REVIEW ARTICLE

Polypharmacy in Clinical Psychiatry-a Brief Review

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ABSTRACT

Psychiatrists in clinical practice choose polypharmacy as a therapeutic strategy to control the symptoms. Polypharmacy is much more common than would be expected in contrast to the available treatment guidelines. Higher rates of relapse in patients receiving monotherapy have been documented. Polypharmacy in general clinical practice may be employed with some justification. Unwanted use of these practices may be avoided for better patient care. Limited knowledge and the wide spread marketing has led to widespread acceptance of polypharmacy practices. Some remedial measures are needed in reducing this practice of polypharmacy in our country. In this article an attempt has been made to highlight this important clinical problem for awareness of mental health professionals.

Key-words: Polypharmacy, psychiatry, clinical practice

INTRODUCTION

Use of two or more medications simultaneously is called polypharmacy.[1] The term polypharmacy contains two components, poly derived from the Greek word polus (many) and pharmacy from the Greek word pharmakon (drug).[2] The word polypharmacy first appeared in the psychiatric literature in 1969 in a published article.[3] Polypharmacy .is commonly observed in clinical practice in India and other developing countries and can be problematic for the patients especially when same class of drugs are prescribed together. It is a matter of concern for mental health professionals and health planners and is a debatable issue in clinical psychiatry. Some authors consider that the concept of adequate prescription is almost as abstract as that of health [4]. There is a strong need to establish the optimal prescriptions of psychotropic medications in today's era of polypharmacy.

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Polypharmacy is making psychiatrists more like a physician or clinical pharmacologist. Due to the recent trend of psychiatrists to prescribe more psychotropic medications, space for psychotherapeutic interventions is limited. This practice will generate physician hood concept among young generation psychiatrists. The concomitant use of psychiatric drugs is probably based more upon experience than evidence. [5]

How common is poly-pharmacy?

The study of the phenomenon of polypharmacy in psychiatry is inherently complex. Excessive dosing and poly-pharmacy is widely prevalent in psychiatry. [6] There are numerous studies on prescription habits showing that polypharmacy is much more common than would be expected in view of the available treatment guidelines.[6-14] Hiroto et al,[6] in a study of schizophrenic patients found that majority of the patients were on polypharmacy. In this study, 179 patients gave consent

for participation. In 34 patients data was incomplete and 6 patients were not on any antipsychotic medication. Out of 139 patients, 102 (73.4%) were on non standardized dosage while 32 (23.02%) were on excessive dosage of medications. In another study by Adi et al, [7] , 93.4% of bipolar patients received polypharmacy. Patients who received fewer drugs reported normal mood frequently and had fewer mood swings. Sachs and Thase[8] analyzed polypharmacy in many clinical trials and revealed that 40% of patients derived little or no benefit. Cuevas and Sanz[9] in a sample of 264 patients of various psychiatric disorders found that the mean number of psychotropic drugs used were 1.63 (range 1-7) and 41.9% of patients received polypharmacy. Sernyak and Roserheck[10] found the rate of polypharmacy in outdoor schizophrenic patients in the range of 6.8-15% while in indoor patients it was 50 %(a high figure).

In a study comprising a review of the clinical records of 209 patients with schizophrenia, 55.5% of patients were found on polypharmacy treatment record. The patients received an average of 3.06 psychotropic drugs upon discharge and an average of 1.61 antipsychotic agents.[11] In a developing country survey of 158 psychiatric patients, the

authors found the pattern of polypharmacy was prevalent in 54% study subjects.[12] In another study of case records and a second phase confirmation strategy through personal interviews, mean number of psychoactive drugs prescribed was 2.22 (range 1-6). The rate of polypharmacy was 67% with 34.1% of patients receiving two drugs, 20.5% receiving three drugs and 12.5% of the patients receiving four or more psychoactive drugs.[13] Johnson and Wright[14] found that in a teaching hospital, 34% of patients were on two or more drugs while 17% were receiving four or more medications. Antiparkinsonian drugs were given regularly to 48% of patients and an antidepressant to 10% of the schizophrenic patients.

