ayurvedic preparation with the modern control, viz. Diazepam and Placebo in 12 patients of Generalised Anxiety Disorder, are presented in this paper. Findings of the psychological parameters show that the Ayurvedic drug is more effective in enhancing the perceptual discrimination and psychomotor performance than the other two control drugs. The data on bio-chemical parameters indicate that the Ayurvedic drug offers protections to the stress induced metabolic changes by decreased urinary outputs of 17 OHCS and VMA. The intra-group comparisons in the Ayurveda group alone indicate that the drug is effective in controlling the somatic and psychic anxiety. Hence, the Ayurvedic drug can be safely prescribed for fairly longer periods without the fear of physical or psychological dependance, in acute and chronic states of anxiety, in old age with no apprehension about the age-related hazards and in cases presenting both the somatic and psychological symptoms.

1. Research Officer (Modern Medicine)
2. Research Officer (Bio-Chemistry)
3. Research Assistant (Social Worker)
4. Research Assistant (Psychology)
5. Research Assistant (Bio-chemistry)
6. Research Assistant (Statistics)
7. Ex. Assistant Director (Ayurveda)

Dr. A. Lakshmipathi Research Centre for Ayurveda (C.C.R.A.S.) V.H.S. Campus, T.T.T.I. Post, Madras-600113.

Introduction

Anxiety neurosis account for 34% of all patients suffering from neurosis in India according to the epidemiological study by Anand Bhushan, Baskaran and Varma (1967). The term anxiety

disorders, as it is currently used is a DSM III (APA, 1980) concept. There are many diagnostic entities under this heading among which generalised anxiety disorders (GAD) are remarkably common state hardly requiring hospitalisation, but definitely requiring careful clinical management.

Benzodiazepines (BZS) remain in the most widely used drugs in GAD. Their main disadvantage is development of tolerance and potential for development of dependance. Troublesome side effects of benzodiazepines are : 1. Decreased motor co-ordination. 2. Memory disturbance. 3. Drowsiness. Withdrawal of BZS results in withdrawal symptoms in about 15% of the users—more among long term users. Roberts and Vass (1986) described the occurrence of Schneiderian First rank symptoms in cases of BZS withdrawal.

Owing to these, quite a number of patients give up treatment at some stage or other and search for alternative medicare system in order to find relief. Even though in the available Ayurvedic classics, no particular condition which can be readily compared with anxiety neurosis is available, while enumerating *nanatmajavatavyadhis* and diseases caused due to *rajas* and *tamas*, a term *'Chittodvega'* is mentioned. In a nutshell, *Chittodvega* can be said as *manasaroga* where both *manasa dosa* (*Rajas*) and *saririka dosa* (*Vata* and *Pitta*) are vitiated producing the symptoms.

A number of Ayurvedic drugs have been tried in anxiety neurosis. Singh and Mehta (1977) observed that *Sankhapushpi* (*Convolvulus pluricaulis*) provided significant relief and improved mental functions in 30 cases of anxiety neurosis after one month. The effect of *Ksirabala taila* in psychogenic headache was examined by Ramu *et al* (1980) who found significant reduction in anxiety symptoms at the end of six weeks. Ten anxiety neurosis patients who have not improved with modern drugs were treated with *Ksiradhara* by Ramu *et al.* (1982). Improvement in the anxiety conditions was noted by all the three assessments— by Ayurvedic physician, Psychiatrist and Clinical psychologist. *Medhyarasayana*—a herbal compound consisting of *Sankhapuspi* (*Convolvulus pluricaulis*) *Guduci* (*Tinospora cordifolia*) *Mandukaparni* (*Centella asiatica*) and *Yasti* (*Glycyrrhiza glabra*) was tried by Koushik and Singh (1982) in 28 cases of anxiety. There was significant reduction in anxiety, increased sense of well being, gain in body weight and correction of pulse rate and B.P. in these cases.

In the present study, the anxiolytic effect of an Ayurvedic compound drug is studied with reference to modern control drug, diazepam and placebo.

