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Research Paper

Beliefs Related to the Efficacy of the Antidepressant Medications: An Exploratory Research

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ABSTRACT

Antidepressant medication has apparently become the most popular treatment for depression in the whole world. This paper explores relevant research data and raises questions about the beliefs related to the efficacy of the antidepressant medications. The title of this research is "Beliefs related to the efficacy of antidepressant medications: An exploratory research". To get an answer for this question, data was collected, in a qualitative way by using interview method from different psychiatrists and clinical psychologists residing in Delhi NCR. At the end, results were concluded that when the severity is more, use of antidepressants is necessary so that the crisis situation is controlled, afterwards therapeutic methods should be used in order to completely recover the individual. But, as the antidepressant medications are a foreign agent, hence, the only use of these as a form of therapy will not completely heal the person, instead, there are more chances of relapse.

Keywords: *Antidepressant Drugs, Depression, Psychotherapy, Psychiatrist*

MDD has been ranked as one of the most common mental health issues and stands at the third position in terms of cause of impediment of disease worldwide, according to the World Health Organisation's data in 2008, which has projected that this disease will rank first by 2030. A person with MDD not only shows mood symptoms of sadness, but also a variety of other symptoms that are more severe than those in milder forms of depression. People may lack energy and the ability to carry out their daily activities. The physical symptoms include loss of appetite and sleep disturbance. People also show cognitive symptoms of worthlessness and thoughts of death and suicide.

At the diagnostic level, there are very high levels of comorbidity between depressive and anxiety disorders. However, the issues surrounding the co-occurrence of depression and anxiety are very complex. Chronic Major Depression has been associated with serious childhood family issues and an anxious personality in childhood.

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DSM criteria for Major Depressive Disorder:

A**.** Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

*Note**:** Do not include symptoms that are clearly attributable to another medical condition.*

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, or hopeless) or observation made by others (e.g., appears tearful).
2. Markedly diminished interest or pleasure in all, or almost all, activities performed in most of the day, nearly every day (as indicated by either subjective account or observation).
3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others; not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other areas of functioning which are important on a day-to-day basis.

C. The episode is not attributable to the physiological effects of a substance or another medical condition.

D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.

E. There has never been a manic episode or a hypomanic episode.

The etiology of Major Depressive Disorder is believed to be multifactorial, including biological, genetic, environmental, and psychosocial factors. MDD is considered to be mainly due to abnormalities in neurotransmitters, especially serotonin, norepinephrine, and dopamine. This has been proven by the use of different antidepressants in the treatment of depression. People with suicidal ideations have been found to have low levels of serotonin metabolites.

Both pharmacotherapy, which includes antidepressants, mood stabilizing drugs and antipsychotic drugs, and psychotherapy, which includes cognitive therapies, behavioural therapies, CBTs, interpersonal therapy and family and marital therapy are used as the treatment methods for Major Depressive Disorder.

Antidepressants Drugs

Antidepressant drugs are the most commonly prescribed psychiatric medications. More than 90 percent of patients being treated for depressive disorders will be given these medications. These are the drugs involved in elevation of mood in a depressed patient (Tripathi, 2003).

Classifications:

I) Monoamine Oxidase Inhibitors (MAOI)

Monoamine Oxidase Inhibitors were the first drug which was introduced clinically as antidepressant. These drugs inhibit monoamine oxidase enzyme. The enzyme is existing in two molecular forms i.e., MAO-A and MAO-B. However, these drugs were initially being studied for the treatment of Tuberculosis, when they were found to elevate the mood of patients. They were later shown to be effective in treating depression. Patients taking MAOIs must avoid foods rich in amino acid tyramine. This limits the drugs' clinical usefulness.

Unwanted Effects

The unwanted effects of MAOI include hypotension, weight gain, dry mouth, blurred vision and urinary retention. Excessive central stimulation leads to tremors, excitement, insomnia and in overdose, convulsions and MAOI of hydrazine type (phenelzine and iproniazid) produce, very rarely, severe hepatotoxicity.

2) Tricyclic Antidepressants (TCA)

TCA is one of the important class, but far from ideal in practice. The TCAs operate to inhibit the reuptake of norepinephrine and serotonin once these have been released into the synapse. The discovery of first TCA, known as imiprine, was also serendipitous as it was being studied as a possible treatment for schizophrenia when it was found to elevate mood. The theory that these drugs work by increasing norepinephrine activity is now known to be oversimplified.

Unwanted Effects

TCA produces unwanted effects that include, weight gain, mental confusion, sedation, weakness, anticholinergic, dry mouth, blurred vision, constipation, bad taste, epigastric distress, urinary retention and palpitation. Sweating and fine tremors are also noted with most TCA. Some patients may switch to hypomania or mania, seizure, postural hypotension (in older patients) and cardiac arrhythmias (Tripathi, 2003).

3) Selective Serotonin Reuptake Inhibitors (SSRI)

Earlier, the antipsychotic medications that were discovered first (so called Classical antidepressants) included monoamine oxidase inhibitors and tricyclic antidepressants (as mentioned above). These were now been replaced in routine clinical practise by 'second generation' treatments such as the SSRIs. SSRIs are chemically unrelated to the older TCAs and to the MAOIs. However, most antidepressants work by increasing the availability of serotonin, norepinephrine, or both. As their name implies, the SSRIs serve to inhibit the reuptake of the neurotransmitter serotonin following its release into the synapse. Unlike the tricyclics, SSRIs selectively inhibit the reuptake of serotonin. SSRIs are easier to use, have fewer side effects, and are generally not found to be fatal in overdose, as the tricyclics can be.

