

THE THERAPEUTIC ROLE OF MAGNESIUM IN DIFFERENT DEPRESSIVE SYNDROMES OF FEMALE PATIENTS

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ABSTRACT:

Numerous studies have proven that low levels of B vitamins, vitamins C and magnesium have been associated with depression. These all help in the brain's production of neurotransmitters and may enhance the effectiveness of antidepressant medications. Calcium and magnesium have a soothing effect on the nerves and can be particularly helpful when depression interferes with sleep. Previous studies have shown that there are depleted magnesium levels in the depressed patients. The present study is based on the finding that magnesium supplements can reduce the signs and symptoms of depression. In this experiment behavioral and somatic features were evaluated such as agitation, guilt feeling, psychomotor retardation, insomnia, anxiety, weight loss, hypochondria which are the hall marks of clinical depression. The female subjects who were diagnosed with clinical depression and premenstrual dysphoric disorder were treated with daily dose of 360 mg. of magnesium. Depression was evaluated for three months. Nearly all the female patients responded positively to the magnesium therapy with elevation of mood, relaxation and sleep duration.

Keywords: Depression, vitamin B, vitamin C, magnesium, antidepressants, anxiety, insomnia, guilt feelings, agitation, hypochondriasis.

INTRODUCTION

Depressive disorders involve the body, mood and thoughts. Major depression is manifested by a combination of symptoms that interfere with the ability to work, study, sleep and enjoy. On the other hand mania often affects the thinking, judgment, and social behavior and can cause serious problems (Nulman 1997).

Depression can occur in families, but can also occur in people with no family history. Medical illnesses such as stroke, heart attack, cancers and hormonal disorder can also cause depressive illnesses. Hence a combination of genetic, psychological and environmental factors are involved in depressive illness. (Hkschfled1997). The rate of incidences of depression is more in women as compared to men (Konstein, 1997). The management of the depression involves the use of antidepressants

and counseling both. Women achieve higher plasma concentration of antidepressants, so may require low doses (Harrison 1990).

The diagnostic criteria for major depression is established as DSM-IV (Diagnostic and statistical Manual of Mental Disorder), which is the same for men and women. The symptoms are sub-grouped into:

Psychological (4 symptoms)
Physical (5 symptoms)

For a person to be declared as depressed he/she should have five symptoms positive and the inclusion, exclusion and duration criterias are also specified.

Patients with mild to moderate depression may respond to psychosocial therapy alone for a limited period, or they may be used in conjunction with antidepressant medicines

(McElhatton 1996). The different types of depression are observed in female and those associated with their reproductive life cycles are:

Premenstrual dysphoric disorder

(The symptoms are mild, begin a week before menses and remit within a few days after onset)

Depression during Pregnancy

(The risk of treatment is prevalent, requires assessment of risks and benefits for both mother and fetus.) (The symptoms may indicate moderate to severe depression and different classes of drugs may be used along with the choice of Electro – Convulsive Therapy.)

Depression during post – partum period

(Mild symptoms observed for four to ten days.) (If physical symptoms and depressed mood persists for more than two weeks then could lead to major depression)

Depression during pre menopausal period

(May be due to vasomotor instability and the symptoms may be moderate and require antidepressant drug therapy.)

Depression associated with infertility, miscarriage or prenatal loss.

(Symptoms may be mild and if persists beyond eight weeks, then treatment is required)

The management of depression includes:

Counseling
Drug Therapy

Along with drug therapy belonging to different classes, it has been demonstrated that the deficiency of vitamins and minerals can also cause depression and the correction of deficiencies often relieves depression. Among vitamins such as Vitamin B₆, folic acid, vitamin C and Magnesium deficiency can also cause numerous psychological changes including depression (Altshuler 1998).

The symptoms of Magnesium deficiency include memory loss, restlessness and insomnia (Durlach 1987). The plasma levels have been found to be low in depressed patients as compared to controls. Magnesium has also been used to treat premenstrual mood changes (Fatemi 1991).