Methods and Materials

Selection of cases

The study sample consists of 12

patients of both sexes in the age range of 20-50 years and falling into generalised anxiety disorder (300.02-DSM-III). Selection and exclusion criteria are based on DSM-III. In addition, patients having anxiety or depressive symptoms secondary to other medical illness or drug intake are excluded.

Design of the study

Sequential cross-over design and double blind method are adopted. The patient receives placebo or diazepam or Ayurvedic drug initially according to the random order. The same patient receives the other two treatments also after a gap of seven days between treatments. The treatment period is 45 days.

Conduct of the study

A detailed clinical and social history is taken. The patients are assessed on M.P.I. to rule out psychosis. The following parameters are included.

Psychological

1. Taylor's manifest anxiety scale. 2. Hamilton anxiety rating scale. 3. Work output. 4. Perceptual discrimination. 5. Psychomotor performance tests—(a) Hand precision, (b) Hand steadiness, (c) Eye-hand co-ordination, (d) Speed of response.

Physiological

1. Blood pressure, 2. Heart rate. 3. Pulse rate, 4. Body weight.

Bio-chemical

1. 17-hydroxy-cortico steroids (Appleby *et al.* 1955), 2. 17-keto steroids (Norymberski, 1953), 3. Vanillyl mandelic acid (VMA or HMMA) Pisano, *et al.* 1962). All these tests are done in the 24-hour urine sample. They are done initially and at the end of 45 days.

Drug administration

The Ayurvedic compound consists of *Mandukaparni* (*Centella asiatica*) *Yasti* (*Glycyrrhiza glabra*) *Jatamansi* (*Nardostachys jatamansi*) in the ratio of 1 : 1 : 2 suspended in the *Ksirabala taila*. The daily dosage of Ayurvedic drug is 3 gms/day in 3 divided doses. Each capsule contains 500 mgs of drug (*Mandukaparni* (120 mgs), *Yasti* (120 mgs), *Jatamansi* (240 mgs) and *Ksirabala taila* (3 drops). The daily dosage of Diazepam is 15 mgs/day also in 3 divided doses. Placebo is plain starch powder.

Result and Discussion

Socio-demographic variables like age, sex, type of onset, precipitating factors and family history of psychiatric illness are found to be similar between groups.

Table-I presents the analysis of psychological parameters Ayurveda group Vs. Placebo and Ayurveda group Vs. Diazepam. For parameters 1 and 2, percentage reduction is a positive sign and for 3-9, percentage increase is a

Table—I
Psychological Parameters

Sl. No.	Parameters	*Treatment Group*								
		AYURVEDA			*PLACEBO*			*DIAZEPAM*		
		Initial score	Final score	% increase/ reduction	Initial score	Final score	% increase/ reduction	Initial score	Final score	% increase/ reduction
1.	Max-Hamilton's Anxiety rating scale	34.3	27.4	—20.2	35.6	25.0	—29.8	30.7	17.3	—43.8
2.	Taylor's manifest anxiety scale	27.9	21.6	—22.5	29.1	25.6	—12.5	27.8	18.3	—34.3
3.	Perceptual discrimination	58.3	72.8	25.0*@@	64.6	70.7	9.6	66.5	58.9	—11.4
4.	Work output	39.3	40.7	3.5	36.8	39.0	5.9	39.7	38.8	—2.3
5.	Memory-forward	5.6	5.9	6.5	5.5	5.9	8.4	5.4	5.8	7.1
6.	Memory-Backwards	4.4	4.4	0.0	4.1	4.2	2.2	3.9	3.6	—6.4
7.	Finger dexterity	58.4	63.3	8.4	59.6	64.6	8.4	55.9	55.4	—0.9
8.	Tapping board	86.2	97.4	13.0	88.8	89.0	0.2	84.7	96.2	13.5
9.	Hand steadiness	10.3	9.3	—9.7	10.8	6.8	—3.8	8.7	8.9	2.1

Note : * $P<0.05$ Ayurveda group campared to Placebo g oup.

