

Inositol:
A Scientific Evaluation of its Clinical
Effectiveness

LTP Technical Writing

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Inositol: A Scientific Evaluation of its Clinical Effectiveness

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Inositol is a naturally occurring isomer of glucose. It is a key intermediate of a second messenger system used by numerous serotonergic, cholinergic and noradrenergic receptors, making compounds containing inositol important in signal transduction. In addition, inositol is a primary component of cellular membrane phospholipids. Clinical research studies indicate that inositol is an effective, safe alternative to antidepressant medication (particularly selective serotonin reuptake inhibitors and tricyclic antidepressants) for the management and treatment of depression, panic disorders and obsessive compulsive disorders (OCD). Inositol's efficacy, in the absence of side effects, makes this nutrient an attractive addition to treatment plans for specific mood disorders. Following is a scientific review of inositol for the treatment of mood disorders, including a discussion of its anecdotal use for the treatment of insomnia and its cautioned use by pregnant women for the prevention of neural tube defects and embryopathies.

Inositol is generally considered to be a member of the B vitamin family and is present mainly as the fiber component, phytic acid. Intestinal bacteria are responsible for liberating inositol from phytic acid. Plant sources include nuts, seeds, whole grains, and citrus fruit. Animal foods

contain inositol primarily in the form of myo-inositol. Interestingly, this isomer of inositol is most abundant in the central nervous system. Inositol has been shown to exert beneficial effects in patients suffering from panic disorder, obsessive-compulsive disorder (OCD) and/or depression (Levine J, 1997; Benjamin J et al., 1995; Levine J et al., 1995; Benjamin J et al, 1995 (2)).

Depression

Depressive patients generally have decreased levels of inositol in their cerebrospinal fluid (Levine J, 1997). Researchers now theorize that inositol shows clinical results in patients with depression due to the intracellular phosphatidyl inositol second messenger cycle serving as a second messenger system for 5-hydroxytryptamine (5-HT₂) receptors. Serotonin selective reuptake inhibitors (SSRI's) have a similar therapeutic profile to inositol in that they inhibit serotonin reuptake in the synaptic cleft (Mishori A, et al. 1999). Researchers performed a double blind controlled trial for 28 days on 28 depressed patients using 12 grams of inositol per day. The Hamilton Depression Scale (HAMD) was used to evaluate patients after the 28-day trial period. Significant overall benefit was confirmed in the inositol group compared to the placebo group. No changes were noted in liver, kidney or hematological function (Levin J, 1995). A second trial confirmed the antidepressant effects of inositol (Benjamin J et al, 1995).

	PLACEBO	INOSITOL
BASELINE	32.87+/- 5.4	33.38 +/- 6.1
AFTER 2 WEEKS	29.27+/-7.2	27.31+/-8.0
AFTER 4 WEEKS	28.93+/-10.4	21.61+/-9.7
TOTALCHANGE	~3.94	~ 11.7 (F _{1,26} = 4.48, p = 0.04)

Table 1. The effect of inositol or placebo treatment for depression on mean +/- S.D. HDS (Levine et al, 1995)

Obsessive-Compulsive Disorder

Levine (1997) completed a meta-analysis of all research studies done using inositol on psychiatric patients. In addition to reviewing the studies on depression, Levine highlighted some interesting findings with obsessive-compulsive (OCD) patients. Serotonin plays a definitive role in obsessive-compulsive disorder. This role is confirmed by the specific effectiveness of SSRI's in OCD patients and the fact that serotonin agonists exacerbate the syndrome. In 1993, Rahman and Neuman effectively reduced serotonin receptor desensitization via the administration of myo-inositol. These research findings, coupled with the knowledge that SSRI's have proven beneficial in the treatment of obsessive-compulsive disorder (OCD) influenced Fux M et al (1996) to complete a double blind placebo controlled random-assignment crossover treatment trial using inositol. Thirteen patients completed the trial and all met DSM-III-R criteria for OCD. Six patients began the trial on placebo and seven began the trial on inositol (18 grams/day) for a total of six weeks for the first phase and six weeks for the crossover phase. The researchers decided to administer 18 grams of inositol versus 12 grams (typical dose for depressive patients) due to the fact that OCD patients generally respond to higher relative doses of SSRI's than is needed to effect a change in most depressive patients. All patients were free of drug and alcohol abuse and had no evidence of diabetes or GI disorder. OCD was assessed using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and depression and anxiety was assessed using the HDS and HAS. The mean improvement from baseline to six weeks in OCD symptoms was 5.9 ± 5.0 for inositol versus 3.5 ± 2.8 ($p=0.04$, paired t-test) on placebo. This indicates a measurable positive response with the administration of inositol in OCD patients. Table 2 further details the results of this study with respect to inositol's effect on subscale obsession, subscale compulsion, anxiety and depression (all of which showed marked improvement with the administration of inositol versus the placebo).