Unwanted Effects

The SSRI produce comparatively less unwanted side effects. However, they frequently produce nausea, nervousness, insomnia, restlessness, anorexia, headache, dyskinesia and diarrhoea. This drug may impair both hepatic and renal function and are contraindicated in

patients with hepatic impairment. Another serious complication secondary to their effects in increasing serotonergic activity is serotonin syndrome. (Tripathi, 2003; Ferguson, 2001).

4) Other Antidepressants

These other antidepressants are known as atypical antidepressants which are compounds with non-selective receptor blocking effects and their antidepressant actions are poorly understood. One of such antidepressants are trazodone. Trazodone (desyrel) was the first antidepressant to be introduced in the United States that was not lethal when taken in overdose. It specifically inhibits the reuptake of serotonin. Trazodone has heavy sedating properties that limit its usefulness.

Bupropian, another atypical antidepressant is not structurally related to other antidepressants. It inhibits the reuptake of both norepinephrine and dopamine. In addition to being an antidepressant medication, bupropion (wellbutrin) also reduces the nicotine cravings, and symptoms of withdrawal in people who want to stop smoking.

Psychotherapy, or talk therapy, is a way to help people with a broad variety of mental illnesses and emotional difficulties. Psychotherapy can help eliminate or control troubling symptoms so a person can function better and can increase well-being and healing.

Psychotherapies can be used to treat the mild to moderate forms of depression. However, for treating severe forms of depression, a combination of both medications and therapeutic approaches may be used. In some circumstances, medication may be clearly useful and in others psychotherapy may be the best option. For many people, combined medication and psychotherapy treatment is better than either alone. Healthy lifestyle improvements, such as good nutrition, regular exercise and adequate sleep, can be important in supporting recovery and overall wellness.

Therapy may be conducted in an individual, family, couple, or group setting, and can help both children and adults. Both patient and therapist need to be actively involved in psychotherapy. The trust and relationship between a person and his/her therapist is essential to working together effectively and benefiting from psychotherapy. Psychotherapy can be short-term, dealing with immediate issues, or long-term, dealing with longstanding and complex issues. The goals of treatment and arrangements for how often and how long to meet are planned jointly by the patient and therapist. Confidentiality is a basic requirement of psychotherapy. Also, although patients share personal feelings and thoughts, intimate physical contact with a therapist is never appropriate, acceptable, or useful.

REVIEW OF LITERATURE

In 2017 a systematic review was published (according to PRISMA) where all relevant databases were searched, both beneficial and harmful effects were systematically assessed, and a predefined assessment of the clinical significance of antidepressants was performed. That review found that SSRIs compared with placebo had a statistically significant effect on depressive symptoms.

Some recent studies have suggested serious potential risks. People who used antidepressants had a 14% higher risk of heart attacks and strokes and a 33% greater risk of death, according to findings in a meta-analysis of 17 studies that was published in 2017 in the journal Psychotherapy and Psychosomatics.

The big danger of going off antidepressants is the risk of relapse. People who have had one episode of depression have a 50% chance of having a second. Those who have had two episodes have an 80% chance of having another. Staying on antidepressant medication can cut the risk of relapse in half, according to a review of 15 clinical trials published in 2014 in the Journal of Clinical Psychiatry.

Regardless of recent controversy about efficacy (Kirsch et al., 2008, Nierenberg et al., 2011), updated evidence has confirmed the positive benefit–risk ratio for antidepressants in the treatment of moderate to severe Major Depressive Disorder (Möller et al., 2012, Dupuy et al., 2011, Vöhringer and Ghaemi, 2011, Horder et al., 2011).

Some recent quantitative research suggests that antidepressant medication is superior to placebo only for patients with very severe depressive symptoms, with negligible treatment effects observed for those with less severe symptoms (Fournier et al., 2010).

In the past decade, numerous new atypical antidepressants (neither tricyclics nor SSRIs) have also become increasingly popular, and each has its own advantages (Marcus & Olfson, 2010). For example, bupropion (Wellbutrin) does not have as many side effects (especially sexual side effects) as the SSRIs and, because of its activating effects, is particularly good for depressions with significant weight gain, loss of energy, and oversleeping. Furthermore, venlafaxine (Effexor) seems superior to the SSRIs in the treatment of severe or chronic depression, however the profile of side effects is similar to that for the SSRIs.

All the guidelines up to 2008, including the one by the American Psychiatric Association, the one by the Canadian Psychiatric Association, the one by the National Institute of Clinical Excellence in the United Kingdom and the Japanese one, recommend that the choice of antidepressants be made "on the basis of adverse effect profiles, cost, and patient preferences" because there are differences in side effect profiles but not in effectiveness among various antidepressants.

The irreversible inhibitors of monoamine oxidase (MAO) are known to block the mitochondrial degradation of enzyme and increase the brain levels of norepinephrine, serotonin and/or dopamine (Bortolato et al., 2008).

In double-blind randomized clinical trials, venlafaxine, a dual reuptake inhibitor of serotonin and norepinephrine was significantly more efficacious than fluoxetine in patients hospitalized with major depressive syndrome and melancholia (Nemeroff ef a/., 2007; 2008)
In the treatment of bipolar depression, lithium may be no more effective than traditional antidepressants (study results are inconsistent), but about three quarters show at least partial improvement (Keck & McElroy, 2007). Nonetheless, treatment with antidepressants is related with substantial risk of precipitating manic episodes or rapid cycling, however the risk of this happening is abridged if the person also takes lithium (e.g., Keck & McElroy, 2007; Thase & Denko, 2008).

Several recent studies have provided additional evidence for early onset of antidepressant effects. Stassen et al. (2007) conducted a pooled analysis (N=2848 patients) of RCTs involving 7 antidepressants and placebo, and found that the mean time to onset of improvement was within 2 weeks.