Justification for polypharmacy

Despite so many advances in treatment of psychiatric patients, 30% of the patients do not respond or only respond partially to pharmacological treatment.[15] Lack of response to treatment in psychiatric patients is a clinical problem in psychiatric practice. Clinician generally chooses polypharmacy as a therapeutic strategy to control the symptoms. Combining multiple agents is the most commonly used clinical practice for treatment of resistant bipolar patients.[16-18] The combination of medications in some controlled studies has demonstrated greater efficacy than monotherapy.[19-21] Response rates for combination treatment of acute mania generally exceed those of treatment with lithium or valproate by 20-25%.[20-21]

Newer drugs generally have improved safety profiles. Use of multiple medications with synergistic effect and with one drug augmenting the effect of the other can be beneficial for some group of patients. Discovery of various receptors with action and specificity for drugs supports the judicial use of combination of drugs having different receptor affinity. Judicial use can augment the desired action without increasing the side effects of the drug. Most Psychiatric disorders are now considered as complete syndrome with no single hypothesis explaining the phenomenology of the disorder. So chances are that monotherapy will not produce the desired results. This may lead to refractoriness of the disorder. Hence, treatment of patient's refractory to monotherapy with combination of medications may be justified.

Associated comorbid disorders are not exception in psychiatry. Combination of two drugs with different action on multiple receptors has proven to be helpful in managing co morbid psychiatric disorders. The large number of medications is now available in the market for the treatment of patients with psychiatric disorders. Pharmaceutical company's claims of safety of the new agents and probably the pressures of pharmaceutical industry have created new opportunities for the use of multiple medications for a single condition. Medical treatment is viewed as more effective, easier to deliver, less expensive and consuming less time and thus all the symptoms are treated medically. Successful use of polypharmacy for other chronic illness such as infection with HIV, Parkinson's disease, cancer and epilepsy.is a common routine clinical practice and has revolutionized the treatment of such chronic illnesses.

Polypharmacy in depression

Large number of depressive patients does not respond to monotherapy Lithium is a classical augmenting agent

for unipolar depression resistant to first line antidepressants. It enhances the action of antidepressant by acting synergistically[22]. Thyroid hormone potentiates the effects of antidepressants[23]. Similarly buspirone has been used as an augmenting agent. Serotonin specific reuptake inhibitors along with estrogen are used in premenopausal and postmenopausal women with refractory depression. This combination has been reported in case reports and clinical trials conducted to assess the efficacy are limited one.

Polypharmacy in bipolar affective disorder

Polypharmacy with two or more psychotropic medications is the rule rather than exception in the treatment of bipolar disorders. First line treatment is with lithium or valproic acid or divalproex. If patient fails to stabilize in manic phase on first line drugs, preferred another line of agent is atypical antipsychotic. With newer evidence, atypical antipsychotic are becoming the first line treatment for mania. If lithium, valporic acid or atypical antipsychotics are not effective, they can be given in combination. If this is not effective, benzodiazepine or conventional antipsychotic can be added to first or second line monotherapies. Neuroleptic should be used for most disturbed and out of control patients but restricted to acute phase only. For maintenance phase, failure to first line antimanic agents(lithium, valproate, divalproex) or atypical antipsychotics, a trial of other anti convulsants(carbamazepine, lamotrigine, gabapentin and topiramate). is given to the bipolar patients

Therapeutic recommendation for maintenance treatment of bipolar affective disorder patient is undergoing rapid changes. Till few years back, lithium was the hallmark of bipolar treatment with antidepressant cotherapy for patients prone to depression. Recently several newer therapeutic molecules are available for treatment. Valproic acid or divalproex is now considered first line choice along with lithium. Atypical antipsychotic are becoming another choice for maintenance therapy of bipolar disorders When lithium or valproic acid alone or in combination fails, atypical antipsychotics are even becoming first line choice for bipolar maintenance With risk of switch to mania or hypomania antidepressants are rarely used these days. The trend today is to use antidepressant sparingly in bipolar depression. This is used only in the presence of robust mood stabilization with mood stabilizers.

With strong evidence of efficacy of lamotrigine and quetiapine in bipolar depression, the use of antidepressant is gradually diminishing. Higher prevalence of comorbidity with bipolar disorder such as substance abuse [24], anxiety disorder [25] necessitates the need for combination treatment. Inherent complexity of the recurrent, episodic and phasic nature of bipolar disorder and lack of understanding of specific pathophysiology, a single drug may not control all symptoms. in bipolar patients.

