

DRUG TREATMENT OF OBSESSIVE — COMPULSIVE DISORDER

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Obsessive compulsive disorder is a common, usually chronic and sometimes disabling neuro psychiatric syndrome of unknown aetiology. In obsessive compulsive disorder, the irrational ideas or the impulse persistently intrudes into the awareness, Obsessions (constantly recurring thoughts such as fear of exposure to germs) and compulsions (repetitive action such as washing hand many times) are recognized by the individual as absurd and are resisted but anxiety is alleviated only by ritualistic performance of the action or by deliberate contemplation of the intruding idea or emotion. Many patients do not mention the symptoms and must be asked about them. Male-female ratio is similar, highest rate of the obsessive compulsive disorder occurring in young, divorced, separated and unemployed (all high stress categories).¹

Findings from the community based epidemiological catchment area survey carried out in USA found that 2-3% of population may suffer from obsessive compulsive disorder at some point during their life time, a prevalence rate which is twenty times, higher than previous estimates. It remained hidden because 60% of all obsessive- compulsive disorder patients were seen by either primary care physicians or other non psychiatric health professionals. Patients were reluctant to talk about their crazy symptoms. Some

patients with long terms and washing compulsions sought treatment from general practitioner or dermatologist for non specific dermatitis of hand before seeking treatment for obsessive compulsive disorder.²

Now greater professional and public awareness coupled with optimistic treatment outlook, may explain why more patients with obsessive compulsive disorder are now being brought to clinical attention.¹

The early diagnosis and treatment of this disorder is essential because it can lead to social consequences like disruption in education, social isolation, marital difficulties and neglect of children.²

A wide variety of treatment are available for the obsessive compulsive disorder. These include:-

1. Physical methods of treatment
 - A. Drug treatment
 - B. Electro convulsive therapy
 - C. Surgical treatment
2. Behavioral therapy
 1. Physical methods of treatment

A. DRUG TREATMENT

The present review aims to highlight the role of drugs in the treatment of obsessive

compulsive disorder in the light of current literature.

i. Role of clomipramine.

Pharmacotherapy is used by some clinicians as a first line approach to the treatment of obsessive compulsive disorder. Clomipramine has become the standard drug for use in obsessive compulsive disorder. Clomipramine is a tricyclic antidepressant and is semi-selective serotonin re uptake inhibitor. It is metabolized into clomipramine and N-desmethylclomipramine in the body. The higher plasma concentration of clomipramine, co related significantly with improvement in obsessive compulsive symptoms, while depression appears to co relate with plasma levels of desmethyl clomipramine. The anti obsessional effects of clomipramine is mediated by its effect on five hydroxytryptamine.³

Griest et al⁴ as a part of 21 site multi-centre investigation, found clomipramine treatment to be associated with statistically significant improvement on several measures of obsessive compulsive symptoms in 32 non depressed obsessive compulsive disorder patients. Although 19% clomipramine treated patients could not tolerate the drug because of side effects, they concluded that clomipramine is an effective and generally well tolerated, short treatment for obsessive compulsive disorder.

Twenty one patients with obsessive compulsive disorder remained improved from 5 to 27 moths with clomipramine. After discontinuation of drug sixteen (16) patients have recurrence of obsessive compulsive symptoms. This finding points toward the prolonged treatment of this disorder. However, the side effect of clomipramine are responsible for the failure of treatment in many cases.⁵

Monteiro et al.⁶ reported that in their study 24 patients on clomipramine developed complete or, partial anorgasmia none of the patient treated with placebo did so.

The complete or partial anorgasmia persisted throughout the course of treatment. Both sexes were equally effected, such side effects can lead to discontinuation of clomipramine therapy. The other common side effects of the clomipramine include dryness of mouth, constipation, increased sweating, anorgasmia in females and retarded ejaculation in males.

The efficacy of clomipramine as short term and generally well tolerated drug in obsessive compulsive disorder has been confirmed by following studies.^{3,7,8,9,10}

ii. The role of selective serotonin re-uptake inhibitors (SSRI's).

There are new group of anti depressants which selectively inhibit the re uptake of serotonin at synaptic level, because of selective action on serotonin re uptake, they are also good anti obsessional agents. Because of more selective nature of SSRIs, they are devoid of anti cholinergic, anti muscarinic and anti adrenergic side effects, which are inherent in classical tricyclics compound.

