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A Review Article-Adverse Drug Reaction Epidemiological Symptoms (EPS) And Adverse Drug Reaction On Selective Serotonin Reuptake Inhibitors And Serotonin Norepinephrine Reuptake Inhibitors

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Abstract: ***If any person suffering from depression, then only one idea that medication can gives him back to the life like- hope, pleasure, loss of love and everything. Pharmacovigilance is the science activities relating to the Detection, Assessment, Understanding and Prevention of adverse drug. Newer antidepressants SSRIs and SNRIs 2nd generation. In 1987 the USFDA (US Food and Drug Administration) approved 1st SSRIs fluoxetine after that in 2002 sertraline, citalopram, Escitalopram and fluvoxamine introduced in the market. The 1st SNRI introduced in 1993.effects or any other types related problems (the importance or Pharmacovigilance, WHO 2002). Clinical trials to examine discontinuation syndrome in term of receptors physiology have been inconclusive. Antidepressants causes higher risk of liver damage and they found that citalopram, Escitalopram, fluvoxamine and paroxetine have lowest risk of liver damage Extrapyramidal Symptoms (EPS) to SSRIs, Fluoxetine - induced Parkinsonism rigidity and dystonic reaction. They assumption that increase in 5-hydroxytryptamine (5-HT) activity resulting from 5-HT reuptake blockade by Fluoxetine inhibited both the tuber infundibular and nigrostriatal dopaminergic neurons, and dystonia, akathisia, and tardive dyskinesia associated with Fluoxetine. Although Fluoxetine has been linked to more case of extrapyramidal systems (EPS) in the literature, the other SSRIs such as Paroxetine, Fluvoxamine, and Sertraline have also been known to cause these types of movement disorders. The most common type of extrapyramidal systems (EPS) associated with Sertraline was akathisia, also reported.***

I. INTRODUCTION

Antidepressants are the medication which used to treat depression and other psychiatric related problems, these drugs designed to balance chemical into the brain. Individually in previous studies suggest that post-marketing clinical trials reported Fluvoxamine is associated with the highest frequency of Gastrointestinal (GI) disturbances, while with Sertraline and Fluoxetine are most often reported - anxiety, agitation, and insomnia. We found that the other studies post-SSRI sexual dysfunction (PSSD) about raised the possibility of long term sexual outcomes for people exposed to SSRIs during pregnancy whereas citalopram or escitalopram the cardiac arrhythmia or it included QT interval prolongation is more frequently reported. Decrease libido, sexual dysfunction, weight gain was infrequently reported during pre-marketing clinical trials from SSRIs. Because of the decrease in weight that occurred during the early, short-term clinical trials with Fluoxetine, it was investigated as a potential decrease in weight agent. Attempt suicide, suicidality and murder were included. We also analyzed the risk factors for extrapyramidal systems (EPS) during treatment with SSRIs, including the Cytochrome - P450 enzyme, serotonin and dopamine transporter and receptor polymorphism and the risk of EPS with SSRIs show to increase with advanced age and the presence of the A1 allele of the dopamine D2 receptor gene Taq1A polymorphism. In 127 published report of SSRIs - induced movement disorder, dystonia in 24%, akathisia was

noted in 38%, dyskinesia in 15%, Parkinsonism in 32%, tardive dyskinesia in 8%, and all mixed disorder in 19% of cases. They also conclude that SSRIs use appeared to be associated with the development of movement disorder, either as a direct result of the drug or due to exacerbation of an underlying condition.

II. MATERIAL AND METHOD

English language studies were included or analyze. We searched many published review article and research papers regarding to this topic including from these sites; PubMed, PsycInfo, Medline, Wikipedia, Journal of clinical psychopharmacology, Journal of clinical Psychiatry, American Journal of Psychiatry and SciHub. And in the exclusion criteria we were selected only those articles who related to SSRIs and SNRIs Drugs.

