Clinical Practice Guidelines for Management of Schizophrenia

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INTRODUCTION

Schizophrenia is a serious mental disorder with prevalence rates of 2-3 per 1000 reported from India. The impact of schizophrenia on patients, their families and the wider society are no different from what has been observed in the rest of the world. However, resource constraints, poverty, lack of education and inadequate access to health care facilities for patients make the problem of providing care particularly daunting in India. In 2005, the Indian Psychiatric Society came up with treatment guidelines for schizophrenia tailored to meet the requirements of our patients in the context of prevailing existing resources. There have been several developments in the management of schizophrenia since then. These new set of guidelines attempt to update the previous guidelines by emphasizing what is new in the field. These guidelines ought to be read in conjunction with the earlier version of the treatment guidelines on schizophrenia as developed and published by the Indian Psychiatric Society in the year 2005.

SCOPE OF THIS DOCUMENT

The major emphasis of the current guidelines is on areas in the management of schizophrenia, which have witnessed significant developments since the publication of the

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previous guidelines. These guidelines are not particularly applicable to any specific treatment setting and may need minor modifications to suit the needs of patients in a specific setting. The recommendations are primarily meant for adult patients. The needs of children or the elderly with schizophrenia may be different. Finally, it is expected that recommendations made will have to be tailored to suit the needs of individual patients.

Assessment and evaluation (table-1)

A comprehensive assessment of the patient and his/her caregivers needs to be carried out. The cornerstone of this assessment is a detailed history and physical and mental state examinations. Efforts should be made to obtain information from all sources, especially the family. Wherever possible, diagnosis of schizophrenia be preferably made according to current diagnostic criteria, as such a diagnosis is more reliable. A reliable diagnosis facilitates communication among clinicians, and allows for better applicability of evidence-based recommendations. Many clinical conditions that may mimic schizophrenia include mood disorders, substance-induced psychoses and psychoses secondary to physical illnesses. These should be ruled out as far as possible by history, examination and additional investigations. In some instances a definitive diagnosis may need time. Further, because of the enormous psychosocial consequences a diagnosis of schizophrenia needs to be made with great caution and sensitivity. In doubtful cases, a medication-free observation period can be considered. However, consideration of medication free period need to be balanced against the risks of delaying treatment or the potential for harm to self and others in acutely ill patients. It is important to remember that diagnosis is not a one-time affair, but a continuous process. Accordingly, based on the subsequent information from patients and caregivers, and on repeated clinical evaluations the diagnosis may need reevaluation.

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The assessment should cover all other areas such as symptom dimensions, symptom-severity, psychiatric and medical conditions, particularly comorbid substance abuse, the risk of harm to self or others, level of functioning and the socio-cultural milieu of the patient. A high index of suspicion along with thorough assessment can help in detecting most patients with comorbid substance abuse/dependence. Wherever, facilities are available, urine or blood screens (with prior consent) can be used to confirm the presence of comorbid substance abuse/dependence. A thorough physical examination need to be done to rule out presence of any physical illness and also to rule out psychoses secondary to physical illnesses. This may be supplemented by the judicious use of investigations. Wherever possible, unstructured assessments need to be supplemented by ratings on appropriate standardized rating scales. Other options such as detailed cognitive testing can be done if required and feasible. The use of neuroimaging may be indicated in those with first-episode psychosis, neurological signs, non-response to treatment and elderly patients.

Assessments of caregivers may focus on areas such as their knowledge and understanding of the illness, their attitudes and beliefs regarding treatment, the impact of the illness on them and their personal and social resources.

It is important to remember that assessment is an ongoing process. As the treatment progresses other areas such as response to treatment, side effects, treatment adherence, the impact of patient's immediate environment, disability assessments, other health-care needs, ease of access and relationship with the treatment team may need to be assessed separately.

Formulating a treatment plan (figure 1)

Formulation of treatment plan involves deciding about treatment setting, treatments to be used and areas to be addressed. Patients, caregivers and staff involved in care may be consulted while preparing the treatment plan. Treatment plans be needs-based, practical, feasible and flexible. These should be continuously re-evaluated and modified as required.

Choice of treatment settings

The basic principle while choosing a treatment-setting is to provide care in the least restrictive setting, which nevertheless meets the needs of patients and caregivers. The commonest treatment settings would be either outpatient clinics or inpatient wards. In some instances resources for long-term inpatient care, or community or residential care may be available. The bulk of the patients would probably receive treatment in outpatient settings. Given their severe shortage, inpatient beds are likely to be scarce. Common indications for inpatient care during acute episodes are shown in table-2. Whenever possible patient admitted to the inpatient setting should have accompanying family caregivers. In case inpatient care facilities are not available,

Table 1: Components of assessment and evaluation

Basic assessments

- Comprehensive assessment of both patients and caregivers
- Complete history with information from all possible sources
- Physical examination- record data such as blood pressure, weight and wherever indicated body mass index and waist circumference
- Mental state examination
- · Establish diagnosis according to current diagnostic criteria
- Differential diagnosis by ruling out secondary psychoses
- Areas to be evaluated: symptom-severity, symptom-dimensions (reality distortion, disorganization, negative, depressive and cognitive symptoms), comorbid physical, psychiatric and substance use conditions, risk of harm to self and others, level of functioning and socio-cultural milieu of the patient
- Basic investigations: haemogram, blood sugars and lipid levels, liver functions, renal functions, electrocardiogram (focus on QTc)
- Assessments of caregivers: knowledge and understanding of the illness, attitudes and beliefs regarding treatment, impact of the illness on them, personal and social resources
- Ongoing assessments: response to treatment, side effects, treatment adherence, the impact of patient's immediate environment, disability assessments, other health-care needs, ease of access and relationship with the treatment team

Additional/Optional assessments

- Use of standardized rating scales to rate all aspects of the illness
- · Psychological testing for cognitive functions
- Neuroimaging especially in those with first-episode psychosis, neurological signs, non-response to treatment and elderly patients

Table 2: Some indications for inpatient care during acute episodes

- Presence of suicidal behaviour which puts the life of the patient at risk
- Presence of severe agitation or violence which puts the life of others at risk
- Refusal to eat which puts the life of patient at risk
- · Severe malnutrition
- Patient unable to care for self to the extent that she/he requires constant supervision or support
- Catatonia
- Presence of general medical or comorbid psychiatric conditions which make management unsafe and ineffective in the outpatient setting

than the patient and/or family need to be informed about such a need and admission in nearest available inpatient facility may be facilitated.

Options for management for schizophrenia

Treatment options for management of schizophrenia can be broadly classified as antipsychotic medications, electroconvulsive therapy (ECT), adjunctive medications and psychosocial interventions (table-3).