Antipsychotic polypharmacy

In routine clinical practice, a patient not responding to conventional or atypical antipsychotic is switched to other atypical antipsychotic. Schizophrenia has positive symptopms, negative symptoms, cognitive symptoms, and mood and behavior symptoms. Probably there are multiple mechanisms leading to different symptoms in these patients, and one can use more than one drug targeting different mechanism. Patients were more likely to receive antipsychotic polypharmacy if they were younger, unmarried, had schizophrenia rather than schizoaffective disorder. Lack of response to treatment in patients with schizophrenia is one of principal concern facing clinician in clinical practice. There are two group of patient with schizophrenia who could benefit from the use of polypharmacy. One group comprises patient presenting a partial response to clozapine. The other group consists of patient who needs admission in psychiatry ward, with acute psychotic processes and with behavioural problems (markedly aggressive patients). Patient given prescription for polypharmacy were more likely to receive antiparkinson medications, antianxiety agents, and mood stabilizers.

Risk of polypharmacy

Polypharmacy increases the chances of drug drug interactions. Polypharmacy is associated with early and sudden cardiac death. [26-27]. Polypharmacy is strongly

associated with excessive dosing usage in clinical practice [28]. The excessive dosage and medications may be dangerous for psychiatric patients and may put them on higher death risk. Higher rate of hospitalization can be attributed to polypharmacy prescription practices. Unwanted use of polypharmacy does not confer any therapeutic advantage, but tends to increase the side effects.

The introduction of combination of antipsychotics with antiparkinsonian agents, combination of various antipsychotics, antipsychotics with antidepressants or anxiolytics is one of the most unfortunate developments in the pharmacotherapy of psychiatric disorder. Asian patients are more vulnerable to side effects and require less antipsychotic medication than European patients[12]. Polyphramacy can lead to increased cost of treatment and poor drug adherence.

Can Polypharmacy be reduced?

Fifty years ago psychiatrists had to manage psychotic patients without the help of psychotropic medications. Nowadays good molecules are available for management. In teaching department polypharmacy practices happens because of a high turnover of staff and where the patient is seen by a new doctor every six months. The easiest thing for the new doctor is to repeat the same medication.

Some measures can be adopted in reducing this practice of polypharmacy. Patrick et al [29]_estimated epidemiological measures of polypharmacy and identified the patients at risk for polypharmacy in order to develop proper interventions that minimize the risks. Regular internal auditing of drug prescriptions was found to be quite useful in decreasing the polypharmacy practices. Adequate knowledge with research literature can help the mental health professionals in reducing this unwanted use of polypharmacy. Educational programmes detailing scientific advances can be effective for health care professionals in the reduction of this trend of polypharmacy. Many psychiatrists do not fully understand the mechanism and advantages of new psychotropic medications. They are reluctant to change their prescribing patterns. Educating the patient and their families about the illness, its treatment, side effects are integral parts of scientific pharmacotherapy. This may improve the compliance to treatment programme. Supervised gradual reduction of medication should be attempted over time. Patient should be treated with flexible dose.

Future Pharmacy

Polypharmacy use should be evidence based [30]. Evidence is now available for district subtypes of bipolar affective disorder patients responding to specific types of mood stabilizers Genetic studies of bipolar affective disorder patients require the ability to precisely define a phenotype. Pharmacogenomic studies in future will be quite useful and will provide a new direction for pharmacy. Such types of studies have demonstrated a significant influence of genetic mechanisms on the efficacy of clinically prescribed drugs. Prescribing guidelines and algorithms and their application in clinical practice may be an essential part of future pharmacy. Long term antipsychotic polypharmacy should be reserved for more severely ill patients with psychotic symptoms rather than mood symptoms. Prescribing too many drugs is not a good practice and should be discouraged.

Conclusions:

Polypharmacy should be judicially used in routine clinical practice. Rational approach in its application is essential for better patient care. Good information about polypharmacy practices in developed and developing countries is available in the literature and steps in regulation of this practice is needed to decrease the risks associated with this practice. Regular monitoring of the prescription pattern is quite helpful in checking the spread of this phenomenon. Educational interventions are beneficial for psychiatrists and other professionals and they must follow treatment guidelines.

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