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To compare the efficacy and safety of Panchgavyaghrit (PGG) administered with escitalopram in mild to moderate depressed patients.

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ABSTRACT

Background: Many drug has been mentioned in Ayurvedic psychiatry. Panchagavya gritha (PGG) is mentioned in *Apasmarachikitsa* and is one of the commonly used yogas not only for *apasmara,* but also many other psychiatric conditions including OCD, depression and schizophrenia.**Objective:**To compare the efficacy and safety of Panchgavyaghrit (PGG) administered with escitalopram in mild to moderate depressed patients against escitalopram only group.**Material & Methods:** The present study was prospective study carried out in outdoor patients in the department of Psychiatry in collaboration with department of Pharmacology, T.S. Misra Medical College& Hospital. The present study was conducted from September 2016 to January 2017.**Results:I**n the present study, we observed that less side effects were reported in patients taking only escitalopram on initial dosage but on increasing dosage more side effects were observed in escitalopramonly group as compared to patients taking escitalopram and PGG. **Conclusion:**PGG with escitalopram have lesser side effects and better compliance.

KEYWORDS PanchGavyaGhrit, Escitalopram Depression, Antidepressants

Introduction

Depression is a complex diagnostic construct, applied to individuals with a particular set of symptoms among which the essential ingredients are depressed mood and loss of interest.[1-2]Across the world, 10.07% of disability can be attributed to unipolar major depression. It contributes to nearly 20% of disease in women aged from 15 – 44 years. W.H.O. expects that by the year 2020, unipolar major depression will be the second leading cause disease burden in the world. Aggregate burden of disability associated with depression of mild severity may be greater than the disability associated with the smaller number of people with the more severe depression[3] Depressive symptoms are not recognized in around 50% of attending patients and aggregate disability is more in them, so sample was drawn from mild to moderate depressed patients.[4] According to Ayurveda, action of a drug is based on its *guna, veerya, vipaaka* and *prabhaava.* These as themselves or as combinations determine the status of drug action in the body. Fate of the drug always depends on *rasapancakaand* it goes in line with modern pharmacodynamics.[5]

Many drug has been mentioned in Ayurvedic psychiatry. *Panchagavya gritha(PGG)* is mentioned in *Apasmarachikitsa* and is one of the commonly used yogas not only for *apasmara,* but also many other psychiatric conditions including OCD, depression and schizophrenia. The combination contains 5 ingredients-*Gosakrt* (Cow's dung), *Godadhi* (Curd), *Goksheera* (Cow's Milk), *Gomootra* (Cow's urine) and *Goghrta* (Cow's Ghee).[6] All the drugs are taken in equal quantities and the gritha is prepared as per the common preparatory techniques.[7] Literature revealed that cow ghee, cow milk and cow urine possesses intellect and memory enhancing, rejuvenating and aphrodisiac activities.[8-10] Cow dung juice has antibacterial[11]and cow curd has aphrodisiac[12]activity. Similarly, various researches are reported on single cow products for their effects on CNS. Thus combination of these products may show cumulative desired effect of PGG on cognition. Previously PGG has been assessed for anticonvulsant[13], hepatoprotective[14] and antiepileptic activities.[15]However, no work has been carried out on assessment of anti-depressant activity of PGG.

Material & Methods:

The present studywas prospective study carried out in outdoor patients in the department of Psychiatryin collaboration with department of Pharmacology, T.S.Misra Medical College& Hospital. The present study was conducted from September 2016 to January 2017. A written consent was taken from participants. A total no. of 275 patients were screened of which 175 patients were excluded on the basis of exclusion criteria. Side effect monitoring was done by a pharmacologist and a psychiatrist using Dosage Record Treatment Emergent Symptom Scale (DOTES scale). The patients diagnosed to be suffering from depression as per diagnostic criteria of International Classification of Diseases-10 (ICD-10) were randomly allocated to either of the two groups. The sample size consisted of 50 patients for each mild to moderate depression were drawn from OPD. Subjects above 18 years of age of either gender, diagnosed to be suffering from depression (F 32.0 or F 32.1 as per ICD -10)with or without somatic symptoms or recurrent depressive disorder (F 33.0 or F 33.1 as per ICD -10), duration of current depressive episode is to be between 4 weeks to 12 months, and scoring >6 and ≤ 34 on MADRS(Montgomery Asberg Depression Rating scale), CGI-S(Clinical global impression)>3 and <5 on the initial visit were enrolled in the study. Patients having Axis I or Axis II disorder other than depressive disorder, scoring> 4 on MARDS items number 10 (suicidal thoughts) at screening or baseline, history of non-response to an adequate (6 week) trial of three or more antidepressants (with or without mood stabilizers) during the current episode, with imminent risk of suicide or injury to self, others, or property, pregnant, lactating women or women not using medically accepted method of contraception were excluded. A detailed baseline assessment was done as per the semi-structured proforma which included psychiatric and medical history, physical examination and detailed mental status assessment. Dosage schedule was random allocation of Escitalopram 20mg (Group A) and Escitalopram 20mg and PGG (Group B) belonging to study population were done. Patients were followed at every2-week interval. At each visit, detailed evaluation pertaining to efficacy and safetywas done by administering scales taking history and observation by the therapist.This study consisted of two periods: a prospective baseline screening period lasting up to 2 weeks (week -2 to week 0, T0), and a treatment period lasting 8 weeks after enrollment (weeks 0-12, T1-T6). The treatment phase consisted of a 2-week titration period (T1) and a 10-week maintenance period (T2-T6). In the either of the groups during the titration period, subjects were given 10mg/day Escitalopram once daily in the first week, followed