According to Poleszak (2004) magnesium has antidepressant and anxiolytic effects without causing tolerance. Magnesium ions regulate Ca ion flow in neuronal Ca channels and help to regulate neuronal nitric oxide production in the deficiency of magnesium, there may be neuronal damage that is manifested as depression (George and Karen 2006).

It has also been reported by Lazaro et al (2007) that hypomagnecemia is independently associated with depressive symptoms in older people with diabetes.

MATERIALS AND METHODS

Thirty females with either chronic depression or with chronic pain with depression were selected. They were diagnosed through Hamilton Rating scale for depression. The patients were evaluated before and after magnesium therapy for following aspects:

- Depressed mood
- Guilt feeling
- Suicidal thoughts
- Insomnia (early, middle or late)
- Functional capabilities
- Psychomotor Retardation.
- Agitation
- Anxiety (psychological, somatic)
- Somatic GI symptoms
- Somatic General symptoms
- Sexual dysfunction
- Weight loss
- Insight

Magnesium was given in the dose of 320 mg/day for three months. This dose was

Table 1
Symptoms present according to age

S #	Symptoms	Age in years					
		15-24		25-34		35-44	
		(n=10)		(n=10)		(n=10)	
		No.	%	No.	%	No.	%
1	Depressed mood	5	50	7	70	6	60
2	Guilt Feeling	6	60	6	60	8	80
3	Suicidal Tendency	5	50	5	50	5	60
4	Insomnia (Early, Middle, Late)	9	90	6	60	6	60
5	Work and activities	7	70	9	90	6	60
6	Retardation-Psychomotor	5	50	6	60	5	50
7	Agitation	2	20	6	60	2	20
8	Anxiety Psychological	2	20	4	40	0	0
9	Anxiety Somatic	6	60	5	50	3	30
10	Somatic Symptoms GI	5	50	5	50	0	0
11	Somatic Symptoms General	5	50	5	50	4	40
12	Sexual Dysfunction / Menstrual Disturbance	4	40	5	50	3	30
13	Hypochondrias	3	30	4	40	1	10
14	Weight Loss	4	40	5	50	3	30
15	Insight	2	20	3	30	1	10

Age in year = 15-24 (n=10) 4.66 + 0.032 (P < 0.05)

Age in year = 25-34 (n=10) 5.4 + 0.04 (P < 0.01)

Age in year = 35-44 (n=10) 3.53 + 0.033 (P < 0.05)

according to RDA approved daily requirement (RDA 1999).

The female patients were divided into three categories according to their ages:

Category I (15 – 25 years)

Category II (25 – 35 years)

Category III (35 – 45 years)

RESULTS

- *Depressed Mood* incidence was decreased after magnesium therapy. The result was significant in all age groups.
- *Guilt feelings* were also reduced in severity in all age groups, but it was more in Category III.
- *Suicidal tendency* also showed reduction in category I and II, but it was not significant, whereas in Category III, no effect was observed.
- *Insomnia* severity was reduced significantly in all age groups, and the effect was on all types of early, middle and late insomnia.
- *Functional capabilities* were improved significantly after magnesium therapy in all age groups and the results were highly significant.
- *Psychomotor Retardation* was also highly improved in all age groups and the results were very significant.
- *Agitation* was also reduced in all age groups, but the results were highly significant for category II and III.