There has long been a belief that antidepressants have delayed onset of action and that clinicians and patients need to wait 6–8 weeks before evaluating whether the antidepressant is having an effect (Taylor, 2007).

Recent studies show pro-inflammatory cytokine process take place during clinical depression, mania and bipolar disorder, and it is possible that symptoms of this condition are attenuated by the pharmacological effect of antidepressant on the immune system [Maes. (2005); Brien.et.al. (2006)].

It has been demonstrated that a combination of SSRIs with a noradrenergic TCA desipramine is more efficacious in the treatment of major depression (Nelson et al., 2004). The results suggest that simultaneous increase in the serotonergic as well as noradrenergic synaptic concentrations may have a synergistic effect that is beneficial for the remission of major depressive disorders (Nelson et al., 2004).

In 2003, the Committee on Safety of Medicines (CSM) in the UK advised that the majority of the selective serotonin reuptake inhibitors (SSRIs) and another new-generation antidepressant, venlafaxine, were not suitable to be used as anti-depressants by those aged under 18 years.

Proposed biological mechanisms to explain the delayed onset of therapeutic action of antidepressants included delayed desensitization of postsynaptic receptors or presynaptic auto receptors and/or downstream effects on postsynaptic signalling (Frazer and Benmansour, 2002).

Venlafaxine has provided one of the first opportunities to examine the hypothesis that a specific dual-action antidepressant would provide a superior clinical response as compared to any single-action agent (Demitrack, 2002).

The efficacy of the tricyclics in significantly reducing depressive symptoms has been demonstrated in hundreds of studies where the response of depressed patients given these drugs has been compared with the response of patients given a placebo. Though, merely about 50 percent indicate what is considered clinically significant improvement, and many of these patients still have major residual depressive symptoms. Fortunately, about 50 percent of those who do not respond to an initial trial of medication will show a clinically significant response when switched to a different antidepressant or to a combination of medications (Hollon, et al., 2002).

Neuroimaging studies have reported a loss of volume in the hippocampus, which regulates the stress response via the HPA axis (Bremner et al., 2000; Frodl et al., 2002a). Importantly, these symptoms of depression cause dendritic atrophy in the hippocampus, which too can be corrected with certain antidepressants (Watanabe et al., 1992; Magarinos et al., 1999; McEwen et al., 2002).

SSRIs are used not only to treat significant depression but also to treat people with mild depressive symptoms (Gitlin, 2002). Many mental health professionals believe that prescriptions for SSRIs are being written for these milder cases at an excessive rate. Prescribing drugs to essentially healthy people merely because the drugs make them feel more energetic, outgoing, and productive raises many ethical questions.

Cyclic antidepressants are used for the treatment of depressive mood disorders, primary major depression. Additionally, imipramine is used in children to treat functional enuresis bed wettings [Maes. (2001)].

Abnormal, excessive activation of the HPA axis is observed in approximately half of individuals with depression, and these abnormalities are corrected by antidepressant treatment (Sachar and Baron, 1979; De Kloet et al., 1988; Holsboer, 2001).

Abnormally high activation of the hypothalamic–pituitary–adrenal (HPA) axis is reported in almost half of the individuals afflicted with depression, and antidepressant treatment is able to reverse many of these aberrations (Sachar and Baron, 1979; Arborelius et al., 1999).

Newer groups of antidepressants regulate the level of serotonin and an additional neurotransmitter, the best-known serotonin and nor epinephrine reuptake inhibitor (SNRI) is venlafaxine. Bupropion is a serotonin and dopamine reuptake inhibitors (SDRI) [Rosowsky. (1984)].

An antidepressant is a psychiatric medication used to assuage mood disorders such as major depression and dysthymia. Though everyone experiences periods of sadness at certain point in their lives; depression is distinguished from this sadness, once symptoms are existent for a period of at least two weeks. Antidepressants are often the first choice of treatment for depression [Smalley. (1984)].

Antidepressants interact with neurotransmitters in numerous ways. They can alter the rate at which the neurotransmitters are either created or broken down within the body [Hall and Nugent. (1992)]. They can block the process by which neurotransmitters are recycled and reused, a process called “reuptake”, by blocking reabsorption of neurotransmitters into the nerve cells. Finally, antidepressants can interfere with the binding of a neurotransmitter to neighbouring nerve cells, thus leaving the neurotransmitter available [Rosowsky. (1984)].

Studies also suggest that depressed people who stop taking tricyclics immediately after obtaining relief have a 40 to 50 percent chance of relapse within six to twelve months. If patients continue to take the drugs for several months after being free of depressive symptoms, however, their chances of relapse apparently decrease to approximately 20 percent (Montogomery et al., 1989; Prien & Kupfer, 1986; Klerman, 1978; Weissman & Klerman, 1977).

In hundreds of studies, mild to severely depressed patients taking tricyclics have recovered considerably more than similar patients taking placebos (Morris and Beck, 1974; Davis, Klerman, & Schildkraut, 1967). When 387 depressed patients were treated with either tricyclic drugs or placebos for ten weeks, the tricyclic patients displayed significantly greater improvement than the placebo patients by the sixth week (Lipman, 1966). Various case reports have similarly described the efficacious impact of these drugs.

A survey of studies involving a total of 5864 patients found that overall, imipramine and two other widely used antidepressants (amitriptyline and isocarboxazid) helped almost 65 percent of the patients for whom they were used. Three other commonly used energizers (phenelzine, malamide, and iproniazid) aided in 40 to 49 percent of the cases in which they were used. Placebo controls were effective in only 23 percent of the cases in which they were employed (Wechsler, Grosser, & Greenblatt, 1965).