Pharmacological treatment

Choice of antipsychotic medication

The essential choice is between using an antipsychotic belonging to the class of typical antipsychotics (FGA- first-generation antipsychotic) or from the atypical group (SGA-second-generation antipsychotic). Since the publication of the previous guideline there is somewhat greater clarity on this matter. The bulk of the evidence including large-scale real-world studies indicates that there is very little difference

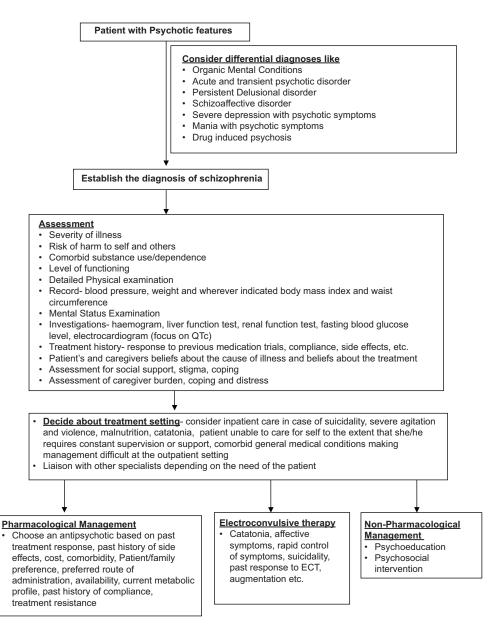


Figure-1: Initial evaluation and management plan for schizophrenia

Table 3: Options for management for schizophrenia

Antipsychotic medications

First-generation antipsychotic medications (Oral/parenteral/depot or long acting- preparations)

Second-generation antipsychotic medications (Oral/parenteral/depot or long acting- preparations)

Somatic treatments

Electroconvulsive therapy (ECT)

Adjunctive medications

Anticholinergics, antidepressants, benzodiazepines, hypnotic-sedatives, anticonvulsants, lithium carbonate

Psychosocial interventions

Family intervention, cognitive behavioural therapy, social skills training, cognitive remediation, individual therapy, group therapy, vocational rehabilitation, early-intervention programmes, case management, community mental-health teams, crisis resolution teams

Other measures

Lifestyle and dietary modifications

in terms of efficacy, adherence and other subjective aspects between the FGA and the SGA group, or between individual antipsychotics belonging to either group. The only exception to this trend is clozapine, which appears to be more efficacious than any other antipsychotic in patients with treatment resistance. It follows from this that the choice of the antipsychotic will depend on factors other than efficacy. Some of these factors are included in table-4.

Dose

The recommended dose of various oral antipsychotics available in India is shown in table-5. In general patients with first-episode psychosis respond to lower doses. The use of high or very high doses (mega doses) of antipsychotics, if required, may be used with caution in exceptional circumstances. It is noted that Indian patients require lower

doses of antipsychotic drugs compared to patients from the West. Although this is suggested by clinical experience and pharmacokinetic studies of Asian patients, there is little evidence for, or against this supposition from clinical trials.

Route of administration

Acutely agitated patients often require parenteral administration of antipsychotics to rapidly control the behavioural disturbance. Liquid or mouth-dissolving formulations are often helpful in non-compliant patients. Depot preparations are generally not used in acutely agitated patients except zuclopenthixol acetate, which has a half-life of about 20 hours. In general, it is recommended that one drug is to be used by one route in order to minimise drug interactions and simplify clinical observations.

Depot preparations (table-6) are often helpful in ensuring medication-compliance and may be used in situations where compliance is a problem. Depot injectables may also be used if patients/relatives indicate a preference for this kind of treatment. Test doses are administered at the start of treatment. When used, depot preparations need to be prescribed within the standard recommended dosage and interval range to achieve optimum effectiveness in preventing relapse.

Adequate antipsychotic trial

The minimum recommended duration of treatment to consider it to be an effective trial for all antipsychotics is use of medication in the highest tolerable dose for 6-8 weeks, with the exception of clozapine, where the minimum period of treatment is at least 3-6 months.

Response

Antipsychotics are known to produce a significant remission of positive symptoms. This could thus be a reasonable goal of treatment during the acute phase. Antipsychotics are less effective in management of negative symptoms, therefore a mild to moderate reduction in negative symptoms is often acceptable. Response indicators for other aspects of the illness (e.g. cognitive symptoms) are not clear. Patients on antipsychotics need to be monitored regularly to ascertain the level of response and the emergence of side effects.

Non-response (Figure-2)

In case a patient fails to respond to an antipsychotic medication, poor compliance or non-compliance need to be evaluated prior to switching the medication to another antipsychotic. If a patient is found to have poor compliance or non-compliance to medications, all efforts are to be made to understand the causes responsible for lack of compliance and appropriate steps need to be taken to handle the problem. However, if a patient fails to respond to an adequate trial of an antipsychotic medication (i.e., adequate dose for at least 6-8 weeks duration) taken

Table 4: Factors that influence selection of antipsychotics

- Past treatment response
- · Cost of treatment, affordability
- Psychiatric comorbidity
- · Medical comorbidity
- · Side effects
- Patient or family preference
- · Preferred route of administration
- · Concomitant medications
- Non-adherence
- · Treatment resistance

Table 5: Recommended therapeutic dose ranges for various antipsychotics

	Usual daily dose	Maximum
	(in mg/day)	daily dose
First Generation Antipsychotics (FGAs)		
Chlorpromazine	300-800	800
Haloperidol	5-20	20
Penfluridol	20-60 mg/week	250 mg/week
Perphenazine	12-64	64
Pimozide	4-10	10
Thioridazine	300-800	800
Trifluoperazine	15-30	30
Zuclopenthixol	10-50	50
Second Generation Antipsychotics (SGAs)		
Amisulpride	50-800	1200
Aripiprazole	10-30	30
Asenapine	10-20	20
Blonanserin	2-8	24
Clozapine	150-600	900
Iloperidone	12-24	24
Olanzapine	10-30	30
Paliperidone	3-12	12
Quetiapine	300-800	800
Risperidone	2-8	16
Ziprasidone	80-200	200
Zotepine	75-300	300

Table 6: Antipsychotic depot preparations available in India

Name of antipsychotic	Usual 2-4 weekly dose in mg	
Zuclopenthixol decanoate	200	
Paliperidone palmitate	234 initially followed by 117 monthly	
Fluphenazine decanoate	12.5-50	
Haloperidol decanoate	50	
Risperidone depot	25-50	
(RisperidalConsta)		
Olanzapine pamoate	210-405	

with good compliance, a change in antipsychotic may be considered. Clozapine need to be considered after failure of sequential trials of 2 antipsychotics (at least one of which is a SGA). Clozapine may also be considered earlier in patients who are violent, at risk for suicide, not responding to their current medication and those experiencing intolerable side effects with two different classes of antipsychotics.