Following are the most commonly studied SSRIs.

1. Fluoxetine
2. Fluvoxamine
3. Sertraline

According to Fineberg et al.¹¹ patients with obsessive compulsive disorder, need short as well as long term symptomatic relief due to the chronic nature of the disorder. As the SSRIs had comparatively early response and incremental reduction of obsessive compulsive symptoms, and they appear well tolerated they should be regarded as the treatment of choice in obsessive compulsive disorder.

Patients suffering from obsessive compulsive disorder were given fixed doses of fluoxetine (20 mg, 40 mg, 60 mg) or placebo for eight weeks. There was significant dose

response relation ship, with best response seen with 60 mg and the poorest response with 20 mg. The results of this study suggests that high doses of fluoxetine are associated with best anti-obsessional response. However, at high doses serotonin syndrome should be kept in mind which is characterized by rigidity, hyperthermia, autonomic, instability, myoclonus, convulsion, confusion, delirium and coma.¹²

Goodmans et al¹³ studied the effect of fluvoxamine and desipramine (a tricycle antidepressant) in obsessive compulsive disorder. Eleven out of 21 patient responded to fluvoxamine compared with 2 out of 19 who responded to desipramine. Fluvoxamine has shorter half life which also allow for rapid clearing if adverse side effect appear. The result of this study provide evidence that 5HT re uptake properties of a drug are predictive of its efficacy as an anti obsessive compulsive agent.

Sertraline in daily dosage of 50-200 mg has been found to be safe and effective treatment for obsessive compulsive disorder and superior to placebo. Author compared these results with clomipramine and concluded with the remarks, that both drugs have significant therapeutic efficacy, but SSRI's were superior to clomipramine, because they have a minimal side effect profile as compared to clomipramine.¹⁴ The commonest side effect due to SSRI's are nausea tinnitus, insomnia, nervousness, akathasia, dyskinesia, retrograde ejaculation and impotence.

iii. Combination treatment with SSRI's

The use of 5HT re uptake inhibitors has led to the meaningful clinical improvement in large number of patients with obsessive compulsive disorder. However, 40 to 60% of patients derive no significant improvement in obsessive compulsive symptoms following monotherapy with these agents.¹⁵

Over the past few years a number of reports describing combination treatment strategies in which an agent which is thought to act synergistically with or to augment ongoing 5HT re-uptake inhibitor therapy has been published. These include following.

- a. Buspirone (5HT1A Agonist)
- b. Lithium
- c. Anti psychotics
- d. Anti depressant
- e. Monoamine oxidase inhibitors
- f. Anxiolytics

a. Buspirone

In an open study buspirone (A 5HT1A agonist) was added to one going fluoxetine treatment in patients with obsessive compulsive disorder. Five out of eleven patients showed at least 25% improvement above and beyond that following fluoxetine therapy alone. They found combination therapy statistically superior to monotherapy.¹⁶

Mcdougle et al.¹⁷ observed that response of addition of buspirone to fluvoxamine refracting obsessive compulsive disorder patient was no better than placebo.

Similar conclusions has also been drawn by Gredy et al.¹⁸

b. Lithium

Lithium is a monovalent cation which has been used as mood stabilizer in affective disorder. Because it increases the serotonergic transmission at synaptic level it has been used as an adjuvant agent along with tricyclic antidepressant tin resistant depression. Lithium has been reported in individual cases to augment the anti obsessional effect of chronic treatment with a variety of tryclic antidepressants.¹⁹ However, a lack of efficacy of lithium augmentation in obsessive compulsive disorder was reported by Blier and Montigny.²⁰

c. Anti psychotics

There is some evidence that obsessive compulsive disorder patients responded when neuroleptic was added to fluvoxamine with or without lithium. Fourteen patients received pimozides two patients received thioridazine for sleep, no other drugs were administered. Formal behavior therapy was not given. Comorbid occurrence of tic spectrum disorders with or of schizotypal personality disorder was associated with response.²¹ However, because of extrapyramidal symptoms (akathasia, dystonia, drug induced parkinsonism, tardive dyskinesia and neuroleptic malignant syndrome) associated with neuroleptic, author of the study advised that adequate trial SSRI be completed before this cocative strategy be used.