While imiprimine has been found to be the most clinically effective of the antidepressant drugs (Klerman & Cole, 1965), recent studies have reported on the similar efficacy of a group of substances known as monoamine oxidase inhibitors. A significant correlation has been found in several studies between clinical improvement in depressed patients and the degree of inhibition of monoamine oxidation produced during drug administration (Feldstein, Hoagland, Oktem, & Freeman, 1965)

Tranquilizing and anti-depressive drugs are effective in the treatment of psychotic disorders. This is the conclusion that emerges from a review of more than 400 research investigations (David, 1965)

One study has associated the effectiveness of antidepressants with respect to non-pharmacological treatment and two studies have compared antidepressants with electroconvulsive therapy for treatment of depression. Another study compared antidepressants with both electro convulsive therapy (ECT) and non-pharmacological treatment.

Seven trials have evaluated the different dosing schedules for treatment of depression. These studies suggest that parenteral imipramine is better than oral imipramine and probably the onset of action is also earlier. Studies have evaluated single dosing against multiple dosing have shown no difference in efficacy except for one study, which showed that single dose nitroxazepine was better than divided doses.

A recently published trial, which evaluated the efficacy of milnacipran, comprised subjects who had agonized from stroke. It is also one of the few trials which have included subjects more than 65 years of age. The trial done by Margoob et al, in addition to the efficacy of escitalopram, have also shown that gene polymorphism plays an imperative role in the treatment response to innumerable antidepressants.

One double blind controlled trial has evaluated the efficacy of clomipramine in the treatment of OCD and revealed that clomipramine was superior to placebo in the management of OCD. This study also disclosed that male subjects showed better response than female subjects.

A small open label study assessed the efficacy of neuroleptic and fluoxetine combination for treatment of obsessive compulsive (OC) symptoms befalling throughout the course of schizophrenia and showed that addition of fluoxetine leads to major improvement in OC symptoms.

Two studies have also studied the effectiveness of antidepressants in common mental disorders. One study showed that treatment completion rates were higher with fluoxetine than imipramine. The trial by Patel et al. included subjects with common mental disorders and evaluated the outcome at one year. It can be considered the longest study which has evaluated the efficacy of antidepressant in Indian subjects.

Studies indicate that the benefit largely depends on the severity of the depression: The more severe the depression, the vaster the benefits will be. So particularly, antidepressants are operative against chronic, moderate and severe depression. They don't help in mild depression.

A review of 14 naturalistic studies of long-term treatment for depression over 10 years found that outcomes for depressed patients were poor, with multiple relapses and large variability, both within and between individuals. Patients in nondrug-treated samples did not show worse outcomes, while some had superior outcomes. (Journal of Affective Disorders, a systematic Review by Hughes S and Cohen D)

A study of antidepressant use over 2 years in primary and secondary clinical care found high rates of recurrence (60%–63%) in patients continuously using adequate dosages of antidepressants.11 Patients not treated with antidepressants after remission had the lowest recurrence rate (26%). (Journal of Psychotherapy and Psychosomatics, research paper published by Bockting C, Ten Doesschate M, and Spijker J, et al.)

Frank et al, have documented response rates for extended treatment with a single effective antidepressant. In that study, the remission rate was 82%, with 75% achieving remission by 140 days. For fluoxetine, 23% of patients who were unimproved at 8 weeks showed full remission at 12 weeks.

Two recent meta-analyses based on a considerable number of placebo-controlled trials in which patients were randomized to either continuation of antidepressants or placebo during the first three months after remission, have shown that continuation treatment with antidepressants significantly decreases relapse rates within the first three months after randomization. This evidence supports the recommendation for continuation treatment with antidepressants during the first months after remission to prevent relapse.

A Danish case-control study examined age and dose effects for selective serotonin reuptake inhibitors and tricyclic antidepressants and found that the fracture risk associated with selective serotonin reuptake inhibitors increased with age but only in medium- and high-dose users, while for tricyclic antidepressants there was only an increased fracture risk in the oldest age group (> 60 years) for the highest dose.

Two studies supported by the National Institute of Mental Health (NIMH), characterized by many methodological strengths, and had lower placebo response rates (33% −35%) and meaningful between-group differences (25%) that support antidepressant efficacy.

Papakostas et al published a systematic review of fixed-dose trials comparing different starting doses of SSRIs. In comparison with starting with the minimum of the standard dose range, starting with the maximum of the standard range may be more effective (RR = 1.12, 95%CI: 0.99 to 1.27) but less acceptable (0.74, 0.54 to 1.00). The response rate may increase from 51% to 54%, at the expense of the dropout rate also rising from 10% to 17%.

Several studies have found upper gastrointestinal bleeding to be more common among patients taking selective serotonin reuptake inhibitors, particularly when used in combination with non-steroidal anti-inflammatory drugs.

Irving Kirsch, professor of psychology at the University of Hull and lead author of the study, said, “Using complete datasets and a substantially larger dataset than previously reported, we found that the overall effect of new generation antidepressant medications is below recommended criteria for clinical significance. Efficacy reaches clinical significance only in trials involving the most extremely depressed patients, and this pattern is due to a decrease in the response to placebo rather than an increase in response to medication.”

A classification-based approach of data from Tranter and colleagues' study suggests that if an early change in positive processing is not seen with antidepressant treatment, patients have little chance of responding to this same treatment later. A similar effect was seen in older adults in which a group of patients with depression who did not show an improvement in the recognition of happy faces after 1 week of citalopram treatment also did not respond after 8 weeks of treatment.

In a recent study, Godlewska and colleagues found that clinical response to escitalopram after 6 weeks of treatment was associated with early change during affective processing in the amygdala, thalamus, cingulate, and insula. The responder group showed a greater reduction in neural response in these areas during the processing of negative versus positive facial expressions, consistent with the hypothesis that these early changes are important for the expression of later clinical benefit.