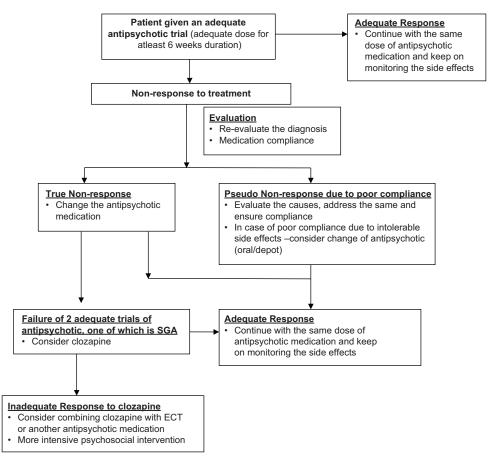


Figure 2: Evaluation of patient with non-response to antipsychotic medications

Combination of antipsychotics

There is limited evidence for the efficacy of combination of antipsychotics. In the initial phase, a clinician may be compelled to use a combination of antipsychotics to manage agitation, but caution need to be exercised while doing so. These should be used on SOS basis and for shortest possible time. Combinations of antipsychotics for prolonged periods may be avoided, except in patients not responding to clozapine.

ADJUNCTIVE MEDICATIONS

Although antipsychotic agents are the mainstay of treatment of schizophrenia, management may involve use of adjunctive treatments like with antidepressants, mood stabilizers or benzodiazepines. However, these can be used with proper rationale and for shortest possible duration. At every assessment a proper evaluation need to be done for the continuation of the same. Lithium and other mood stabilizers can be prescribed in agitated, overactive patients or those with affective symptoms responding poorly to their current drug. Benzodiazepines can be useful in managing agitation and sleep disturbance. Antidepressants may be of use in post-psychotic depression and may be avoided when the patient has florid psychotic symptoms. In general prophylactic use of anticholinergics

is not recommended. It is better to start these drugs when the patient actually develops extrapyramidal side effects. Whenever anticholinergic agents are required, use may be limited to lowest possible doses and for shortest possible time.

ELECTROCONVULSIVE THERAPY (ECT)

As in many other developing countries ECT is used quite frequently in schizophrenia in India. The evidence for efficacy of ECT in the acute phase of schizophrenia is somewhat controversial. There is evidence for augmentation and acceleration of response. ECT is used in conjunction with antipsychotics in the acute phase, but the extent of the benefit of adding ECT to antipsychotics is unclear and the positive effects seem to last only for the first few weeks of treatment. However, there may be some merit in adding ECT to the treatment regimen in patients who respond poorly to antipsychotics. The more unequivocal indications for ECT in combination with antipsychotics are included in table-7. ECT is not useful in chronic schizophrenia and there is not enough evidence to recommend its use in the longer term except in exceptional circumstances. Finally, whenever ECT is used adequate information and support for patients and caregivers, informed consent, proper administration and careful monitoring of response and side effects be done.

PSYCHOEDUCATION FOR PATIENTS AND OR FAMILY (TABLE-8)

Psychoeducation may be considered both for the patient and family members. The aim is to educate the patient and family about the illness. Simple and brief explanations about the nature of the patient's illness, treatments, likely side effects, likely length of treatment etc. can be offered. Relatives also need to be given time to confront the painful fact of the illness, and what it entails for the patient and the family as a whole. It is important that professionals are careful and considerate, but clear and thorough in their use of clinical language and in the explanations they provide. No blame is to be attached to the family. Treatment adherence will be another main objective at this stage. Prior to every session, feedback of the previous sessions may be taken and psychoeducation is to be tailored to the needs of the patient and the caregivers.

PSYCHOSOCIAL INTERVENTIONS

Psychosocial interventions are acknowledged to be an integral part of management of schizophrenia. Different psychosocial interventions including family treatments, cognitive behavioural therapy, social skills training, cognitive remediation, individual supportive therapy, group therapy, vocational rehabilitation, case management, use of community

Table 7: Possible indications of use of ECT in patients of schizophrenia

- Catatonic symptoms
- · Affective symptoms
- Need for rapid control of symptoms
- Presence of suicidal behaviour which puts the life of the patient at risk
- Presence of severe agitation or violence which puts the life of others at risk
- · Refusal to eat which puts the life of patient at risk
- · History of good response in the past
- Patients not responding to adequate trial of an antipsychotic medication
- Augmentation of partial response to antipsychotic medication
- · Clozapine resistant schizophrenia
- Not able to tolerate antipsychotic medications

Table 8: Basic components of Psychoeducation

- Assessing the knowledge of the patient and caregivers about aetiology, treatment and prognosis
- Introducing the diagnosis of schizophrenia into discussion
- · Discussing about various symptom dimensions
- · Providing information about aetiology
- Providing information about treatment in terms of available options, their efficacy/effectiveness, side effects, duration of use
- Discussing about importance of medication and treatment compliance
- Providing information about possible course and long term outcome
- Discussing about problems of substance abuse, marriage and other issues
- Discussing about Communication patterns, problem solving, disability benefits
- Discussing about relapse and how to identify the early signs of relapse
- Dealing with day today stress
- Improving insight into illness
- Handling expressed emotions and improving communication
- Enhancing adaptive coping to deal with persistent/residual symptoms

mental-health teams and of crisis resolution teams have been proven to be useful in the management of schizophrenia. The usefulness and delivery of psychosocial treatments has probably not attracted the research attention it deserves in the Indian context. Nevertheless, there is ample Indian evidence and experience with family treatments, rehabilitation and other modalities such as community programmes, yoga and cognitive remediation. Based on these data, psychosocial interventions, from the simple to the complex, can be recommended for patients with schizophrenia and their families. An approach which prioritizes the needs of patients and their families could be followed.

FAMILY INTERVENTIONS

There has been a long tradition in India of involving families in the care of their members with mental illness. There are several studies documenting the delivery of family interventions. Several formats of predominantly psychoeducational treatments such as informal or unstructured programmes, structured treatments, groupbased interventions, and integrated psychosocial treatments have been tried. From the number of controlled trials it appears that a wide range of interventions and treatmentdelivery, from the simple to the complex, may be useful in the Indian context. The basic emphasis need to be on continued contact and medication adherence while offering emotional and practical support. A needs-based approach, in which interventions are tailored to the background and needs of the families, is more likely to enhance their acceptability and positively influence the readiness of families to participate in such interventions.

ADVISE FOR LIFE STYLE AND DIETARY MODIFICATIONS

All the patients are to be advised for a change in the life style and diet to reduce the risk of metabolic side effects and cardiovascular morbidity and mortality. These include physical exercises, dietary modifications and abstinence from smoking etc.

REHABILITATION

Similar to family treatments, rehabilitation programmes need to be be culturally moulded and adapted to the needs of patients and their families. However, unlike family interventions, resources for more elaborate rehabilitation strategies may not be available in every centre. Nevertheless, relatively simple and inexpensive strategies can form a part of the overall psychosocial intervention package.