by 20 mg/day escitalopram in divided doses (twice daily) in the second week. When subjects could not tolerate this target dose, the initial dose was continued through T6. Escitalopram was given as per the dosage schedule and in the second group PGG 5ml OD before food once daily in the first week, which was increased to 5ml BD before food in the second week. When subjects could not tolerate this target dose, the initial dose of escitaloprama long with PGG was continued through T6.

Drugs &Instruments used were:

- Escitalopram- Obtained from Sun-Pharmaceutical Industries Ltd.
- PGG- obtained from ParthvimedhaGau Pharma Pvt. Ltd.
- Semi-structured proforma for socio demographic details.
- Details of psychiatric history and examination
- Montgomery Asberg Depression Rating Scale (MADRS) [16]
- Clinical global impression (CGI-S)[17]
- Dosage Record Treatment Emergent Symptom Scale (DOTES)[18]

At every visit depressive symptom were measured by using Montgomery-Asberg Depression Rating Scale (MADRS). At initial visit severity of symptoms were assessed by CGI-S. At visits, space between every two weeks; Clinical global impression – improvement (CGI-I) were given to the subjects. Adverse effects were also either recorded by the patient, reported by the patient, observed by the therapist or either elicited by the therapist on each visit. The results are based on the data obtained from100 participants. Data were analyzed using MS Excel 2007 and summarized as counts and percentages.

Results:

Regarding socio-demographic variables, both escitalopram and escitalopram and PGG group had no significant difference. Pertaining to clinical variables like duration of illness, type of onset, episodicity and family history of similar illness statistical analysis revealed that there was no significant different in duration, onset, episode and family history between the two groups in present study. (Table-1) It was observed that there were significant changes in mean in MADRS scores in the both the group from the base line and revealed significant reductions in MADRS score at end of 2-12 weeks. Escitalopram and PGG group had slightly more reduction of MADRS scores than Escitalopram group however not clinically significant. (Table-2) Overall there was more reduction in CGI scores in Escitalopram and PGG group as compared to escitalopramgroup at the end of 12 weeks. (Table-3) Patient discontinued more in escitalopram group as compared to escitalopram and PGG group. In PGG group, there were less side effects and better tolerance. In the present study, we observed thatless side effects were reported in patients taking only escitalopram on initial dosagebut on increasing dosage more side effects were observed in escitalopramonly group as compared to patients taking escitalopram and PGG. (Table-4)

Discussion

Among the huge treasures of drugs mentioned in the Ayurvedic treatise, PGG is considered very important in *Apasmarachikitsa,* paralleling psychiatry in modern medicine.It is alsocleansing the channels in the body which brings clarity to the mind and its functions thus PGG is effective in improving the cognitive functions. A study conducted by FibiMol et al. concluded that medhya drugs like gritha improves the intellectual functions.[19] A study was done by Kakkassery et al. to evaluate the effect of PGG inthe management of schizophrenia and it was found to be effective.[20]A previous study on PGG revealed that it was effective in both the obsessive and compulsive part of OCD.Above studies also revealed that PGG is effective in management of some psychiatric disorders. Besides that, the gritha is the best drug for potentiating dhee, dhriti and smrithi, which are the components of budhi.[21]. In the present study, when PGG and escitalopram combination showed greater efficacy, lesser side effects and better compliance.

Conclusion:

PGG with escitalopram have lesser side effects and better compliance.But there is need of further studiesto prove the findings of present study.