Table 2
Symptoms rating according to age

S #	Symptoms	Rating	Age in years					
			15-24		25-34		35-44	
			(n=10)		(n=10)		(n=10)	
1	Depressed mood	Mild	3	30	3	30	5	50
		Moderate	2	20	4	40	1	10
		Severe	0	0	0	0	0	0
2	Guilt Feeling	Mild	2	0	3	30	6	60
		Moderate	3	30	3	30	2	20
		Severe	4	10	0	0	0	0
3	Suicidal Tendency	Mild	3	30	5	50	5	50
		Moderate	1	10	0	0	1	10
		Severe	1	10	0	0	0	0
4	Insomnia (Early, Middle, Late)	Mild	8	80	6	60	4	40
		Moderate	0	0	0	0	2	20
		Severe	1	10	0	0	0	0
5	Work and activities	Mild	5	50	6	60	5	50
		Moderate	1	10	2	20	1	10
		Severe	1	10	1	10	0	0
6	Retardation-Psychomotor	Mild	2	20	6	60	4	40
		Severe	1	10	1	10	0	0
		Moderate	3	30	0	0	1	10
		Severe	0	0	0	0	0	0
7	Agitation	Mild	0	0	4	40	2	20
		Moderate	2	20	2	20	0	0
		Severe	0	0	0	0	0	0
8	Anxiety Psychological	Mild	0	0	3	30	0	0
		Moderate	2	20	1	10	0	0
		Severe	0	0	0	0	0	0
9	Anxiety Somatic	Mild	2	20	2	20	2	20
		Moderate	3	30	2	20	0	0
		Severe	1	10	1	10	1	10
10	Somatic Symptoms GI	Mild	4	40	4	40	0	0
		Moderate	1	10	1	10	0	0
		Severe	0	0	0	0	0	0
11	Somatic Symptoms General	Mild	4	40	4	40	3	30
		Moderate	1	10	1	10	1	10
		Severe	0	0	0	0	0	0
12	Sexual Dysfunction / Menstrual Disturbance	Mild	3	30	4	40	2	20
		Moderate	0	0	0	0	0	0
		Severe	1	10	1	10	1	10

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- *Anxiety* was very significantly reduced in all age groups, but the results were highly significant in the category II for psychomotor anxiety. The somatic anxiety was also reduced significantly in all age groups after the administration of magnesium as compared to Control.
- *Somatic GI symptoms* were also reduced in all age groups and the results were significant, whereas the *General Somatic*

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S #	Symptoms	Rating	Age in years					
			15-24		25-34		35-44	
			(n=10)		(n=10)		(n=10)	
13	Hypochondrias	Mild	2	20	4	40	0	0
		Moderate	0	0	0	0	0	0
		Severe	1	10	0	0	1	10
14	Weight Loss	Mild	0	0	2	20	0	0
		Moderate	0	0	0	0	0	0
		Severe	0	0	0	0	0	0
15	Insight	Mild	1	10	2	20	1	10
		Moderate	1	10	1	10	0	0
		Severe	0	0	0	0	0	0

- symptoms* were either not present or were not affected by magnesium therapy.
- *Sexual dysfunction* particularly menstrual disturbances were improved significantly in Category I and II. The results were not significant in Category III.
 - *Weight loss* was improved in all age groups after the magnesium therapy and the results were significant.
 - *Insight* was not affected by magnesium therapy and no effect was observed in any Category of Patients.

DISCUSSION

Magnesium deficiency is one of the causes of depression and magnesium therapy can be useful in recovery from depression (Dahle 1995). Virtually all significantly depressed patients are deficient in Magnesium and clinicians should consider the use of Magnesium for therapeutic benefits in chronic depression (Rockville 1993). Urinary magnesium excretion is increased by most diuretics, as well as by epinephrine, nor epinephrine and caffeine (Cox 1991).

Magnesium is a major regulator of all membrane potential and the deficiency of magnesium prevents normal nerve cell stability and can lead to symptoms of depression (Facchinetti *et al.*, 1991).

Magnesium has an important role in the conversion of propionic acid to propionylCoA and succinylCoA, where succinylCoA serves as a precursor of myelin sheath of the nerve, which is very essential for the normal generation and propagation of action potentials. Also according to Ananda and Anil (2010) the depletion of magnesium is observed in animal brain and in human blood after brain injury, and the treatment with magnesium attenuates the pathological and behavioral changes in rats with brain injury.

Magnesium is also required for decreasing the formation of free radicals and scavenging the reactive oxygen species (Chambers 1996). Magnesium is also required for the synthesis of ATP, for the synthesis of protein, anaerobic breakdown of glucose and removal of toxic substances such as ammonia from the body (Durlach 1987).

The reduction in anxiety is possibly due to the increase availability of dopamine, as magnesium and vitamin B6 deficiency causes a reduction in the production of dopamine. Increased dopamine modulates the negative effects of excitatory amines by inducing relaxation (Muneyvirici 1998). Magnesium sulphate can act as an anticonvulsant by blocking the action of acetylcholine at central level, which can lead to anxiety symptoms.