INDIVIDUAL SUPPORTIVE THERAPY

A supportive empathic relationship between patients and professionals, in which good listening promotes a lasting therapeutic alliance is an essential part of good practice. Additional elements could include support and advice, encouraging continued engagement, treatment-adherence and healthy lifestyles. Efforts to minimize stress may also be beneficial. Individual support along with medication is the most commonly practiced treatment in schizophrenia. Patients and families consistently rank individual support as among the most highly valued services offered to patients with schizophrenia.

OTHER PSYCHOSOCIAL INTERVENTIONS

Other interventions that hold promise are home-based care, support groups for caregivers, community-based interventions, cognitive training or remediation, and yoga. More research on the efficacy of these strategies and their wider implementation is needed.

Basic components of any psychosocial intervention are depicted in table-9. For more specific recommendations other sources may be consulted.

TREATMENT ADHERENCE

Adherence is defined as "the extent to which the patients' behaviour, in terms of regular clinic visit, taking medications, following diets, executing lifestyle changes, coincide with the clinical prescription". Non-adherence in this context thus denotes failure to enter a treatment programme, premature termination of treatment, or incomplete implementation of instructions, including those that pertain to medication administration. Evidence suggests that about half of the patients with schizophrenia do not comply with the treatment recommendations, about one-third miss their appointments with the clinicians and 20-60% of patients drop out from treatment. Common factors associated with poor medication noncompliance are shown in table-10. Factors consistently linked to non-adherence include poor insight, negative attitude or subjective response to medication, comorbid substance abuse, and poor therapeutic alliance. Clinicians need to make efforts to reduce the rates of medication compliance and treatment non-adherence. It is important for the clinicians to understand that besides the contextual or situation factors, patient related factors and illness related factors, certain clinician related factors are responsible for poor medication compliance and higher dropout rates. Some of the common clinician related factors which may be relevant in Indian context include poor communication between the clinician and the patient/caregiver, poor therapeutic alliance and noncollaborative decision-making. Hence, clinicians need to focus on better communication and improve therapeutic alliance with patient and the family to improve overall outcome. Whenever clinicians encounter poor medication

Table 9: Recommendations about psychosocial interventions

- Assessment of psychosocial factors involving the patient and the family is an integral part of psychosocial interventions.
- There is a wide range of interventions that have proved useful in Indian
- Choice of the intervention will be shaped by the needs of patients and their families as well as the resources available.
- Basic components of any intervention include: promoting a therapeutic alliance with the patient and the family, encouraging ongoing engagement, information about various aspects of the illness, focusing on treatment-adherence and healthy lifestyles, and offering emotional and practical support.

Table 10: Factors associated with poor medication compliance

Demographic risk factors

• Younger age, male gender, unemployment, lower socioeconomic status

Patient related factors

· Knowledge about illness and treatment, perceived need for treatment (insight), motivation, beliefs about treatment risks and benefits, past experiences/"transference", past history of adherence, self-stigma

• Living independently, poor social support, poor financial support Clinical risk factors

• Poorer premorbid functioning, earlier age of onset, prior history of non-adherence

Symptom-related risk factors

· Lack of insight, paranoia, grandiose delusions, conceptual disorganization, impaired cognition, substance abuse, comorbidities, depression, refractoriness, spontaneous remissions

Treatment-related risk factors

• Medication side effects, poor treatment alliance, complex dosing, negative experience of medication, route of administration, length of treatment, cost of treatment, number of medications

Service-related risk factors

• High cost of medication, poor accessibility of treatment services Family/caregivers-related risk factors

• Lack of supervision, negative attitudes towards treatment, lack of knowledge about medicines, nature of relationship with patient, perceived need for treatment, beliefs about benefits and risks with continued treatment, involvement in treatment, stigma, financial constraints, support from other sources

Clinician/provider related factors

• Therapeutic alliance, frequency and nature of contact with clinicians, expected duration of treatment, duration of past treatment, accessibility to clinicians and services, reimbursement, psychoeducation and psychosocial treatment, complexity of administration

or treatment compliance, all efforts need to be made to understand the reasons behind the same. Proper evaluation of non-adherence need to cover assessment of familial, social, biological and pharmacological perspectives. Patients/caregivers concerns need to be addressed by proper psychoeducation and modification of pharmacological treatment. Medication compliance can be improved by using depot preparations and use of mouth dissolving formulations under supervision. Evidence also suggests beneficial effects of cognitive-behavioural approaches and motivational interviewing.

PHASES OF ILLNESS/TREATMENT

Management of schizophrenia can be broadly divided into three phases, i.e., acute phase, continuation treatment or stabilization phase, maintenance or stable phase. Some patients may present very early in a prodromal phase and appropriate strategies for detection and management for this phase might be required.

Prodromal stage

It is now well known that onset of frank psychosis is often preceded by psychological and behavioral abnormalities involving cognition, emotion, perception, communication, motivation and sleep. These symptoms may precede the psychosis by weeks to years. Various diagnostic systems categorise the symptoms as: basic symptoms, attenuated positive symptoms, brief limited intermittent psychotic symptoms, features of schizotypal personality disorder, genetic risk paired with functional deterioration, as well as general symptoms that are not specific to psychosis. Evidence also suggests that many patients with prodrome, especially the high risk group have higher chance of conversion to frank schizophrenia. Conversion rates have been reported to range from 25-40%. Further, prodrome itself may have negative impact on the social, emotional and cognitive development. Therefore, now more and more emphasis is laid on early detection and intervention. Factors which have been shown to predict conversion to psychosis include presence of genetic risk with recent deterioration in functioning, higher degree of unusual thought content, suspiciousness/paranoia, presence of social impairment, longer duration of symptoms, high levels of depression, reduced attention and history of substance abuse. In terms of management of prodrome it is suggested that treatment ought to be based on the needs of the patient. There is some evidence to suggest that use of antipsychotics in prodromal phase can delay the conversion to psychosis and antidepressants may be useful in symptomatic improvement in a sub-group of patients. However, at present evidence for use of antipsychotics in prodromal phase is not convincing to recommend its use in all patients. There is also preliminary evidence to suggest the beneficial effect of certain agents like omega-3 fatty acids. In contrast, evidence suggest that psychological interventions like cognitive behaviour therapy, cognitive therapy, psychosocial stress management, etc can improve functioning and symptomatology during the prodromal phase, although the active components of these treatments are not well known. Accordingly, whenever a patient presents with symptoms suggestive of prodromal phase of schizophrenia, initial management is done in the form of psychosocial intervention. Use of pharmacotherapy need to be weighed against the side effects of antipsychotics and sensitization of dopamine receptors in brain, which can possibly lead to supersensitivity psychosis or rapid-onset psychosis following stoppage of antipsychotic medication.

MANAGEMENT IN THE ACUTE PHASE OF TREATMENT

Most patients in this stage are likely to exhibit florid psychotic symptoms such as delusions or hallucinations, disorganized thinking and behavioural disturbances. Their functioning may be severely impaired and they can be at risk of harming themselves or others. Additionally both the patient and the family might have considerable difficulty in coming to terms with the onset of acute symptoms. The various aspects of management in the acute phase are included in table-11.

