ABSTRACT

Introduction of potent antipsychotics for the treatment of schizophrenia not only brought changes in the outlook for management of this disorder but also infused optimism and hope. However, substantial number of patients fail to respond to conventional antipsychotics thus creating a class of patients who are termed as treatment resistant, treatment refractory or difficult to treat patients. This update focuses on such patients and provides description of various options for their management. Though atypical antipsychotics offer respite to a vast number of such difficult to treat patients, their efficacy is perhaps over-emphasised. Conversely, the potential of psycho-social therapies in such patients has not been fully exploited. Management of such patients in the community is a challenge and in taking up this gauntlet, a judicious mix of pharmacotherapy and psychosocial intervention strategies, close monitoring of the patients with a view to detect prodromes of relapse and early intervention are likely to play increasingly important part.

Key Words: Schizophrenia, management, psycho-social, psychopharmacology

The Kraepelinian-Bleulerian concept of schizophrenia which so heavily dominated psychiatric thinking viewed this disorder as a chronic and progressively debilitating condition. Both Kraepelin and Bleuler believed that in this condition, restitution to premorbid level of functioning was not possible. However, despite evidence to the contrary, somehow, chronicity implying poor prognosis and outcome became an integral part of criteria for the diagnosis of schizophrenia. "Six month duration of illness", an essential feature of diagnostic guideline for the diagnosis of schizophrenia of the American Psychiatric Association is a reflection of extension of this concept in contemporary psychiatry.

In the light of the above mentioned perspective, the management of schizophrenia was considered difficult. Reviews by Bleuler (1978) and Ciompi (1980) showed that treatment offered to the patients did not have substantial impact and a sizeable number of patients became chronic. A general consensus emerged that roughly one third of the patients recovered, one third became chronic and the remainder followed an in between course. Introduction of chlorpromazine in the 50’s and later of haloperidol and pimozide ushered in an era of psychopharmacology which brought optimism. Even then it soon became apparent that many patients did not derive any benefit from such treatment and thus were resistant or refractory to treatment.

Schizophrenia patients who are treatment resistant or refractory to treat have now become focus of intense research activity particularly from psychopharmacology point of view. However, in the context of the conceptual thinking about this disorder in which chronicity is either implicit or explicit, the notions of resistance to treatment or refractoriness to treatment become difficult to understand. Thus, designating such patients as “difficult to treat” may be more appropriate, less emotive and a
shade less controversial. This paper focuses on issues pertaining to the management of difficult to treat patients and takes a look at various options available to help such patients.

Difficult to treat patients

The term difficult to treat schizophrenia patient is broad and includes not only the so-called resistant or refractory patients, but also those patients who for some reasons fail to show desired response to therapy be it drug therapy, psycho-social therapies or a combination of the two. Difficult to treat patients also includes those patients who may be non-compliant, aggressive and violent. Difficult to treat patients may also mean those patients who for some reason evoke negative responses from caregivers including mental health professionals. In this article, the terms difficult to treat, resistant to treat and refractory to treatment would be interchangeably used.

In order to formulate an effective management strategy for such difficult patients, it is essential to have some criteria for calling a patient as treatment resistant or refractory. It is generally agreed that treatment refractoriness refers to assessment of response to conventional drug therapy in a given patient. It is also generally agreed that treatment refractoriness implies that correctly diagnosed patients had been given a fair trial of different classes of antipsychotics by different routes in adequate doses and for adequate length of time and, that despite these the patients failed to show the desired response.

Herein lies the first difficulty. There is a need to have consensus on how to define varying degrees of response to treatment in individual patients. Response to treatment in schizophrenia patients is not a single dimension but has various facets. Clinical outcome, psychosocial outcome, work outcome and satisfactory attainment of the goals of specific therapies or programmes are some of the areas, diverse in nature, which reflect response to treatment. Thus, when discussing refractoriness to treatment, one has to define the frame of reference and also operationalise criteria for categorising response. Consensus about adequacy of dose and duration of treatment is also needed.