III. DISCUSSION AND RESULT

Tim J. Wilkinson, et al., studies suggest that after 4 phase of clinical trials they have reported highest rate of sexual dysfunction as high percentage as 75%. According their study SSRIs induced Hyponatraemia was not reported in the clinical trials phase, in post – marketing clinical trials it is occur in 1 to 200 elderly patients per year receiving the therapy with Fluoxetine and Paroxetine medications. Individually in previous studies suggest that post-marketing clinical trials reported Fluvoxamine is associated with the highest frequency of Gastrointestinal (GI) disturbances, while with Sertraline and Fluoxetine are most often reported - anxiety, agitation, and insomnia. And they found that during long-term therapy of SSRI, the most troubling adverse reaction are Increase or decrease libido, sexual dysfunction, changes in weight, and sleep problems. A review article of Post-SSRI sexual dysfunction (PSSD) about raised the possibility of long term sexual outcomes for people exposed to SSRIs during pregnancy and in young age. SSRIs induced sexual dysfunction. There are published 300 cases of long suffering from sexual dysfunction in which 221 cases were after the previously use of selective serotonin inhibitors. They studied that male and female were suffering from decrease libido, loss of interest in sex. SSRIs are associated with particular adverse effects that other SSRIs drugs may not arise as frequency as well e.g. citalopram or Escitalopram and dose dependent which high risk of QT prolongation. Authors Funk KA et al studies suggest that recently a review of QT interval prolongation potentially amongst SSRIs pointed to a numerous limitation in interpreting data, but not least that trials are not designed to examine QT interval changes. However, Torsade de points (TDp) with citalopram or Escitalopram the cardiac arrhythmia or it included QT interval prolongation is more frequently reported, it is a current evidence indicates. Where other drugs of SSRIs are concerned, TDp and QT prolongation are limited to case reported, so it is proven that paroxetine, fluoxetine, fluvoxamine and sertraline has appeared lowest the risk for QT interval prolongation of SSRIs.

Mechanism of action is common of Selective Serotonin Reuptake Inhibitors (SSRIs) and generally, therefore, pharmacodynamics with all SSRIs, are likely to occur drug interaction with the other drugs for e.g. all SSRIs drugs are contraindicated in combination with monoamine oxidase inhibitors (MAOIs) due to risk of serotonin syndrome and there is an increased risk of upper GI bleeding when aspirin is administered with SSRIs. Newer antidepressants SSRIs and SNRIs 2nd generation. In 1987 the USFDA (US Food and Drug Administration) approved 1st SSRIs fluoxetine after that in 2002 sertraline, citalopram, Escitalopram and fluvoxamine introduced in the market. Comparison with the SSRI and SNRI class tends to induce more insomnia, dry mouth, nausea, and in some cases both class elevated blood pressure or QT prolongation. Antidepressants causes higher risk of liver damage and they found that citalopram, Escitalopram, fluvoxamine and paroxetine have lowest risk of liver damage [9]. If the addition of triptans with SSRIs and SNRIs so that they cause of serotonin syndrome but lack of insufficient data available of these drugs whether or not of serotonin syndrome.

SSRIs are typically associated with weight loss during initial therapy, weight is often regained after 6 months and can be followed by additional increase weight with long-term use. Dis-continuation reaction have been reported after withdrawal of prolonged SSRIs treatment and constitute a syndrome that is not well characterized. Symptoms include nausea, dizziness, lethargy, agitation, anxiety, and headache. These are generally mild, begin within a week of dis-continuing SSRIs therapy, and resolved within three weeks. Some of the reported problems are more disabling, for example, falls and absence from work. As an expected, withdrawal adverse reaction is more common with SSRIs that which have the short half – life (Paroxetine, Fluvoxamine). PSSD is a persistently sexual dysfunction that occurs after dis-continuation of SSRIs indication. They commonly reported symptom include - erectile dysfunction genital, anesthesia, decreased sex drive, pleasure-less orgasm, decrease libido or absence of erection, vaginal lubrication issues, premature ejaculation, and nipples insensitivity in women's. Higher risk of cardiovascular adverse reaction from SSRIs whenever SNRIs also have showed adverse reaction. Particular, SSRIs were suspected to have the potentially induce QTc interval prolongation, & therefore increase the risk of ventricular arrhythmia. SNRIs, SSRIs, and other antidepressants accounted for 10–15% each of case of collapse or hypotension. SSRIs showed a significantly lower risk than all other antidepressants ($p = 0.007$, imputed alone). In other study 68% SNRIs were imputed to cause the adverse drug reaction and showed an importantly higher risks of this adverse drug reaction in case in which SNRIs had been imputed alone. Especially Venlafaxine median dosage 150 mg/day was revealed to have an importantly higher risk of hypertension than all the other antidepressants.