MANAGEMENT IN THE CONTINUATION TREATMENT PHASE

This phase begins once the acute symptoms reduce in severity or remit and conventionally lasts for about 6-12 months. Different components of this phase are shown in table-12. Consolidation of remission, continued reduction in symptoms and prevention of early relapses are the usual treatment objectives during this phase. Reduction of stress on the patient and the family by continuing engagement

Table 11: Management in the acute phase

Comprehensive assessment (psychiatric/medical/psychosocial) Deciding on goals of treatment

Patients

Eliminate/reduce symptoms of schizophrenia and improve the level of functioning

Promote safety, reduce risk of harm, reduce stress

Caregivers

Minimise caregiver distress

Offer help to enable them to cope with the illness in their relative

Both

Develop a therapeutic alliance and provide opportunities for patients and caregivers to actively engage in treatment

Offer basic information and support tailored to needs of patients and caregivers

Choice of treatment setting

Antipsychotic treatment Choice of drug

Dose

Dose Route of administration

Duration of treatment

Determining response or non-response

Combining antipsychotics

Use of adjunctive medications when indicated

Use of ECT when indicated

Psychosocial interventions- relatively basic and mainly for the purpose of fulfilling the goals of treatment listed above

Planning for further treatment

Table 12: Management in the continuation treatment phase

Determining goals

Further assessment

Antipsychotic treatment

Psychosocial interventions

Monitoring for response, side effects and treatment adherence

and support and enhancing their adaptation to life after discharge from the hospital, are other important goals of management. Management includes continuing medication treatment, monitoring of response and side effects and furthering psychosocial interventions. Medications need to continue preferably at the same dose for the next 6-12 months. The continued goals of psychosocial treatment are to maintain treatment engagement and adherence, offer support for patients and their families and help prepare the patient for life in the community. More elaborate psychosocial interventions may be tried at this stage. Finally, regular monitoring of response, side effects and treatment-adherence needs to continue.

MANAGEMENT IN THE MAINTENANCE OR STABLE PHASE

During this phase of illness, symptoms are stable and usually less severe than in the acute stage. Negative symptoms may predominate and deficits in social and occupational functioning become more apparent. Maintaining or improving level of functioning, prevention of recurrences and promoting psychological/personal recovery are the major aims of treatment during this phase of management. Different components of this phase are shown in table-13.

During this phase, follow-ups can be scheduled once every 2-3 months and more frequently in times of crises, or if desired by the family. During this phase of management, regular feedback need to be obtained from the family. Any new issues that arise are discussed and some of the previous issues may need reemphasis. Management in the stable phase involves carrying forward the gains achieved. The management plan should be relooked for any need for change. It also involves determining the goals, continuing further assessment, continuing with antipsychotic medications and monitoring of side effects and furthering the psychosocial interventions. In addition the management need to focus on rehabilitation, enhancing personal recovery.

Goals of treatment: The goals of treatment during this phase are to maintain or improve functioning, improve quality of life and facilitate personal recovery. Psychotic exacerbations need to be effectively treated. Adverse effects are to be noted and managed.

Table 13: Management in the maintenence phase

- Determining goals
- Re-evaluating/modifying the treatment plan
- · Assessments and monitoring
- · Antipsychotic treatment
- · Psychosocial interventions
- Monitoring for response, side effects and treatment adherence
- Early intervention for relapses

Re-evaluating/modifying the treatment plan: As time elapses the nature of the illness, problems faced by the relatives, needs of the patient and the family and previously determined targets are all expected to change. Regular contact, awareness and monitoring are needed to detect these changes. Ongoing assessment is thus essential. It allows those modifications to be made in the treatment plan, which are required to accommodate any new problems or demands that may have arisen.

Assessments and monitoring: Monitoring is required for assessing response and for side effects that may emerge. Further assessments may be required during this period especially if psychosocial treatments are being planned. Information should be obtained from the patients, family members, and other available sources. Frequency of contact will depend on several factors such as clinical state, the distance of the hospital from the patient's home, social support available for the patient, the type of treatment being administered etc.

Antipsychotic treatment

Dose: The dose of the antipsychotic needs to be individualized. A balance has to be struck between the need to reduce side effects and the need to prevent relapse. Stable patients who do not have positive symptoms may be candidates for reduction in doses. Doses need to be reduced gradually at the rate of about 20% every 6 months till a minimum effective dose is reached.

Reduction of dose/ withdrawal of antipsychotic medication may be be undertaken gradually whilst regularly monitoring signs and symptoms for evidence of potential relapse. Following withdrawal from antipsychotic medication, monitoring for signs and symptoms of potential relapse, need to continue, for at least 2 years after the last acute episode. Any re-emergence of symptoms is to be immediately treated.

Duration of treatment: Duration of treatment depends on a number of factors and will need to be individualized. The suggested guidelines are as follows:

- First-episode patients ought to receive 1-2 years of maintenance treatment
- Patients with several episodes or exacerbations are to receive maintenance treatment for 5 years or longer after the last episode
- Patients with history of aggression or suicide attempts should receive treatment for longer period or lifelong.

The usual indications for use of long term or lifelong antipsychotic medications are shown in table-14.

Psychosocial interventions

The psychosocial interventions started in the previous treatment phases is to be continued and the gains obtained till now should be evaluated. Further, the clinicians should evaluate as to whether any change is required in terms of goals and strategies used.

Table 14: Indications for life long/long term use of antipsychotic medications

History of multiple relapses while on treatment
History of relapses when the medications are tapered off
History of 2 episodes in last 5 years
History of suicidal attempts
Presence of residual psychotic symptoms
Family history of psychosis with poor outcome
Comorbid substance dependence

Rehabilitation

Facilities for vocational rehabilitation are scarce. However, if the patient is already working efforts can be made to help out in any problems at the work place, which could be due to the effects of the illness. If the patient is unemployed, their suitability for work needs to be assessed. If he is ready for work, he is to be encouraged to seek appropriate jobs. However, if the patient requires rehabilitation then culture-specific characteristics for that rehabilitation programme need to be adopted in order to be successful.

Early intervention for relapses

The management plan needs to be organised to respond as quickly as possible to any relapses in the patient's condition. Patients and relatives need to be educated to recognise early symptoms of a relapse. They need to be told about the need for early intervention in impending cases of relapse. They need to have easy access to treatment facilities such as emergency services or inpatient settings, which will cater to the needs of a patient on the verge of a relapse. Contact need to be increased during this phase. Crisis intervention measures such as brief admissions or frequent home visits need to be adopted, whenever feasible. All these are important steps in efficient detection and treatment of relapses.

SPECIAL SITUATIONS

Clinicians often encounter certain clinical situations which either require special attention or can influence treatment decisions. Management of these situations is summarised in table-15.