@@ $P<0.01$ Ayurveda group compared to Diazepam group.

2. Negative sign indicates reduction.

positive sign. On the anxiety ratings, as measured on parameters 1 and 2, all the groups show reduction, the diazepam group showing the highest reduction, but not statistically significant reduction. Ayurveda group shows a statistically significant increase in perceptual discrimination in comparison to both Placebo and Diazepam groups. Ayurveda group shows a numerical percentage increase in many psychomotor performance tests as compared to the placebo groups. This favourable effect of the Ayurvedic drug is especially significant in contrast to the impaired perceptual and psychomotor performance as a result of both acute and chronic ingestions of benzo-diazepines (Petursson *et al*, 1983). Skegg *et al.* (1979) also found that the risk of a serious traffic accident was five times greater for BZS users than for normal controls. Tasks involving eye-hand coordination, hand steadiness, perceptual discrimination etc. are encountered many a times in everyday life and the Ayurvedic drug scores a point in this respect over Diazepam.

Table-II presents the analysis of physiological parameters. None of the values attain significance.

Table-III shows the data on biochemical parameters. The reduction in VMA levels and 17 hydroxy-corticosteroids in the Ayurveda group is statistically significant when compared to the diazepam group. Studies have well documented the increased activity of adrenocortical and the sympathetic adrenomedullary systems during stress (Cannon, 1929). A sequence of studies in the 1960s and 1970s focussed on the excretion of the metabolite 17-hydroxy corticosteroids (17—OHCS). Marked elevations in urinary 17—OHCS occured in traumatic situations suggesting increased adrenocortical function (Friedman *et al*, 1963; Teece *et al.* 1966). In the light of the above observations, the findings in this study about the significantly marked reduction in the 17-OHCS and VMA levels in the Ayurveda group as compared to Diazepam group assumes significance. This result is indicative of the protective action of the drug against the stress induced metabolic changes.

Table-IV presents the intra-group comparisons in the Ayurveda group only. Significant results alone are presented. As can be seen, the percentage of increase/reduction in the desirable direction is seen in psychological, physiological and bio-chemical parameters. Anxiety ratings, both somatic and psychic assessed as separate clear entities in the Taylor's scale and Hamilton scale show significant percentage reduction in the Ayurveda group. It is worth recalling the fact here that in the modern system, patients suffering from generalised anxiety disorder who show predominance of somatic symptoms are given another group of drugs viz., beta adrenergic blockers like propranolol instead of

Table – II
Physiological Parameters

S. No.	Parameter	Treatment Group								
		AYURVEDA			*PLACEBO*			*DIAZEPAM*		
		Initial score	Final score	% increase/ reduction	Initial score	Final score	% increase/ reduction	Initial score	Final score	% increase/ reduction
1.	Weight	50.9	50.7	—5.7	57.5	57.7	0.5	52.7	53.4	1.3
2.	Systolic BP	126.4	124.0	—1.9	127.1	126.4	—0.6	128.6	122.4	—4.8
3.	Diastolic BP	87.3	79.1	—9.4	92.7	84.6	—8.8	89.0	84.0	—5.6
4.	Pulse rate	87.8	83.0	—5.5	79.6	83.2	4.4	89.3	86.2	3.5

Table—III
Bio-chemical Parameters

S. No.	Parameter	*Ayurveda Treatment*			*Placebo Treatment*			*Diazepam Treatment*		
		Initial Mean ± SE	Final mean ± SE	Mean diff. ± S.E.	Initial mean ± SE	Final mean ± SE	Mean diff. ± SE	Initial mean ± SE	Final mean ± SE	Mean diff. ± SE
1.	17-Ketosteroids mg/day	15.96± 2.57	12.61± 1.45	—3.35± 2.96	13.92± 1.78	15.19± 2.44	1.27± 2.05	15.73± 2.13	10.44± 1.50	—4.29± 2.29
2.	17-Hydroxy/ steroids mg/day	26.93± 4.23	15.90± 3.05	—11.03±** 4.72	24.83± 5.19	23.90± 4.00	—0.93± 4.50	21.89± 4.03	17.42± 2.45	—4.47± 4.01
3.	VMA/mg/day	4.38± 0.65	3.22± 0.49	—1.16±* 0.49	3.69± 0.40	2.84± 0.39	—0.85± 0.71	2.64± 0.47	3.65± 0.45	1.01± 0.48