Table 3a
Symptoms rating (%) before and after treatment with magnesium according to age

S #	Symptoms	Severity	Age in years					
			15-24		25-34		35-44	
			(n=10)		(n=10)		(n=10)	
			Pre	Post	Pre	Post	Pre	Post
1	Depressed mood	None	50	70	30	70	40	60
		Mild	30	30	30	30	50	40
		Moderate	20	0	40	0	10	0
		Severe	0	0	0	0	0	0
2	Guilt Feeling	None	40	50	40	50	20	70
		Mild	20	50	30	50	60	30
		Moderate	30	0	30	0	20	0
		Severe	10	0	0	0	0	0
3	Suicidal Tendency	None	50	60	50	40	40	40
		Mild	30	30	50	1	50	60
		Moderate	10	10	0	0	10	0
		Severe	10	0	0	0	0	0
4	Insomnia (Early,	None	10	70	40	80	40	60
		Mild	80	30	60	20	40	40
		Moderate	0	0	0	0	20	0
		Severe	10	0	0	0	0	0
5	Work and activities	None	30	80	10	50	40	80
		Mild	50	20	60	50	50	20
		Moderate	10	0	20	0	10	0
		Severe	10	0	10	0	0	0
6	Retardation-	None	50	70	40	70	50	80
		Mild	20	30	60	30	40	20
		Moderate	30	0	0	0	10	0
		Severe	0	0	0	0	0	0

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After administration of magnesium in our study the reduction in the somatic symptoms of GI involves the action through hormones that is magnesium can enhance insulin secretion and also improves incorporation of glucose due to which facilitation of sugar metabolism and utilization takes place. The general somatic symptoms were also improved due to the better delivery of glucose indicating

that magnesium is very important in glucogenesis reactions of the mitochondria (Emelianova 1996).

The premenstrual symptoms were improved after magnesium supplementation because the magnesium concentration of RBCs was found to be low in women with premenstrual syndrome. The calcium to

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S #	Symptoms	Severity	15-24		25-34		35-44	
			(n=10)		(n=10)		(n=10)	
			Pre	Post	Pre	Post	Pre	Post
7		None	80	90	40	80	80	90
		Mild	0	10	40	20	20	10
		Moderate	20	0	20	0	0	0
		Severe	0	0	0	0	0	0
8	Anxiety Psychological	None	80	90	60	90	100	100
		Mild	0	10	30	10	0	0
		Moderate	20	0	0	0	0	0
		Severe	0	0	0	0	0	0
9	Anxiety Somatic	None	40	70	50	60	0	80
		Mild	20	30	20	30	20	20
		Moderate	30	0	20	10	0	0
		Severe	10	0	10	0	10	0

magnesium ratio is also affected by hormonal fluctuations leading to premenstrual symptoms (Facchinetti 1991).

The effect on the weight loss is due to the effect on insulin release and proper utilization of glucose, along with magnesium playing a positive role in the functioning of parathyroid glands, metabolism of vitamin D, and adequate sensitivity of bone to parathyroid hormones and vitamin D (Elamin and Tuvemo 1990).

Magnesium deficiency might also contribute to the development of Pre-Eclampsia and to impaired neonatal development. Neurologically the inhibition of Ca channels and the antagonism of NMDA receptors rises the possibility of neuronal protection, also magnesium administration to women with premature labor may decrease the incidence of cerebral palsy (James 2009).

According to James *et al* (2000) magnesium can increase the antimanic efficacy of verapamil by mechanism that operate at intracellular level. The Mg – verapamil combination may have clinical application as an adjunct to verapamil in the maintenance therapy of mania.

It is concluded that magnesium therapy is very effective in reducing the signs and symptoms of depression and premenstrual dysphagia in the females of all age groups with no evident adverse effects. Dietary intake of high magnesium containing food is also recommended, and the magnesium can act synergistically with other antidepressant medications. The work could be further extended to observe the effects of magnesium in male depressed patients also.

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