SIDE EFFECTS AND THIER MANAGEMENT

Antipsychotics are associated with many side effects, which require intervention. Some of the common side effects that can be very distressing to the patients include extrapyramidal side effects, cardiovascular side effects, sexual dysfunction and metabolic side effects. The cardiovascular side effects can be life threatening too. The common management strategies for these side effects are shown in table-16.

Extrapyramidal side effects: Extrapyramidal side effects (EPS) are often noted in patients receiving FGAs, especially high potency antipsychotic medications. However, EPS is

also seen with SGAs. The acute EPS include acute dystonia, pseudo-parkinsonism and akathisia. Acute EPS is usually seen during the first few days or weeks of starting treatment, is dose dependent and subsides with stoppage of offending agent. Chronic EPS is usually seen after prolonged use (months to years) of antipsychotics and these include tardive dyskinesia, tardive dystonia and tardive akathisia. It is important to note that chronic EPS is not dependent on the dose of antipsychotics and persists even after stopping the offending agent. It is important to be aware of the risk factors for development of these side effects (table-17).

In case a patient is experiencing Parkinsonism during the initial phase of treatment, the first step of management involves lowering the dose of the antipsychotic medication. If reduction in dose is associated with unacceptable efficacy than change of antipsychotic medication may be considered. When change of antipsychotic medication is considered, a medication with lower EPS potential need to be opted. In patients who respond to an antipsychotic and continue to experience Parkinsonism, a short course of anticholinergic medications may be considered.

Acute dystonia is also seen during the initial phase of treatment, i.e., after receiving first few doses of antipsychotics. Acute dystonias respond dramatically to administration of parenteral anticholinergic or antihistaminergic medications. Recurrence of acute dystonias can also be prevented by using a short course of anticholinergic medications.

First step in management of acute akathisia involves reduction in dose or changing the antipsychotic to a medication with lower EPS potential. Some patients may require the use of medications like beta-blockers and benzodiazepines like clonazepam or lorazepam for management of akathisia.

Neuroleptic Malignant Syndrome (NMS): It is an acute psychiatric emergency, which has been reported to occur more often with FGAs. However, data in the form of case reports and case series also suggest association of almost all SGAs with development of NMS. Various factors which increase the risk of NMS are shown in table-18. Management involves stopping the antipsychotic medication, supportive measures and use of bromocriptine, amantadine or dantrolene. Use of lorazepam may also be helpful and those patients with NMS, who donot respond to these treatments, may benefit with ECT.

Sedation: Many antipsychotics are known to cause sedation by virtue of their antihista-minergic, antiadrenergic, and anti-dopaminergic action. The risk of sedation is high with chlorpromazine, clozapine and quetiapine. Initial strategy should be to wait and watch and if this is not beneficial, if possible dose reduction must be considered.

C	Table 15: Issues related to special situations			
Special situation	Strategies			
First-episode psychosis and early intervention	 Longer duration of untreated psychosis is powerful predictors of subsequent poor outcome Attempts need to be made to reduce the duration of untreated psychosis, to promote remission through effective pharmacological and psychosocial interventions, to maximize functioning, and to prevent relapse and other adverse outcomes 			
	• Early detection, comprehensive assessment, emphasis on continued engagement, and flexible treatment enable early intervention services to meet these goals			
	 It is still not clear for how long patients with first-episode psychosis are to continue maintenance antipsychotic medication A 1-2 year period is usually recommended, though many patients may require longer periods, and some may require shorter periods of treatment 			
Suicidality in	• Suicide is more common during the initial period after discharge from the hospital			
schizophrenia	 Risk factors which have been specifically associated with suicide among patients with schizophrenia include younger age, high socio-economic status, high premorbid scholastic achievement and high intelligence quotient, high aspirations and expectations, early age of onset, younger age at first hospitalization, a chronic and deteriorating course with multiple relapses and higher level of insight into the illness 			
	• Some of the treatment related issues which have been shown to be associated with suicide include inadequate treatment, poor medication adherence, poor response to treatment and akathisia			
	 As it is not possible to predict suicidal behaviour, clinicians need to pay greater attention to presence of suicidal ideations, which are predictors of suicidal attempt and suicide at every phase of treatment 			
	• High risk management need to be followed during the initial phase of admission and every effort need to be made to retain the patient in the inpatient set-up			
	• Adequate treatment of psychotic symptoms with antipsychotic medication and of depression when present with appropriate therapy can prevent suicide			
	• Clozapine has been shown to reduce the risk for suicidal behaviours. Accordingly, it may be preferred for patients who have multiple suicide attempts or persistently report suicidal ideations.			
	 Psychoeducation of patient and family need to focus on discussing about warning signs of suicide. Patients experiencing severe distress due to a feeling of loss, stigma etc., need to be provided psychological support and monitored closely. 			
Violence and Aggression in	 All patients are to be evaluated for violence and dangerousness during every assessment, especially during the acute phase of illness 			
Schizophrenia	 Whenever a patient is found to have serious threat for violence or exhibits violence, inpatient management is to be considered 			
Comorbid Substance	 Injectable antipsychotics like haloperidol or lorazepam can be used for management of violence and aggression Presence of substance use disorder is often associated with overall poor outcome of illness 			
use Disorders	Clinicians also need to pay attention to these disorders and the additional aims of the treatment are abstinence from the substances or at least harm reduction			
	Pharmacological agents shown to be effective for management of detoxification and pharmaco-prophylaxis for different substance use disorders may be considered if required			
	 Psychosocial interventions like relapse prevention counselling, cognitive behavioural interventions and motivation enhancement treatment may be included in the treatment plan 			
	Patients are to be continuously monitored for relapse of substance use disorder			
Depression	 A rational approach to treating depression in schizophrenia first needs to consider and rule out organic conditions, negative symptoms, antipsychotic associated side effects (dysphoria, akinesia and akathisia), schizoaffective depression, stress-related reactions, and an impending psychotic episode 			
	 Controlled trials with SGAs have shown that they are superior to FGAs in their antidepressant efficacy. Clozapine may be particularly effective in patients at high risk for suicide 			
	Antidepressants are generally ineffective during the acute phase. They may even worsen the psychosis, and are best avoided			
	• On the other hand, results of controlled trials have demonstrated the efficacy of adjunctive antidepressant therapy in post-psychotic depression			
a •	Clinical experience suggests that ECT may be helpful			
Catatonia	 Whenever a patient with schizophrenia presents with catatonia, all possible differential diagnosis for catatonia is to be considered. Appropriate investigations may be carried out and the underlying causes are to be managed Initial management may involve use of benzodiazepines, especially lorazepam, which leads to symptomatic relief in 			
	significant proportion of cases • In case the catatonia does not respond to benzodiazepines or relapse after stopping benzodiazepines, ECT is to be			
Negative symptoms	considered • First step in management of predominant negative symptoms is to rule out secondary negative symptoms. However, if			
	negative symptoms persist, they are presumed to be primary negative symptoms of the deficit state • No treatments have proven efficacy for management of primary negative symptoms, although some benefit has been reported			
	with clozapine and amisulpride • Psychosocial interventions in the form of social skill training, token economy may be attempted			

Contd...