Table-1: Depicts the sociodemographic variables of the 60 subjects enrolled in the study

Variables	Escitalopram(n=50)	Escitalopram and PGG (n=50)		
	N	%	N	%
Age (in yrs)				
Up to 30	5	10.0	2	4
31-45	45	90.0	48	96
Sex				
Male	17	34	20	40.0
Female	33	66.0	30	60.0
Marital status				
Married	21	42	19	38
Single	29	58	31	62
Duration				
<1 Months	14	28	11	22
1-6 Months	30	60	28	56
> 6 Months	06	12	11	22
Onset				
Insidious	24	48	22	44
Acute	26	52	28	56
Episode				
1	41	82	42	84
>1	09	18	08	16
Family history of similar illness	Present	11	22	10
	Absent	39	78	40

Table – 2: Mean change in MADRS score from baseline in two groups

Change from baseline	Escitalopram(n = 50)	Escitalopram and PGG (n = 50)
	Mean	Mean
After 2 weeks (T1)	4.30	5.86
After 4 weeks (T2)	8.83	9.80
After 6 weeks (T3)	12.33	15.73
After 8 weeks (T4)	16.21	20.36
After 10 weeks (T5)	20.21	25.78
After 12 weeks (T6)	24.36	29.45

Table – 3: Change in CGI Score from Baseline

Change from baseline	Escitalopram (n = 50)			Escitalopram and PGG (n = 50)		
	No Change No. (%)	Decrease No. (%)	Increase No. (%)	No Change No. (%)	Decrease No. (%)	Increase No. (%)
After 2 weeks (T1)	20 (40.0)	26 (52.0)	4 (8.0)	20 (40.0)	32 (64.0)	8 (16.0)
After 4 weeks (T2)	12 (24.0)	35 (70.0)	3 (6.0)	8 (16.0)	40 (80.0)	2 (4.0)
After 6 weeks (T3)	12(24.0)	37 (74.0)	1(2.0)	3 (6.0)	47 (94.0)	0 (0)
After 8 weeks (T4)	10 (20.0)	38 (76.0)	2 (4.0)	2 (4.0)	48 (96.0)	0(0)
After 10 weeks (T5)	8 (16.0)	40 (80.0)	2 (4.0)	1 (2.0)	49(98.0)	0(0)
After 12 weeks (T6)	7 (14.0)	41 (82.0)	2(4.0)	0	50 (100.0)	0(0)

Table– 4: Side effects assessed by DOTES AND Side effect (either reported by the patient, observed by the clinician or elicited by the therapist)

Side Effects	Escitalopram (n = 50)							Escitalopram and PGG (n = 50)						
	DAY							DAY						
	0	14	28	42	56	70	84	0	14	28	42	56	70	84
Flatulence	-	1	2	2	2	2	1	-	1	1	1	1	1	-
Somnolence	-	1	2	2	2	2	2	-	1	1	1	1	1	1
Decreased libido	-	1	2	2	2	2	2	-	-	1	1	1	-	-
Anxiety	-	1	1	1	1	1	1	-	-	1	1	-	-	-
Orgasmic Abnormality	-	1	2	2	2	2	2	-	1	1	1	-	-	-
Lethargy	-	1	2	2	2	2	2	-	1	1	1	-	-	-
Dream Abnormality	-	1	2	2	2	2	2	-	1	1	1	1	-	-
Yawning	-	1	2	2	2	2	2	-	1	1	1	1	1	-
Vomiting	-	1	2	3	-	-	-	-	-	1	1	-	-	-
Palpitation	-	1	2	2	2	2	3	-	1	1	1	-	-	-
Indigestion	-	1	2	3	2	2	2	-	-	1	1	-	-	-
Abdominal Pain	-	1	2	3	2	1	1	-	-	1	1	1	1	-
Influenza like symptoms	-	1	2	1	-	-	-	-	1	2	1	-	-	-
Fatigue	-	1	2	3	2	2	2	-	-	1	1	-	-	-
Ejaculation Disorder	-	1	2	3	3	3	3	-	1	2	1	1	1	-
Impotence	-	1	2	2	2	2	2	-	-	1	1	-	-	-
Anorgasmia	-	1	2	3	3	3	3	-	1	1	1	1	-	-
Rhinitis	-	1	2	3	2	2	2	-	-	2	1	1	--	-
Sinusitis	-	1	2	3	2	2	2	-	-	1	1	-	-	-
Dizziness	-	1	2	3	3	3	3	-	-	1	2	1	-	-
Decreased appetite	-	-	1	2	2	2	3	-	-	1	1	1	-	-
Headache	-	2	2	3	4	5	7	-	1	2	1	1	-	-
DOTES Scale														
a.Behavioral toxicity														
Insomnia	-	1	2	4	6	8	9	-	1	2	2	2	1	-
b.Autonomic and GIT														
1. Dry mouth	-	1	2	3	3	3	3	-	1	1	1	-	-	-
2.Constipation	-	1	2	3				-	-	1	1			
3.Increased Salivation	-	1	2	3	3	3	3	-	1	1	2	1	-	-
4.Sweating increased	-	1	2	3	3	4	4	-	-	1	1	-	-	-
5. Nausea	-	2	4	6	7	8	8	-	2	3	3	2	2	2
6. Diarrhea	-	1	2	4	5	6	7	-	1	2	2	2	2	2
d. Others														
1.Dermatologic														
2. Weight gain	-	-	1	2	3	3	3	-	1	1	1	-	-	-

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