Factors which make patients difficult to treat

Many factors make a patient difficult to treat. Some of the major factors are as follows:
1. Inadequate response to conventional antipsychotics.
2. Problems of adverse drug effects.
3. Problems of compliance.
4. Problems of comorbid conditions and
5. Treatment failure-relapse on adequate drug dosage.

1. Inadequate response to conventional antipsychotics: After the introduction of chlorpromazine as an antipsychotic, many other such agents made their way. In a well-conducted trial, Cole et al. (1966) showed that nearly 70% of the study subjects had substantial improvement on antipsychotic medication. Since then it was generally believed that drug therapy had powerful impact on the patients though factors predicting response to pharmacotherapy were not delineated with any degree of confidence. More recent drug trials, however, do not support the view that antipsychotics are as beneficial as was suggested by earlier investigations. It is now generally held that no more than 50% of the patients of schizophrenia derive marked benefit from these medications (Von Putten et al., 1990; Rifkin et al., 1991; McEvoy et al., 1991). The reasons for this apparent change are not clear though changes in nosology, stringent and operationalised criteria for diagnosis of schizophrenia, thorough patient selection for controlled drug trials as well as assessments of response, changes in criteria for hospitalisation and discharge from in-patient care, the potential role of concomitant substance abuse and other comorbid conditions e.g. depression in diminishing effectiveness of
drug therapy are cited as reasons for this change.

In the above context, it is difficult to accurately estimate prevalence of difficult to treat patients. One approach that has been frequently used for such estimates is to survey populations of schizophrenia patients and ascertain the number of patients who would meet eligibility criteria for clozapine therapy. Many studies are now available in which this approach has been adopted (Terkelsen and Grosser, 1990; Essock et al., 1996). The estimates of poor or non responders to conventional drug therapy as reported by these surveys are not uniform and vary from a low of 18% for in-patients to a high of 60% for the same patients population. It is also reported that these patients do not differ much on symptomatology from those who have responded better to drug therapy (Kane et al., 1988, 1995; Liberman et al., 1991; Breier et al., 1994). However, there is evidence to suggest that patients who have abnormalities on brain imaging, soft neurological signs or poor premorbid social adjustment tend to respond poorly to conventional drug therapy (Weinberger et al., 1980; Pandurang et al., 1989; Vita et al., 1991; Liberman et al., 1992, 1993a,b; DeLisi et al., 1992). It has also been shown that presence of antisocial and violent behaviour, irritability and aggression in patient makes him more difficult to treat (Remington et al., 1993; Honigfield et al., 1996).

3. Problems of compliance: One of the most frequent reasons for relapse and rehospitalisation in patients of schizophrenia is noncompliance. For a variety of reasons patients come off antipsychotics—some because of distress of side-effects, some because of lack of insight whilst still psychotic, some because of the conviction that as they have been well for some time they do not need medicines and some because of mistaken notion that they are not vulnerable to relapse. Often lack of adequate information about the nature of the illness, poor awareness of the need to continue with medicines despite being well and barren preparation of the patients to cope with distressing side-effects are the main reasons contributing to noncompliance. The net result of noncompliance in majority of cases is a difficult to treat patient because such patient becomes chronic, has relapses and repeated hospitalisation. Rates of noncompliance are difficult to ascertain, however, as many as 30% of the patients become noncompliant in the first year of treatment (Kane, 1985) and this figure may perhaps be higher for our country because of added reasons of financial constraints on the part of patients and poor accessibility of psychiatric services.

4. Problems of comorbid conditions: It is now increasingly becoming obvious, particularly in
the West, that a sizeable number of schizophrenia patients abuse drugs such as alcohol and cocaine. Many surveys of schizophrenia patient populations put these figure to range from 47% to 58% for substance abuse and 17% to 27% for cocaine abuse (Galanter et al., 1988; Regier et al., 1990; Shaner et al., 1993). Substance abuse is known to aggravate symptoms of the disease and also makes prognosis poorer. Substance abuse contributes to poor drug compliance and makes the patients more vulnerable to become homeless (Drake et al., 1991). Concurrent use of substances like amphetamines, cocaine and alcohol tend to make patients more aggressive and antisocial in addition to worsening of the symptoms (Yesavage & Zarcone, 1993).