See Table on Following Page.

Patient	Total change in Y-BOCS score	Baseline	Placebo (6 wks)	Inositol (6 wks)
1	-10	22	17	11
2	-5	17	15	12
3	-7	27	24	20
4	-8	30	27	22
5	-11	14	13	3
6	-15	28	20	13
7	-11	16	8	5
8	-3	21	17	18
9	-4	18	11	14
10	+1	24	23	25
11	+1	24	23	23
12	0	34	35	34
13	-2	26	23	24
HAS +/-	N/A	15.00+/-	13.50+/-9.5	12.33+/-10.3
HDS +/-	N/A	14.83+/-8.6	13.75+/-9.6	11.0+/-9.1

Table 2. The effect of Inositol on OCD patients: Placebo vs. inositol using Y-BOCS scores (Fux M et al, 1996).

Panic Disorder

Some antidepressants are effective against panic disorder leading researchers to study the effects of inositol on these patients as well. Twenty-one patients diagnosed with panic disorder with or without agoraphobia were given 12 grams of inositol per day or a placebo. The severity and frequency of panic attacks declined significantly with minimal associated side effects noted. The average number of panic attacks per week in patients treated with inositol fell from 10 per week to 3.5. The researchers concluded that these results were "clinically meaningful" in the management of panic attacks (Benjamin et al, 1995).

Inositol Compared to Antidepressant Medications

Inositol has therapeutic effects in mood disorders that are generally

responsive to serotonin selective reuptake inhibitors (SSRI's). Clinical results suggest that conditions including depression, panic disorder and obsessive-compulsive disorder (OCD) show beneficial results with the use of inositol (Levine J, 1997; Benjamin J et al., 1995) when prior benefit was confirmed with the use of SSRI's. One study revealed that the therapeutic results of inositol for depression were similar to tricyclic antidepressant (TCA) drugs but without the adverse side effects commonly noted with TCA's (Benjamin J et al., 1995).

Insomnia

Inositol may assist patients suffering from insomnia. Researchers speculate that inositol's documented effects on regulating serotonin levels may aid in stimulating relaxation in an insomniac. However, as of yet, there are no valid double-blind controlled studies confirming its use for insomnia.

Not for Use During Pregnancy

Researchers have documented the preventive effect of inositol in folate-resistant neural tube defects in rats and mice (Greene ND et al, 1997;Reece E et al, 1997), as well as its positive effect in treating hyperglycemia-induced embryopathy (Khandelwal M et al, 1998). However, inositol is a calcium agonist. Specifically, oxytocin, a key uterine stimulator, activates phospholipase C in order to produce inositol-1,4,5-triphosphate which releases calcium from intracellular stores and stimulates uterine contractions (Colodny L et al, 1998). Calcium agonists such as inositol have been shown to affect dose-related myometrial contractions in laboratory mice (Chien E et al., 1996). Thus, it is possible that inositol may in fact stimulate uterine contractions indirectly via its intimate relationship with oxytocin making it potentially dangerous for pregnant women.

It appears that inositol's efficacy coupled with the absence of significant side effects make this nutrient an attractive addition to treatment plans for patients suffering from panic disorder, clinical depression and/or obsessive-compulsive disorder.

Indications for Use

Mild to moderate depression (*Levine J et al, 1995*)

Obsessive-compulsive disorder (OCD) (*Fux M et al, 1995;Rahman S et al, 1993*)

Panic attacks (*Benjamin J et al, 1995*)

Potential Indications for Use

Diabetes (*preliminary report published by Cai F et al, 1990*)

Insomnia (*anecdotal*)

Alzheimer's Disease (*Barak Y et al, 1996 – indicated slight improvement in cognitive function but concluded that trend shown for increased improvement was not significant*)

Liver Disorders (*anecdotal*)

Drug/Nutrient Interactions: Inositol works synergistically with methyl donors.

Dosage Recommendations: See the reports of clinical trials summarized herein

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