	Table 15: Contd
Special situation	Strategies
Obsessive	Obsessive compulsive disorder/Obsessive compulsive symptoms are common in patients with schizophrenia and these may
compulsive	be part of the prodrome of schizophrenia, may be part of clinical manifestation of schizophrenia along with other symptoms
symptoms in	may be treatment emergent or may precede the onset of schizophrenia
schizophrenia	• Treatment emergent obsessive compulsive symptoms are commonly reported with SGAs like clozapine, olanzapine and
	risperidone
	• There is little evidence in the form of randomized controlled trials for management of obsessive compulsive symptoms in
	schizophrenia
	• In general it is suggested that if the obsessive compulsive symptoms appear to be part and parcel of schizophrenia, initially
	patients may be treated with antipsychotics only and the obsessive compulsive symptoms need to be monitored
	• If the obsessive compulsive symptoms are considered to be treatment emergent then reduction in dose of antipsychotic,
	change of antipsychotic or use of antiobsessional agents are to be considered
	 Among the antiobsessional agents, there is some data for the efficacy of clomipramine and fluvoxamine Cognitive behaviour therapy in the form of exposure and response prevention has also been tried with beneficial effects
Comorbid Physical	• Patients with schizophrenia have high rate of physical illnesses
illnesses	• All patients need to receive thorough assessment for possible physical illnesses and depending on the feasibility may be
micsscs	investigated as per the requirement
	Those with comorbid physical illnesses need to be continuously monitored during all the phases of treatment
	• Comorbid physical illnesses and concomitant medications need to be taken into account while selecting the treatment setting
	and antipsychotic medication per se
Treatment-resistance	• The first step in the management of treatment-resistance is to establish that the disorder has failed to respond to adequate
schizophrenia (TRS)	trials of antipsychotics in terms of dosage, duration and adherence
	• Other causes of non-response need to be considered such as, non-compliance, adverse effects, comorbid conditions such as
	substance misuse, before actually diagnosing treatment refractoriness
	• Clozapine has been reported to be beneficial among patients with TRS
	• The role of ECT in TRS has not been examined, although studies suggest that it could be useful
	• Chosocial interventions such as cognitive therapy, family treatment, assertive outreach or crisis intervention are also
Claration .	beneficial.
Clozapine – resistance	 There is some evidence to suggest that combining ECT with clozapine improves the outcome of patients who do not respond to clozapine alone
Tesistance	• Evidence for usefulness of combining clozapine with other antipsychotics, antidepressants, mood stabilizers is limited and
	not convincing
Difficult to treat	• Factors which make the patient difficult to treat include: inadequate response to antipsychotic, problems of adverse drug
schizophrenia	effects, poor medication compliance, comorbidities, treatment failure and relapse on adequate drug dosages
· · · · · · · · · · · · · · · · · · ·	• Issues related to medication compliance and adverse effects need to be addressed
	• Antipsychotic need to be selected keeping the medical and psychiatric comorbidities in mind
	• Patients with treatment resistance may be treated with clozapine.
	• Patients having relapse of symptoms despite adequate dosages of 2 or more antipsychotics may also be treated with clozapine
	 Psychosocial factors influencing medication compliance need to be evaluated and addressed
Pregnancy	• Many patients with schizophrenia have unplanned pregnancies and because of illness related variables, compared to those
	without schizophrenia, women with schizophrenia more commonly have pregnancy outcomes in the form of low birth
	weight, preterm birth, still birth and perinatal deaths
	• Patients and caregivers need to be counselled about pregnancy and the risks and unplanned pregnancies may be avoided
	• Most of the psychotropics belong to category 'C' or 'D', except for clozapine
	• In general it is said that high potency antipsychotics have lower risk of foetal malformations
	• Any decision to start antipsychotics, continue or discontinue antipsychotics need to take into account current level of
	symptomatology, longitudinal course of symptoms, risk of relapse with stoppage of medication, effect of a particular
	antipsychotic on foetal malformation and obstetrical complications • All decisions about medications are to be taken after proper consultation with the patient, spouse and caregivers. A close
	• All decisions about medications are to be taken after proper consultation with the patient, spouse and caregivers. A close liaison with the obstetricians is helpful in monitoring patients during the pregnancy
	nation with the observations is neighbor in morntoning puterits during the pregnancy

Anticholinergic and antiadrenergic side effects: These side effects manifest as dry mouth, blurred vision, constipation, urinary retention, thermoregulatory effects, impaired learning and memory and slowed cognition. Some patient may develop confusion, delirium, somnolence and hallucinations due to severe anticholinergic side effects. Anticholinergic side effects are more commonly seen with clozapine and chlorpromazine. It is reported that the anticholinergic side effects are usually dose-dependent and reduce with reduction in the dose of antipsychotic or concomitantly used anticholinergic agent.

Cardiovascular side effects: Among the cardiac side effects, the commonly encountered side effects include QTc prolongation, orthostatic hypotension and tachycardia. QTc interval of more than 500 milliseconds is associated with elevated risk of ventricular arrhythmias, known as "torsades de pointes", which may lead to ventricular fibrillation and sudden cardiac death. Among the older antipsychotics, thioridazine, pimozide and high dose of intravenous haloperidol are reported to be associated with increased risk of QTc prolongation. Among the SGAs, ziprasidone is reported to have higher risk of QTc prolongation; however, this has not been shown to be

	Table 16: Management of Side Effect	
Side effect	First Step	Other options
Antipsychotic induced Parkinsonism	Reduce the dose	Change the antipsychotic to an antipsychotic with lower EPS potential
Acute dystonia	Parenteral - anticholinergic or antihistaminergic medications	Short term use of anticholinergics to prevent recurrence
Acute Akathisia	Reduce the dose	Change the antipsychotic to an antipsychotic with lower EPS potential
		Use- beta-blockers, benzodiazepines
Tardive dyskinesia	Stop the offending agent	Clozapine in case there is worsening of psychosis Vitamin-E, benzodiazepines, anticholinergics
Tardive dystonia	Stop the offending agent	Clozapine in case there is worsening of psychosis
Neuroleptic malignant syndrome	Stop the offending agent Supportive measures	In treatment refractory NMS consider ECT
	Bromocriptine, amantadine, dantrolene Lorazepam	
QTc prolongation	Reduce the dose	Stop the offending agent Change the antipsychotic to an antipsychotic with lower potential for QTc prolongation
Orthostatic hypotension	Reduce the dose	Stop the offending agent Change to an antipsychotic with lower antiadrenergic or no antiadrenergic activity Use of stockings, increasing the salt intake, fludrocortisone
Tachycardia due to anticholinergic action	Wait and watch for sometime in those without cardiac disease	Peripherally acting beta-blockers
Hyperprolactinemia and Sexual dysfunction	Reduce the dose	Change to an antipsychotic with lower potential to cause hyper-prolactinemia Consider use of bromocriptine or amantidine if there is hyperprolactinemia Sexual dysfunction not associated with hyperprolactinemia- Yohimbine, Cyproheptadine, Imipramine (for retrograde ejaculation), Phospho-diaesterase inhibitors (for erectile dysfunction), antidepressants like paroxetine, dapoxetine (for premature ejaculation)
Sedation	Wait and watch – most patients develop tolerance	In case of persistent sedation Reduce the dose Change to night time dose, if using the medication in divided doses Change to a less sedating agent
Anticholinergic and antiadrenergic side effects	Stop concommitant anticholinergic agent if used Reduce the dose In case of severe side effect like delirium stoppage of offending agent may be required	Change to an antipsychotic with lower anticholinergic properties Constipation- high fibre diet, increase water intake, laxatives