Depression, anxiety, panic and obsessive compulsive phenomena and disorders frequently accompany schizophrenia. These comorbid psychiatric disorders confound diagnostic and treatment issues. But for post-psychotic depression, other conditions have not been that well researched. In our country, the exact extent of comorbid conditions, particularly drug abuse, is not known but its occurrence cannot be denied though it is probably not as high as that seen in the USA.

5. Treatment failure-relapse on adequate drug dosage: There are many patients who despite adequate maintenance therapy and seemingly good compliance relapse or have exacerbation of symptoms. This has been shown in numerous long-term trials of maintenance therapy in schizophrenia. These patients are not necessarily treatment defaulters but for reasons which have still not been elucidated do have relapses. There is no evidence to suggest that these patients who relapse on maintenance therapy have any special clinical, socio-demographic or treatment characteristics which make them more prone to relapse. Management guidelines for such patients who are likely to become difficult to treat are not available.

The above mentioned factors make it obvious that many reasons contribute towards a patient becoming difficult to treat and that in times to come this would become a challenging problem which needs to be contained.

Strategies for managing difficult to treat patients

The strategies which are employed to deal with difficult to treat patients can be broadly grouped as follows:

1. Strategies pertaining to classical neuroleptics,
2. Use of atypical antipsychotics and
3. Psychosocial management strategies.

1. Strategies pertaining to classical neuroleptics: Since drug noncompliance is often the major reason for a patient to become a difficult to treat subject, as a first step efforts should be made to increase compliance. This can be achieved by educating the family and the patient about the virtues of taking medicines regularly and in prescribed doses. This approach does pay dividends many times. Next, the compliance and monitoring of the patient can be improved by putting him/her on a long acting depot preparation. If the patient does not take medicines because of real and distressing side effects, then, these should be alleviated by appropriate therapeutic measures. Also, the dose of medicines should be very carefully titrated so that the lowest effective dose is taken by the patient and thus side-effects are minimised and compliance optimised.

Psychiatrists often consider increasing the dose of conventional antipsychotics when the patient does not show the desired favourable response. Some advocate the use of megadoses of antipsychotics. However, there is no strong evidence to suggest that prescription of such megadoses to patients who are otherwise non responsive to standard doses is beneficial. On the contrary many professionals believe that megadoses of neuroleptics may cause side effects and point out that cardiotoxicity related to megadoses is a dangerous situation. It has been shown that systematic reduction of dose of antipsychotics from a high level is often beneficial in
treatment resistant cases as such an approach has been shown to reduce both the symptoms and side-effects (Von Putten et al., 1993).

It is a common clinical practice to prescribe combinations of more than one antipsychotics to a patient. The consensus view of the professionals is that this practice is hazardous and undesirable. The Royal College of Psychiatrists does not recommend use of combination of neuroleptics as a routine and suggests that it should be used in a very few selected cases where the treating psychiatrist utilises years of experience dealing with the patient to prescribe him a combination.

When the above mentioned strategies do not pay dividends and when there is clinical evidence to suggest that the patient has depression, anxiety, episodicity or violence, then use of adjuncts such as antidepressants, lithium, carbamazepine, ECT and benzodiazepines is advocated.

Though at times it is difficult to differentiate between clinical manifestations of depression and negative symptoms in schizophrenia, yet clinical experience suggests that many patients when given the benefit of doubt and are prescribed antidepressants, they improve. It has also been shown that antidepressants are especially helpful in post schizophrenic depression (Meltzer, 1992).

Lithium has often been used as an adjunct in the management of treatment resistant schizophrenia cases. Many studies testify to effectiveness of lithium in reducing psychotic symptoms in patients who only partly respond to classical neuroleptics. However, when combining lithium with haloperidol, caution should be exercised as irreversible toxicity is known to occur especially if the patients is on high doses of haloperidol.

In schizophrenia patients who have EEG abnormalities or episodes of violence and manic symptoms, addition of carbamazepine may be helpful. Because of risk of neutropenia which is likely to be aggravated, carbamazepine should not be combined with clozapine.