Data from preclinical studies show that a single dose of ketamine produces rapid antidepressant-like effects in rodent models and reverses the depressive behaviours caused by chronic stress. The results also show that a single dose of ketamine rapidly increases synapse number and function in medial prefrontal cortex neurons, and reverses the synaptic deficits caused by chronic stress.

A recently published review assessing results after 24 weeks showed that the longer-term effects of antidepressants (SMD 0.34) seem as small as the short-term effects. A clinical practice guideline from NICE showed similar results (SMD 0.28).19 It is possible that long-term treatment with antidepressants may even worsen outcomes.

A recently published review found that a significant proportion of people who experience withdrawal symptoms after treatment with antidepressants do so for more than 2 weeks and that it is not uncommon for people to experience withdrawal for several months.

Ferguson has investigated the causes of various side effects profiles, especially the causes of sexual dysfunction, weight gain, and sleep disorders. An occurrence of side effects in long-term SSRI therapy is most concerning. Ferguson’s results comply with ours. The statistically significant side effects of SSRI antidepressants in correlation with the duration of the treatment in our subjects are: perception of increased sleep (0.039) as well as decreased sleep ($P = 0.009$), sweating ($P < 0.001$), sudden heat stroke ($P < 0.001$), being without orgasm ($P = 0.004$), decreased libido ($P < 0.001$), weight loss ($P = 0.045$).

A review of 14 naturalistic studies of long-term treatment for depression over 10 years found that outcomes for depressed patients were poor, with multiple relapses and large variability, both within and between individuals. Patients in nondrug-treated samples did not show worse outcomes, while some had superior outcomes. (Journal of Affective Disorders, a systematic Review by Hughes S and Cohen D).

METHODOLOGY

In order to reach upon a solution that whether antidepressants are the best form of therapy or not, we used the qualitative method of research and interviewed various psychiatrists and clinical psychologists residing in Delhi NCR. The questions were open ended and hence the participants were free to give their responses. The personal information of the participants is also kept confidential and therefore, is anonymous. At the very beginning, a short

introduction about the research topic was also given to all the participants and their responses for each question was recorded.

An interview is a qualitative research method that relies on asking questions in order to collect data. Interviews involve two or more people, one of whom is the interviewer asking the questions. There are several types in which the structured interview was used for our research paper. A structured interview method is a data collection method that relies on asking questions in a set order to collect data on the topic. Although, in research these are often quantitative in nature, however, they also can be used in qualitative research if the questions are open ended, which is evident in our paper.

Mr. G is a psychiatrist working in a very reputed hospital. The interview was started with a statement based question that "women are more prone to be diagnosed with depression", do you agree with this statement? If yes, why. The answer, according to him was, yes they are, and he further added that the prevalence of depression among women is more, as emotionality and the thought processes are predominantly associated with the females than the males. Henceforth, the ratio is approximately 2:1. This is even validated by other researchers also. Mr. G included in his statement that however the risk of suicide is more in males than females, but the prevalence of depression is more in that of the females. The next question was "which age group of people are more prone to be diagnosed with depression", to which the answer was middle age. However, he continued, that the onset of depression is multimodal, so it can start from an early age of 10-15 where the stress may be primarily related to academics. Nevertheless, dispositional age for the initiation of depression is 20-35, prevalence of geriatric depression can also be seen among individuals aging 55 and above. Mr. G, during the interview had opined about the usage of these antidepressants as, in the case of Mild Depression, non-pharmacological techniques are way better than the pharmacological methods used for the treatment, as it is less severe and the reasons behind depression are primarily the lack of coping skills. Although, when it comes to treating Moderate Depression, the severity is more, for this reason, SSRIs or the SNRIs can be prescribed for the client depending on the tolerability of doses along with the psychotherapies being given. When it comes to more severe forms of depression, higher dysfunctionality, chronicity, and most importantly treatment resistance among the clients is noticed, therefore, the pharmacological methods of treatment are used primarily. Once the crisis situation has been managed, psychotherapies are given to improve their coping skills. According to Mr.G the side effects of antidepressants varies from patient to patient. Nonetheless, the primary side effects of antidepressants what we observe usually are nausea, vomiting, abdominal discomfort, weight gain, bloating, and gaseous abdomen. Other side effects which are much milder in intensity and can be managed with other medications are associated anxiety, switch phenomenon, neurological side effects, and bleeding disorders. The next question was "can psychotherapies alone be given without antidepressants in treating a person suffering from depression"? The answer recorded was as follows, yes therapeutic approaches alone can be used but only in the treatment for the mildest forms of depression or those who are in the maintenance stage of chronic depression. As stated by Mr. G, the primary line of management with depression is to reduce the severity of the symptoms, prevention and the management of the crisis situation, management of the associated conditions related to depression which is accomplished with the help of antidepressants. The last question been asked was "according to you, are antidepressants the best form of therapy?" for which the answer recorded was as follows, no, antidepressants are not completely the best form of therapy, rather a blend of both pharmacotherapy and psychotherapy must be used in treating the more severe forms of depression such as Major

Depressive Disorder. However, psychotherapies alone can be given in treating the mildest forms of depression.