A positive effect of augmentation with haloperidol in resistant obsessive compulsive disorder patients has been reported, but better response was seen with concomitant tic disorder of Tourette's syndrome a condition thought to be closely associated with obsessive compulsive disorder.²²

Augmentation of SSRI's with the atypical neuroleptic (a neuroleptic with least extra pyramidal symptoms) risperidone has been suggested to be useful in obsessive compulsive disorder. Controlled trials of risperidone augmentation in such patients are needed, in particular it is necessary to determine an appropriate dose range to minimize adverse effects.²³

d. Anti depressants

The notion that only potent serotonin reuptake inhibitors are effective in obsessive compulsive disorder is supported by the failure of trazodone to achieve a response in patients suffering from obsessive compulsive disorder.²⁴

However, the trazodone fluoxetine combination offers advantage in the treatment of obsessive compulsive disorder, because combination of these agents may allow a

potentiated therapeutic effects without the increased sedation associated with higher doses of trazodone, or the insomnia associated with higher doses of fluoxetine.²⁵

e. Monoamine oxidase inhibitors

According to Vallego et al²⁶ phenelzine (a monoamine oxidase inhibitor irreversible type-A) is as effective in obsessive compulsive disorder as clomipramine. However, this was a small study without placebo compression; therefore proper conclusion regarding efficacy of phenelzine in obsessive compulsive disorder cannot be withdrawn.

f. Anxiolytics

These drugs may be beneficial in the acute decompensated stage of obsessive compulsive disorder. But because of chronic nature of illness many patients became habituated to anxiolytics drugs such benzodiazepines.²⁷ However, combined therapy of clonazepam and clomipramine has beneficial effects in obsessive compulsive disorder.²⁸

B. ELECTRO CONVULSIVE THERAPY

Electro convulsive therapy cause striking changes in depressive disorder and results in substantial reduction in chronicity and mortality. The subsequent addition of brief anaesthesia and muscle relaxant made the treatment safe and acceptable. It increase the post synaptic receptors of serotonin, dopamine and catecholamine.

Electro convulsive therapy has no role in obsessive compulsive disorder. If depressive features with suicidal ideation are followed by primary illness then it can be given to patient suffering from it.²⁹

C. SURGICAL TREATMENT

Psychosurgery refer to the use of neurosurgical procedure to modify the

symptoms of psychiatric illness by operating either on the nuclei of brain or the white matter. The stereotactic operations currently employed are tractotomy, limbic, leukotomy and amygdalotomy.

Psychosurgery has a limited place in selected cases of un remitting obsessive compulsive disorder, the stereo tactic techniques now being used including modified cingulotomies are great improvement over the crude methods of the pst moreover, these procedures have improved the efficacy of subsequent pharmacotherapy and behavior therapy.³⁰

2. Behavioral therapy

Although it is as effective treatment as drugs, but will only briefly be mentioned here as this review is mainly concerned with drug treatment. The best proved behavioral technique for obsessive compulsive symptoms are invivo exposure and response prevention. The first involves exposing the patient to the stimulus for the compulsion e.g., if the patient fears contamination and washes excessively, he or she might be exposed to dirt by rubbing his or her hands along the floor. In response prevention, the patient is made to stop performing the ritual no matter how strong the urge is. This requires a level of control ranging from relying on the patients self control to physically preventing the behavior by having someone to stop the patient or by placing the patient in an environment where the rituals cannot be done.

Dar and Criest³¹ found behavioral therapy helpful in fifty percent of patients with obsessive compulsive disorder.

Combination of behavioral therapy and drugs.

Marks et al³² treated chronically obsessive compulsive disorder patients with clomipramine, self exposure and therapist aided exposure. Self exposure was most

potent of all three therapeutic factors. Clomipramine played a limited adjuvant role and therapist aided exposure a marginal one. In short term both antidepressant and exposure therapy were effective treatment for obsessive compulsive disorder.

Drummond³³ examined patients who were being treated with SSRI for over three years with no significant therapeutic response. He started in patient exposure therapy in these patients which resulted in a significant clinical improvement. The gains of treatment were maintained at nine month follow up period.

CONCLUSION

It is evident from literature, for most patients, a combination of SSRI and behavior therapy is optimal treatment. Medication decreases obsessions and rituals making behavioral therapy easier to initiate, gains form behavioral therapy are long lasting and may permit medication to be stopped. Modern psychosurgery has apart to play in the overall management of obsessive compulsive only in severely disable patients who are unresponsive to other forms of treatment.

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