ECT has been shown to be of some value in treatment resistant cases. However, the response to ECT is often transient. The role of maintenance ECT in resistant cases is debatable but many clinicians believe that in resistant cases maintenance ECT is necessary to maximise therapeutic benefit to the patient. Addition of benzodiazepines to neuroleptics helps in reducing psychotic agitation as well extra pyramidal symptoms. Some researchers believe that benzodiazepines also improve hallucinations, delusions, thought disorders and social withdrawal.

2. Atypical antipsychotics: There are many antipsychotics which are termed as “atypical” because of their chemical structure, unique affinity for neuroreceptors, effect on prolactin levels, capacity to induce catalepsy in experimental animals and property of causing less EPS. Sulpiride, clozapine and risperidone are well known and well established atypical antipsychotics. In addition, olanzapine, sertraline and sertindole are establishing themselves as newer antipsychotics. All of these have been shown to be useful in the management of schizophrenia.

a. Sulpiride: Sulpiride is a benzamide. In various clinical trials it has been shown to have efficacy equivalent to haloperidol. However, it has fewer side effects. Sulpiride in low doses is beneficial in treating negative symptoms and because it causes less EPS, it is notably helpful in those patients who are sensitive and prone to develop extra pyramidal symptoms (Farmer & Blewett, 1993).

b. Clozapine: Introduced in 70s, clozapine was observed to be a potent antipsychotic, but its tendency to cause agranulocytosis led to its downfall. The multicentre Clozaril Collaborative Project with its improved system of monitoring and early detection of agranulocytosis showed that clozapine was significantly more effective than chlorpromazine in a group of patients who had earlier shown poor response to classical neuroleptics (Kane et al., 1988). This drug trial
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made it possible to explore the role of clozapine in treatment resistant cases on a wider scale and it soon became apparent that this drug had efficacy against negative symptoms (Farmer & Blewett, 1993).

Over the years it has been shown that clozapine has clear advantage over other currently available drugs with regard to management of severely ill but resistant to treat patients (Marder & Van Putten, 1988; Kane, 1992). It is now well established that 30% to 60% of treatment refractory patients derive substantial benefit from prolonged therapy with clozapine. It is also well documented that clozapine exerts its beneficial effects in both positive and negative symptoms (Kane et al., 1988). Clozapine has less adverse effects on cognitive and psychomotor functions, does not cause acute EPS, has lower rates of induced tardive dyskinesia and improves quality of life (Kane et al., 1988; Lindstrom, 1988; Meltzer et al., 1990; Piker et al., 1992; Lader, 1994). Thus, the following categories of schizophrenia patients should receive clozapine:

1. Treatment refractory patients.
2. Patients with prominent negative symptoms not responding to conventional psychopharmacology.
3. Patients who are sensitive to classical neuroleptics in terms of developing EPS chiefly akathisia or dyskinesia.

Risk of neutropenia and agranulocytosis are the main limitations to the use of clozapine and because of these risks close haematological monitoring of the patients is necessary. Epidemiological surveys of patients on clozapine indicate that about 1% of patients receiving clozapine develop agranulocytosis and that nearly 95% of such agranulocytosis develops within the first 20 weeks of treatment and the risk falls markedly after the first year of treatment. It is also noted that older patients i.e. patients 50 years and above are substantially more at risk of developing agranulocytosis. Females are more prone to develop agranulocytosis than males. It should also be remembered that the side effect of agranulocytosis is not dose dependent (Alvir et al., 1993; Atkin, 1994). Production of seizures is another distressing and dramatic side-effect of clozapine. About 1% to 5% of patients on clozapine may develop seizures and this side-effect is a dose-related occurrence.