Ms. S is a clinical psychologist who works in a very reputed hospital. The interview was started with a statement-based question that "women are more prone to be diagnosed with depression", do you agree with this statement? If yes, why. The answer, according to her was, yes they are, usually mental illness in women are diagnosed later, and hence the precipitating factors can be mostly disturbed marital relationships, domestic violence, or due to some traumatic incidents. However, men are also diagnosed with depression, but the prevalence may be too less due to the stigmatization by the society. According to many researchers, the occurrence of depression in males can be seen in their adolescence or early adulthood stages. Hence, the report of depression is more in women, but the prevalence may be equal. As per Ms. S experience, women between the ages of 30-45 are more prone to be diagnosed with depression, while in males it is 25-35. The risk of suicide is more in males than in females. The next question been asked was "are antidepressants used only in the treatment of Major Depressive Disorder or these can be used to treat other forms of depression too?", for which the answer was as follows, the antidepressants can be used in treating other forms of depression too including mixed anxiety and depression, depression with psychotic symptoms or without psychotic symptoms, OCD with depression, RDD, atypical depression. There are some antidepressants used specifically for MDD, where some are used in the dual diagnosis disorders. Though the ones used for treating MDD can be used to treat other forms too. According to Ms.S, when the clients have severe depression with psychotic symptoms, the side effects of antidepressants observed are gaining weight, tremors, and drowsiness which are very common. The next question was "can psychotherapies alone be given without antidepressants in treating a person suffering from depression"? The answer recorded was as follows, yes, psychotherapies alone can be given if the client becomes treatment resistant and does not respond to the antidepressants. Psychotherapies help in a very beneficial way, especially in treating anxiety, depression or neurotic disorders and are not a foreign agent, consequently, do not have any side effects. As stated by Ms. S, by taking antidepressants the client gets immediate relief, mood stability can be seen, has good decision making power, has positivistic view towards the future, improvement in sleep and appetite, and a decline in suicidal thoughts are also seen, whereas psychotherapies takes a lot of time for the client to deal with recovery and healing. The last question been asked was "according to you, are antidepressants the best form of therapy?" for which the answer recorded was as follows, no, a client who is suffering from any severe disorder needs a combination of both pharmacotherapy and psychotherapy in order to deal with recovery. Antidepressants cannot be the best form because ultimately the client has to depend upon a foreign agent completely, yet, initial improvement can be seen, but there are more chances of relapse once the medications being taken are stopped. Thus, people are usually unwilling to take these medications.

Mr. R is a psychiatrist working in a very reputed hospital. The interview was started with a statement based question that "women are more prone to be diagnosed with depression", do you agree with this statement? If yes, why. The answer, according to him was, yes, as the responsibilities held by a women are more than that of men. Another reason can be their hormonal instability which contributes to their mental health issues and they have double the chances of having depression than men. The next question was "which age group of people are more prone to be diagnosed with depression", to which the answer was, there is no specific age group. Nowadays, the younger generation are more prone to be diagnosed with having depression. However the psychosocial causes may be different, but every age group

is equally prone. Mr. R, during the interview had opined about the usage of the antidepressants as, these are used not only in the treatment of MDD but can be used for treating Bipolar Depression, Dysthymia, and apart from depression these are used for treating anxiety disorders, headaches, OCD, phobias, etc., although the severity matters. Antidepressants are mostly prescribed only when the symptoms of the disorder are severe, otherwise psychotherapies alone can be used in treating any disorder. According to Mr.R the side effects of antidepressants depends on the classification of these. TCAs have more of constipation, dry mouth, blurring of vision, sedation whereas SSRIs have sexual side effects, acidity, gastric side effects. SNRIs have gastric side effects, constipation, dry mouth, increased sedation and drowsiness. Nevertheless, these side effects also depend on the tolerability of the dosage prescribed by the psychiatrists. The next question was "can psychotherapies alone be given without antidepressants in treating a person suffering from depression"? The answer recorded was as follows, no, I don't think psychotherapies alone can help in treating MDD. Yes, however, I agree that the therapy can be very useful in the treating the mild to moderate forms of depression, but when the severity is more, medication is a necessity. As stated by Mr. R, by taking antidepressants the client gets immediate relief, mood stability can be seen, has good decision-making power, has positivistic view towards the future, improvement in sleep and appetite, and a decline in suicidal thoughts are also seen, whereas psychotherapies takes a lot of time for the client to deal with recovery and healing. The last question been asked was "according to you, are antidepressants the best form of therapy?" for which the answer recorded was as follows, no, antidepressants are not completely the best form of therapy, rather a blend of both pharmacotherapy and psychotherapy must be used in treating the more severe forms of depression such as Major Depressive Disorder. Though, psychotherapies alone can be given in treating the mildest to the moderate forms of depression.

Mrs. M is a psychiatrist working in a very reputed hospital. The interview was started with a statement based question that "women are more prone to be diagnosed with depression", do you agree with this statement? If yes, why. The answer, according to her was, yes they are, and there are many factors which contribute to it. The first reason is the biological factor which include hormonal changes, pregnancy and child birth. Also, there are many psychological factors, for instance, women are more emotionally expressive than men. Women in the patriarchal societies are more prone to be diagnosed with depression which comes under the social factors. The next question was "which age group of people are more prone to be diagnosed with depression", to which the answer was middle age. However, she continued, that all the age group of people are equally prone to be diagnosed with depression nowadays. Mrs. M, during the interview had opined about the usage of these antidepressants as, in the case of mild and moderate forms of depression, non-pharmacological techniques are way better than the pharmacological methods used for the treatment, as it is less severe and the reasons behind depression are primarily the lack of coping skills. Although, when it comes to treating more severe forms of depression medications must be prescribed for the early recovery from the symptoms along with psychotherapies for the complete recovery and healing. According to Mrs. M, the side effects of antidepressants varies from patient to patient. Nonetheless, the primary side effects of antidepressants what we observe usually are nausea, vomiting, abdominal discomfort, weight gain, bloating, gaseous abdomen, and drowsiness, which can be cured if the dosage given is properly adjusted by the psychiatrist. The next question was "can psychotherapies alone be given without antidepressants in treating a person suffering from depression"? The answer recorded was as follows, yes therapeutic approaches alone can be used but only in the treatment for the mildest to moderate forms of depression or those who are in the maintenance stage of chronic

depression. As stated by Mrs. M, antidepressants are very much effective as the client responds rapidly to these medications. Also, the client is again able to carry out the daily activities in a proper manner, where psychotherapies take a long time to heal and recover a person completely. The last question been asked was "according to you, are antidepressants the best form of therapy?" for which the answer recorded was as follows, no, antidepressants are not completely the best form of therapy, rather a blend of both pharmacotherapy and psychotherapy must be used in treating the more severe forms of depression such as Major Depressive Disorder. The reason behind this is that medications work biologically whereas psychotherapies work on our thinking pattern, that's why both are necessary in the treatment of a disorder.