Note : * $P<0.01$ Ayurvedic drug group compared to Diazepam drug group.
** $P<0.05$ Ayurvedic drug group compared to Diazepam drug group
SE—Standard Error.

Table—IV
Ayurvedic Treatment Group

S. No.	Parameter	Initial scores	Final scores	Percentage of increase/ reduction	Level of signifi-cance
1.	Diastolic BP	87.3	79.1	—9.4	$0.05<P<0.1$ (approaches significance)
2.	Hamilton Anxiety rating scale	34.3	27.4	—20.2	$0.05<P<0.1$ (approaches significance)
3.	Taylor's manifest anxiety ratings	27.9	21.6	—22.5	$P<0.02$
4.	Perceptual discrimination	58.30	72.8	25.0	$P<0.01$
5.	Finger Dexterity	58.4	63.3	8.4	$0.05<P<0.1$
6.	Speed of response	86.2	97.4	13.0	$P<0.01$
7.	V.M.A. levels mg/day	4.3	3.2	—25.5	$P<0.02$

benzodiazepines. Outside of medical supervision, many patients are seen to switch from benzodiazepine to propranolol and vice versa and escalate the dosage and show frank addictive behaviour through tolerance. (Paul and Merrett, 1985). Such gross drug abuse is more common in the elderly patients. Confusional states, ataxia and falls among the elderly have been reported as a result of benzodiazepine consumption (Jarvis, 1981). In such cases, the present drug, a herbal preparation can be safely prescribed even in advancing years and also in controlling both psychic and somatic anxiety symptoms.

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REFERENCES

Anand Bhushan, Bhaskaran, K. and Varma L.P.	1967	Socio-economic Class and Neurosis, *Indian Journal of Psychiatry*. 9(4) 334.
American Psychiatric Association	1980	DSM III, Washington D.C. APX Press.
Appleby, J.L. and Norymberski, J.K.	1955	Quoted in Practical Clinical Bio-chemistry, Vol. II, Herold Varley, Alan, H. Gower lock and Maurice Bell, 5th edition. William Heinamen Medical Books Ltd., p. 66.
Cannon, W.B.	1929	Bodily changes in Pain, Hunger, Fear and Rage, Appleton, New York.
Caraka	——	*Charaka Samhita*, Chikitsasthanam, Chapter Rasayana, 1/3 : 30-31, 1/3 : 33, 24-29.
Friedman, S.B., Mason, J.W. and Hamberg, D.A.	1963	Urinary 17-hydroxycortico-steroid levels in parents of children with neoplastic disease. *Psychosomatic Med.*, 25, 364-76.
Jarvis, E.	1981	Drugs and the elderly patient. *Adverse Drug Reaction Bulletin*, 86, p. 312-315.
Koushik, A.K. and Singh, R.H.	1982	Clinical evaluation of Medhya Rasayana compound in cases of Non-depressive Anxiety Neurosis *Ancient Science of Life*, Vol. 2, No. 1 : 11-16.
Norymberski, J.K., Stubbs, R.D. and West, H.F.	1953	Quoted in Practical Clinical Bio-chemistry Vol. II. Herold Varley, Alan H. Gowerlock and Maurice Bell, 5th Edition, William Heineman Medical Books Ltd., p. 58.
Paul, Grantham and Merrett, C.	1985	The valium victim; rhetoric or reason. Paper presented at the World Congress for Mental Health, Brighton, England.
Peturrson, H., Gudionsson, G. and Lader, M.H.	1983	Psychometric performance during chronic benzodiazepine treatment and withdrawal, *Psychopharmacology*, 81, p. 345.