associated with sudden cardiac deaths. In case, there is QTc prolongation, change of antipsychotic is to be considered.

Hypotension associated with various antipsychotics is attributed to antiadrenergic activity. It is commonly seen with clozapine, risperidone, quetiapine. Among the FGAs, hypotension is often seen with chlorpromazine. Hypotension can be prevented by starting with lower doses and slow upward titration of medication. When a patient develops hypotension with a particular antipsychotic medication, the first step in management is to reduce the dose of the offending agent. If this does not help than switching to another agent with lower antiadrenergic activity is to be considered. Additional management strategies include use of stockings, increasing the salt intake and use of fludrocortisone, which is a fluid retaining corticosteroid.

Tachycardia may be associated with hypotension or it may result due to anticholinergic activity. Tachycardia due to anticholinergic activity, as seen with clozapine may be managed with low dose peripherally acting beta-blockers.

Hyperprolactinemia and Sexual dysfunction: All antipsychotics are shown to be associated with sexual dysfunction, although the rates vary with different antipsychotics. In general, rates of sexual dysfunction are reported to be higher with FGAs and risperidone. One of the common causes for sexual dysfunction with FGAs and risperidone is increase in prolactin levels, which leads to disruption of hypothalamo-pituitary-gonadal axis. Females have been reported to be more sensitive to hyperprolactinemia related sexual dysfunction. First step in management of hyperprolactinemia and sexual dysfunction is reduction in the dose of antipsychotic medication. If this option is not acceptable, change in antipsychotic is to be considered. If change of antipsychotic is not possible, than management with bromocriptine or amantidine may be considered to lower the prolactin levels.

Table 17: Risk factors for acute and tardive extrapyramidal side effects with antipsychotics

Acute Dystonia

Use of high potency FGAs

Young age

Male gender

High doses

Intramuscular administration of antipsychotic medications

Acute Akathisia

Use of high potency FGAs

Tardive dyskinesia

Older age

Female gender combined with postmenopausal status

Use of FGAs

Use of high doses of antipsychotic medications

Antipsychotic-induced parkinsonism

Concurrent general medical conditions like diabetes

Affective disorder (particularly major depressive disorder)

Tardive dystonia

Use of high potency FGAs

Neuroleptic Malignant syndrome

Young age

Male gender

Use of high potency antipsychotic

Rapid increase in the dose of antipsychotic

Use of intramuscular preparation

Acute agitation

Preexisting neurological disability

Comorbid physical illness

Dehydration

Table 18: Risk of Metabolic side effects associated with various antipsychotic medications⁶

Antipsychotic medications	Risk of lipid and/or glucose metabolism abnormalities	Risk of weight gain
FGAs		
Chlorpromazine	High (limited data)	Substantial
Fluphenazine	Low (limited data)	Neutral/low
Haloperidol, Perphenazine	Low	Neutral/low
Thioridazine	High (limited data)	Intermediate
SGAs		
Clozapine, Olanzapine	High	Substantial
Quetiapine	Moderate	Intermediate
Risperidone, Iloperidone,	Mild	Intermediate
Paliperidone, Sertindole		
Lurasidone	Low (limited data)	Intermediate
Zotepine	Not reported	Intermediate
Asenapine	Low (limited data)	Low
Amisulpride	Mild	Neutral/low
Ziprasidone, Aripiprazole	Low	Neutral/low

Monitoring for metabolic side effects: It is now well known that compared to subjects in the general population, patients with schizophrenia have high rates of metabolic syndrome. Higher prevalence of metabolic syndrome suggests that clinicians need to monitor the patients for emergence of metabolic side effects and manage the same to reduce the cardiovascular morbidity and mortality. Antipsychotics have also been shown to increase the risk of development of diabetes mellitus. Further evidence suggests that there is some discriminatory effect of various antipsychotic medications on metabolic profile. Clozapine and olanzapine have been reported to be associated with highest risk for development of weight gain, lipid abnormalities and elevation in blood glucose levels (See table-18).

Considering the metabolic side effects associated with antipsychotics, various guidelines have been proposed and there are certain variations in the proposed monitoring frequency. In general it is suggested that patients need to be monitored for metabolic disturbances at baseline, at 4-6 weeks and 12 weeks after starting antipsychotic and then after every 3 months or at least annually (table-19). However, those who have personal and family history of obesity, diabetes mellitus, dyslipidemia, hypertension and/or cardiovascular disease are to be monitored 3 monthly.

However, in Indian setting, due to poor follow-up rates and available resources, it may not be feasible to monitor all the parameters regularly. Efforts need to be made to monitor the weight and fasting blood glucose levels at every treatment facility. Patients managed at training centres and resourceful settings may consider complete monitoring of metabolic parameters.

If a patient develops metabolic abnormalities, switching of antipsychotic may be considered. In general if a patient gains more than 7% of the baseline weight or develops hyperglycemia, hyperlipidemia, hypertension or any other significant cardiovascular or metabolic side effect, then a change in antipsychotic is to be considered. However, while considering switching, clinicians need to take into consideration the entire course of the illness, comorbid physical illnesses, side effect profile of medication which

	Baseline	6 weeks after starting antipsychotics	12 weeks after starting antipsychotics	Atleast annually thereafter
Medical History	X	1 0		
Weight/waist circumference/BMI	X	X	X	X
Blood Pressure	X	X	X	X
Fasting glucose levels	X	X	X	X
Fasting lipids	X	X	X	X
Lifestyle modification advise	X	X	X	X

caused metabolic side effects and the potential side effects with proposed medication to be used after switching. If switching of antipsychotic is not possible then medications like metformin or topiramate may be considered, along with more intensive dietary and life style modifications. A close liaison need to be maintained with endocrinologist and cardiologist to provide best quality care to patients.

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