Mrs. P is a clinical psychologist who works in a very reputed hospital. The interview was started with a statement based question that "women are more prone to be diagnosed with depression", do you agree with this statement? If yes, why. The answer, according to her was, yes they are, and she further added that the prevalence of depression among women is more, as emotionality and the thought processes are predominantly associated with the females than the males. Another reasons are hormonal instability, unwanted pregnancy. Hence, the risk of suicide is more in males than in females. The next question was "which age group of people are more prone to be diagnosed with depression", to which the answer was the middle age of 25-40. In this age, work pressure is more and the individuals have more responsibilities where they have to take care of the family and also that of the career. At this age, men become as the bread earners and the women have to fulfil the household chores and also have to take care of their children. Mrs. P, during the interview had opined about the usage of these antidepressants as, in the case of Mild Depression, non-pharmacological techniques are way better than the pharmacological methods used for the treatment, as it is less severe. When it comes to more severe forms of depression, higher dysfunctionality, chronicity, and most importantly treatment resistance among the clients is noticed, therefore, the pharmacological methods of treatment are used primarily. Once the client gets recovery from the severe symptoms, psychotherapies are given in order to treat the client completely. According to Mrs. P the side effects of antidepressants varies from patient to patient and are very mild in severity. Some of the common side effects are headaches, drowsiness and sedation, gaseous abdomen, loss of appetite. Although, these can be cured with some modifications done in the dosage given by the psychiatrists. The next question was "can psychotherapies alone be given without antidepressants in treating a person suffering from depression"? The answer recorded was as follows, yes therapeutic approaches alone can be used but only in the treatment of mild and the moderate forms of depression. As in the case of severe depression, the best method of treatment is the blend of both medications and psychotherapies. As stated by Mrs. P, firstly we should know what to prescribe and that too where. Antidepressants are very much effective when the severity of the symptoms are more. These provide an immediate relief from such symptoms and help the client in his recovery. The last question been asked was "according to you, are antidepressants the best form of therapy?" for which the answer recorded was as follows, antidepressants are very much important in treating an individual suffering from severe depression, but these are not the best form of therapy as they have many side effects and once these are stopped, there are more chances of relapse. According to me, the blend of psychotherapy and pharmacotherapy can be the best form, where medications are prescribed first and once the severity reduces, therapeutic approaches are used for the complete recovery of the client.

DISCUSSION

This qualitative study highlights the impact of antidepressants and whether these can be used as the only form of treatment for MDD. An antidepressant is a psychiatric medication used to assuage mood disorders such as major depression and dysthymia. Though everyone experiences periods of sadness at certain point in their lives; depression is distinguished from this sadness, once symptoms are existent for a period of at least two weeks. Antidepressants are often the first choice of treatment for depression [Smalley. (1984)]. In many cases, these can be prescribed to treat other health conditions such as anxiety, pain, and insomnia. Antidepressants interact with neurotransmitters in numerous ways. They can alter the rate at which the neurotransmitters are either created or broken down within the body [Hall and Nugent. (1992)]. They can block the process by which neurotransmitters are recycled and reused, a process called "reuptake", by blocking reabsorption of neurotransmitters into the nerve cells. Finally antidepressants can interfere with the binding of a neurotransmitter to neighbouring nerve cells, thus leaving the neurotransmitter available [Rosowsky. (1984)]. Newer groups of antidepressants regulate the level of serotonin and an additional neurotransmitter, the best known, serotonin and norepinephrine reuptake inhibitor (SNRI) is venlafaxine. Bupropion is a serotonin and dopamine reuptake inhibitors (SDRI) [Rosowsky. (1984)]. Cyclic antidepressants are used for the treatment of depressive mood disorders, primary major depression. Additionally, imipramine is used in children to treat functional enuresis bed wettings [Maes. (2001)].

In this study, we explore into both the pharmacological and the therapeutic approaches of treatment for depression. The population of the study included both psychiatrists and clinical psychologists. A total of 5 participants were interviewed for the study. To begin with, I shall explain the effectiveness of the antidepressants with respect to other methods of treatment. One study has associated the effectiveness of antidepressants with respect to non-pharmacological treatment and two studies have compared antidepressants with electroconvulsive therapy for treatment of depression. Another study compared antidepressants with both electro convulsive therapy (ECT) and non-pharmacological treatment. Two studies have also studied the effectiveness of antidepressants in common mental disorders. One study showed that treatment completion rates were higher with fluoxetine than imipramine. The trial by Patel et al. included subjects with common mental disorders and evaluated the outcome at one year. It can be considered the longest study which has evaluated the efficacy of antidepressant in Indian subjects. Tranquilizing and anti-depressive drugs are effective in the treatment of psychotic disorders. This is the conclusion that emerges from a review of more than 400 research investigations (David, 1965). Some recent quantitative research suggests that antidepressant medication is superior to placebo only for patients with very severe depressive symptoms, with negligible treatment effects observed for those with less severe symptoms (Fournier et al., 2010). Participants too had opined about the effectiveness of antidepressants. To quote them, they mentioned "the primary line of management with depression is to reduce the severity of the symptoms, prevention and the management of the crisis situation, management of the associated conditions related to depression which is accomplished with the help of antidepressants'. Also they had stated about the usage of these antidepressants. The participants mentioned, "Antidepressants can be used in treating other forms of depression too including mixed anxiety and depression, depression with and without psychotic symptoms, OCD with depression, RDD, atypical depression, Bipolar Depression, and Dysthymia".