Pisano, J.J., Crout, J.R. and Abraham, D.	1962	Quoted in Practical Clinical Bio-Chemistry, Vol. II, Herold Varley, Alan H. Gowerlock and Maurice Bell. 5th Edition, William Heineman Medical Books Ltd., p. 209.
Ramu, M.G., Janakiramaiah, N. Mukundan, H., Shankara, M.R., Leelavathy, S. Narasimhamurthy, N.S. and Venkataraman, B.S.	1982	Ksiradhara in Anxiety Neurosis (Chittodvega)—A pilot study, *JRAS*, Vol. 3, No. 3 & 4, p. 126-132.
Ramu, M.G. *et. al.*	1980	Controlled study on Role of *Ksheerabala taila* in Psychogenic Headache (*Vataja Shirah shoola*) *JRAS*, Vol. 1, No. 2, p. 291-300.
Roberts, K. and Vass, N.	1986	Schneiderian First rank symptoms caused by BZS withdrawal. *British Journal of Psychiatry*, 148, p. 593.
Singh, R.H. and Mehta, A.K.	1977	Studies on Psychotropic effect of the Medhya rasayana drug, Shankapushpi (*Convolvulus pluricalis* Part I. (Clinical studies) *J. Res. Ind. Med. yoga and Homoeo.* Vol. XII, No. 3, p. 18-25.
Skegg, D., Richards, S., Doll, R.	1979	Minor tranquillizers and road accidents. *British Medical Journal* 1, p. 917-19.
Teece, J.J., Friedman, S.B. and Mason, J.W.	1966	Anxiety, defensiveness and 17-hydroxy corticosteroid excretion, *J. Nerve. Ment. Disease.* 141, p. 549-54.

हिन्दी सारांश

एक आयुर्वेदीय योग का चिन्ता हर प्रभाव—एक विनिमयज प्रयोग

के. कुप्पुराजन, सी. शेषाद्रि, वी. राजगोपालन, कंचना श्रीनिवासन, आर. सीतारामन, जानकी इन्दुर्ती एवं एस. वेंकटराघवन

इस शोध पत्र में एक अज्ञात द्वय क्रिमक विनिमयज प्रारूप द्वारा आयुर्वेदिक योग के प्रभाव की तुलना आधुनिक औषधि एवं छद्मौषधि के 12 चिन्ता रोगग्रस्त आतुरों पर किए गए कार्यों के परिणाम समाहित हैं। मनोवैज्ञानिक मानदण्डों के निष्कर्ष दिखाते हैं कि आयुर्वेदिक योग ग्रहण विवेक एवं मानसिक तथा क्रियात्मक उपलब्ध दोनों औषधियों से अधिकृत प्रभावकारी हैं। जैव-रसायनिक मानदण्ड तथा प्रयोगफल के आंकड़े भी इंगित करते हैं कि आयुर्वेदिक औषधि तनाव को चयोपचयजन्य मूत्रोत्पत्ति को कम कर के (17 ओ एच सी एस एवं वी एम ए) तनाव से सुरक्षा प्रदान करते हैं। आयुर्वेदिक समूह की अभ्यान्तरिक तुलना दर्शाती है कि यह औषधि शरीरिक एवं मानसिक चिन्ता पर अंकुश लगाने में प्रभावकारी है। अतः आयुर्वेदिक औषधि का प्रयोग निम्न स्थितियों में सुरक्षित है—

1. शरीरिक एवं मानसिक अबलम्बन रहित आशंका के दीर्घकालिक प्रयोग।
2. चिन्ताग्रस्त भीषण एवं चिरकाल के रोगियों पर।
3. वृद्धों में बिना किसी आयु संबंधी अहित की आशंका के।
4. ऐसे रोगियों पर जिनमें शारीरिक एवं मानसिक दोनों ही प्रकार के लक्षण विद्यमान हों।