Meltzer HY, et al., published 1 of the earliest report linking Extrapyramidal Symptoms (EPS) to SSRIs. They reported in their study case of Fluoxetine - induced Parkinsonism rigidity and dystonic reaction. They assumption that increase in 5-hydroxytryptamine (5-HT) activity resulting from 5-HT reuptake blockade by Fluoxetine inhibited both the tuber infundibular and nigrostriatal dopaminergic neurons.

Shitij Kapur and Remington have supported in this hypothesis [16]. Manufacturer of Fluoxetine, had in their database 218 cases of dystonia, 375 cases of akathisia, and 7 cases of tardive dyskinesia associated with Fluoxetine. The most common type of extrapyramidal systems (EPS) associated with Sertraline was akathisia, but other extrapyramidal systems (EPS) types were also reported. The past reported case of reversible choreiform dyskinesia and extrapyramidal systems (EPS) in a patient treated with Sertraline. We also analyzed the risk factors for extrapyramidal systems (EPS) during treatment with SSRIs, including the Cytochrome - P450 enzyme, serotonin and dopamine transporter and receptor polymorphism. They also found that the risk of extrapyramidal systems (EPS) with SSRIs show to increase with advanced age and the presence of the A1 allele of the dopamine D2 receptor gene Taq1A polymorphism. In 127 published report of SSRIs - induced movement disorder, dystonia in 24%, akathisia was noted in 38%, dyskinesia in 15%, Parkinsonism in 32%, tardive dyskinesia in 8%, and all mixed disorder in 19% of cases. They also conclude that SSRIs use appeared to be associated with the development of movement disorder, either as a direct result of the drug or due to exacerbation of an underlying condition. Extrapyramidal Symptoms (EPS) associated with cyclic antidepressant drugs and attempt to consolidate the hypothesis regarding causation of these adverse reaction. They found that TCAs, miscellaneous agents, MAOIs, and SSRIs were associated, respectively, with akathisia, 26%, 34%, 17%, and 39%; parkinsonism, 0%, 14%, 33%, and 19%; dystonia, 17%, 17%, 17%, and 32%; reversible dyskinesia, 52%, 20%, 33%, and 10%; and neuroleptic malignant syndrome (NMS), 4%, 14%, 0%, and 10%. Amongst SSRIs, Fluoxetine was associated with the highest number of Extrapyramidal Symptoms (EPS) report (63%). Authors concluded that SSRIs drugs may be more common offenders in producing these adverse reaction and that the final common pathway for production of Extrapyramidal Symptoms (EPS) appeared to be caused by indirect modulation of dopaminergic function by serotonin/norepinephrine. A case-control study using spontaneous report collected by the Netherlands Pharmacovigilance Foundation Lareb for the period 1985-1999, a total of 24,263 case reports, 61 case were reports of EPS associated with antidepressants. Both SSRI and EPS reports were more frequent, compared with EPS associated with other antidepressants. The ADR reporting odds ratio for SSRI was 2.2 (95% confidence interval [(CI), 1.2 to 3.9)]. Patients using Antipsychotic drugs concurrently, the risk estimate was higher, at 6.9 (CI, 0.7 - 68.0). The other interesting finding in this study was that Paroxetine had the highest number of reports among all antidepressants (38%) and SSRIs (49%), compared with 23% for all non SSRI antidepressants. Fluoxetine had the highest number of report. The year of Fluoxetine in market introduced was 1987, did not appear to have any significant relation to the number of reports. However venlafaxine, sertraline, and mirtazapine, which were marketed in the 1994 in Netherland, had only 1 report each. This finding might suggest that the inherently pharmacodynamics properties of Fluoxetine may be responsible for its extrapyramidal symptoms (EPS) potential, rather than the timing of its market introduction or number of years on the market. According to their study SSRIs were associated with dystonia (27%), Parkinsonism (49%), dyskinesia (20%) and akathisia (2%). They show that the frequency of akathisia reports (2%) was strikingly lower than the previous US and Canadian reports (38% to 45%). This may be related to the definition of akathisia in different countries or the diagnostic expertise of the reporting personnel. Our analysis of the FDA AERS indicates a 15% frequency of akathisia reports. Incidental evidence of SSRI induced sexual adverse reaction continuing after surcease of the medication. Patients were switched either to Amineptine (n=47), an atypical tricyclic antidepressants that is no longer available, or to Paroxetine (n=38). A third group of depressed patients was treated with Amineptine only (n=26) and had no prior SSRI treatment. All three groups were followed with multiple assessment over a 6 month period. In the previous study we found that overdose the cases against the drug companies, wrote that half his patients did well on Fluoxetine, but Cohen noted a high incidence (50%) with side-effects. Cohen also cited a pre-approval study showing that the standard 20 mg per day starting dose helped 65% of patients, while 5 mg helped 54%, so Cohen became 1 of the pioneer in using lower doses before the researcher Lilly made them available. In the 1996 Physicians' Desk Reference (PDR) entry for Paroxetine at least confirmed that seventeen most common adverse reaction were dose-dependent. In1998 meta-analysis of 47 trials on antidepressants medication including selective serotonin reuptake Inhibitors (SSRIs) indicated that 75% of the response to them was duplicated by placebo. In their meta-analysis study was criticized on several grounds. Therefore, Irving Kirsch, with other authors, obtained data submitted to the USFDA on every placebo-controlled clinical trial on the 6 most widely used SSRIs, and published a meta-analysis on 47 trials, finding a small, clinically insignificant effect. And this work plan was updated in the 2008 [25]. We conclud the updated findings from 35 carefully vetted trial smuggest that, compared with placebo, the four new-generation antidepressants - fluoxetine, paroxetine venlafaxine, and nefazodone, they do not produce clinically special improvement in depression in patients who initially have severe or even moderate depression. Statistically significantly effects but clinically minor effects only in the most severe depressed peoples. Furthermore, the significance of the effect probably is based on a decreased responsiveness to placebo, rather than increased responsiveness to medication. Given these results, they conclude that there is little reason to prescribe new generation antidepressant medications to any but the most severely depressed patients unless alternative treatments have been ineffective. In addition, they write that decreased placebo response in extremely depressed patient, combined with a response to antidepressants comparable to that of less severely depressed patient, is a potentially important insight that should be investigated further. In a controlled trial of Paroxetine vs. Clomipramine presenter by GlaxoSmithKline, 75% of patients had an adverse reaction on Paroxetine, 21% patients had a severe adverse reaction, and 13% committed a suicidal behavioral. In the 1996 Physician Desk Index (PDI) entry for Paroxetine lists 17 adverse reaction with an incidence of 5%greater than for approved doses. These are - constipation, decreased appetite, sweating,