Through the interview process, I also got to know the side effects of antidepressants. Participants mentioned, "The side effects varies from patient to patient. Nonetheless, the

primary side effects of antidepressants what we observe usually are nausea, vomiting, abdominal discomfort, weight gain, bloating, and gaseous abdomen". Another participant said, "When the clients have severe depression with psychotic symptoms, the side effects observed are gaining weight, tremors, and drowsiness which are very common". One other participant said, "The side effects depend on the classification of antidepressants. TCAs have more of constipation, dry mouth, blurring of vision, sedation whereas SSRIs have sexual side effects, acidity, gastric side effects. SNRIs have gastric side effects, constipation, dry mouth, increased sedation and drowsiness". The big danger of going off antidepressants is the risk of relapse. People who have had one episode of depression have a 50% chance of having a second. Those who have had two episodes have an 80% chance of having another. Staying on antidepressant medication can cut the risk of relapse in half, according to a review of 15 clinical trials published in 2014 in the Journal of Clinical Psychiatry. Some recent studies have suggested serious potential risks. People who used antidepressants had a 14% higher risk of heart attacks and strokes and a 33% greater risk of death, according to findings in a meta-analysis of 17 studies that was published in 2017 in the journal Psychotherapy and Psychosomatics.

This study also explores whether psychotherapies can be used as the only form of therapy. Participants had mentioned, "Yes, therapeutic approaches alone can be used but only in the treatment for the mildest forms of depression or those who are in the maintenance stage of chronic depression." Another participant said, "Yes, psychotherapies alone can be given if the client becomes treatment resistant and does not respond to the antidepressants. Psychotherapies help in a very beneficial way, especially in treating anxiety, depression neurotic disorders and are not a foreign agent, consequently, do not have any side effects." One participant had added, "I don't think psychotherapies alone can help in treating MDD. Yes, however, I agree that the therapy can be very useful in treating the mild to moderate forms of depression, but when the severity is more, medication is a necessity." Another participant said, "Yes, therapeutic approaches alone can be used but only in the treatment of mild and the moderate forms of depression. As in the case of severe depression, the best method of treatment is the blend of both medications and psychotherapies."

Now we shall be exploring, whether antidepressants are the best form of therapy or not. Studies indicate that the benefit largely depends on the severity of the depression: The more severe the depression, the vaster the benefits will be. So particularly, antidepressants are operative against chronic, moderate and severe depression. They don't help in mild depression. Studies also suggest that depressed people who stop taking tricyclics immediately after obtaining relief have a 40 to 50 percent chance of relapse within six to twelve months. If patients continue to take the drugs for several months after being free of depressive symptoms, however, their chances of relapse apparently decrease to approximately 20 percent (Montogomery et al., 1989; Prien & Kupfer, 1986; Klerman, 1978; Weissman & Klerman, 1977). There has long been a belief that antidepressants have delayed onset of action and that clinicians and patients need to wait 6–8 weeks before evaluating whether the antidepressant is having an effect (Taylor, 2007). Several recent studies have provided additional evidence for early onset of antidepressant effects. Stassen et al. (2007) conducted a pooled analysis (N=2848 patients) of RCTs involving 7 antidepressants and placebo, and found that the mean time to onset of improvement was within 2 weeks. A classification-based approach of data from Tranter and colleagues' study suggests that if an early change in positive processing is not seen with antidepressant treatment, patients have little chance of responding to this same treatment later. A similar effect was seen in older adults in which a group of patients with depression who did not

show an improvement in the recognition of happy faces after 1 week of citalopram treatment also did not respond after 8 weeks of treatment. Participants had mentioned, "No, antidepressants are not completely the best form of therapy, rather a blend of both pharmacotherapy and psychotherapy must be used in treating the more severe forms of depression such as Major Depressive Disorder. However, psychotherapies alone can be given in treating the mildest forms of depression". Another participant said, "No, a client who is suffering from any severe disorder needs a combination of both pharmacotherapy and psychotherapy in order to deal with recovery. Antidepressants cannot be the best form because ultimately the client has to depend upon a foreign agent completely, yet, initial improvement can be seen, but there are more chances of relapse once the medications being taken are stopped. Thus, people are usually unwilling to take these medications". One other participant said, "Antidepressants are very much important in treating an individual suffering from severe depression, but these are not the best form of therapy as they have many side effects and once these are stopped, there are more chances of relapse. According to me, the blend of psychotherapy and pharmacotherapy can be the best form, where medications are prescribed first and once the severity reduces, therapeutic approaches are used for the complete recovery of the client". A recent analysis by Sado et al. (2009) shows that combined therapy for depression appears to be cost-effective from both health care system and social perspective.

CONCLUSION

The aim of this study was to know whether antidepressants are the best form of therapy or not. Data collected from different sources and our participants who were clinical psychologists and psychiatrists working in various hospitals, concluded that only the use of antidepressants cannot completely cure an individual who is suffering from major depression. Rather a blend of pharmacotherapy and psychotherapy must be used where the medications will help in reducing the severity of the symptoms and the therapeutic approaches will further recover and heal the individual completely.

List of Abbreviations:

DSM – Diagnostic and Statistical Manual of Mental Disorders
MDD – Major Depressive Disorder
CBT – Cognitive Behavioral Therapy
PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses
NICE – National Institute for Health and Care Excellence
NCR – National Capital Region

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