asthenia, nausea (up to 36%), diarrhea (up to 15%), dry mouth (up to 21%), tremor (up to 15%), nervousness, anxiety, dizziness, paresthesia, somnolence (up to 22%), blurred vision, impotence, male genital disorders and other abnormal ejaculation. Fully 31 additional side effects with an incidence at least ≥1% placebo was listed, including unmanageable yawning. Attempt suicide, suicidality and murder were included. Nor were they on corresponding lists for Fluvoxamine, and Sertraline. The majority ADRs reported 26.87% out of 160 patients who took antidepressants and they found that no one any case of certain in their study. Mishra S found also that mostly ADRs observed with the polypharmacy drugs.

IV. CONCLUSION

Epidemiological Symptoms (EPS) and adverse drug reaction are the serious issue with SSRIs and SNRIs because these drug are those who treat depression not for cause reaction and other like symptoms or discontinuous symptoms. The completion of this review in our opinion is that pharmacist, physician, and doctors to aware all human who received these medicament. SSRIs and SNRIs responsible for Epidemiological Symptoms (EPS), common symptoms like-dystonia (27%), Parkinsonism (49%), dyskinesia (20%) and akathisia (2%). They commonly reported symptom include - erectile dysfunction genital, anesthesia, decreased sex drive, pleasure-less orgasm, decrease libido or absence of erection, vaginal lubrication issues, premature ejaculation, and nipples insensitivity in women's and higher risk of cardiovascular adverse reaction from SSRIs whenever SNRIs also have showed adverse reaction. It would be adorable that a suitable management system should be refined for antidepressants drug taking into account the prescribing trends, potential risks, & benefits, adverse drug outcomes, management and prevention protocols for depressive or psychotic patients. Symptoms include nausea, dizziness, lethargy, agitation, anxiety, and headache.

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