All in all, the introduction of clozapine, its low side-effect profile and cost-effectiveness has brought about considerable change in the outlook about the treatment of refractory patients. Close haematological monitoring and effective control of seizures have enhanced acceptance of clozapine by the patients. Though data pertaining to symptomatic improvement with clozapine are quite impressive, psychiatrists have also become aware of general improvement in quality of life of patients on clozapine (Green, 1996).

c.Risperidone: Risperidone, a benzisoxazole derivative, has high affinity for both dopaminergic and serotonergic receptors. It has been shown to be superior than conventional antipsychotic and exerts beneficial effects on both positive and negative symptoms yet has low propensity for producing EPS (Ereshefsky, 1993; Chouinard & Arnott, 1993). In a Canadian Multicentre placebo controlled double blind trial, the antipsychotic activity and side-effect profile of risperidone was compared with haloperidol and placebo. A total of 135 patients of chronic schizophrenia diagnosed according to DSM-III-R criteria participated in the study. At the end of 8 week trial, risperidone was shown to be superior both in clinical efficacy as well as in side-effect profile in comparison to haloperidol (Chouinard et al., 1993). Marder and Meibach (1994) conducted a multi-site double blind controlled study to investigate the safety and efficacy of risperidone. Another objective of their investigation was to determine the optimal dose of risperidone. A total of 388 patients entered the trial. Patients were randomly assigned to 8 week’s treatment with placebo, one of the four doses of risperidone (2, 6, 10 or 16 mg/day) or
20 mg haloperidol per day. It was shown that the optimal daily dose for most schizophrenia patients was 6 mg/day and that risperidone was superior to placebo or haloperidol in clinical efficacy. More and more research evidence shows that risperidone is a potent compound in alleviating positive and negative symptoms which has low incidence of side-effects, as good as clozapine and effective in the long terms as well (Heinrich et al., 1994; Kliesser et al., 1995; Lindstrom et al., 1995). Thus, risperidone is an important agent in the management of refractory patients where negative symptoms or side-effects are vital considerations. Moreover, as this drug does not have serious side effects like neutropenia and seizures and as no regular blood monitoring is required, risperidone would appear to be a worthy alternative to clozapine in the management of treatment refractory schizophrenia.

3. Psychosocial management strategies: It is now increasingly recognised that the notion of refractoriness to treatment in schizophrenia is not merely restricted to effectiveness of drugs in alleviating positive or negative symptoms but it also encompasses consideration of psychosocial functioning of the patient. There are many patients who despite remarkable symptomatic (positive and negative symptoms) improvement continue to have cognitive, behavioural (e.g. disruptive behaviour, aggression etc.) or social difficulties that make it difficult for them to achieve independent community living, desired degree of psychosocial rehabilitation or social reintegration. Wykes & Carson (1896) regard violence, expressed emotions, life events, homelessness and cognitive deficits as possible psychosocial toxic factors in schizophrenia patients that have implications for rehabilitation and community care. Psychosocial interventions are now regarded as essential and integral part of management of schizophrenia and not just luxury or worthy extras (Kane & McGlashen, 1995).

Psychosocial interventions focus on two types of dysfunctions that the patients have - i) specific to schizophrenia (e.g. coping with distressing hallucinations and delusions) and ii) dysfunctions which are common to many chronic and debilitating disorders (e.g. living in the family) but are complicated by core features of schizophrenia.

Psychosocial intervention strategies can be broadly grouped under three heads:
1. Individual patient interventions
2. Family interventions and
3. Community based interventions.

1. Individual Patient Interventions

a. Enhancement of compliance: One of the major reasons for treatment resistant is noncompliance on the part of the patients. There are multiple reasons for noncompliance and attention needs to be given to all these reasons to enhance compliance.

At times patients and their caregivers do not fully understand the importance of drug therapy. In such situations and perhaps as a routine in treatment resistant cases, educating the patients and their significant key relatives about the nature of the illness, the nature of the treatment, the importance of regular intake of medicines, adherence to maintenance therapy and reaming in regular follow-up improve compliance.

Presence of side-effects or apprehensions of developing side-effects are also possible reasons for noncompliance. Here, all efforts should be made to minimise, if total elimination is not possible, side-effects by titration of dose or addition of medicines to counteract side-effects. Demonstration that side-effects can be minimised or improved, may result in better compliance.

Denial of illness and lack of insight often lead to patients not taking medicines or giving them up. In such a situation cognitive behavioural therapy may be of help. Cognitive behavioural therapy helps the patients in reattributing their illness from a delusional explanation to a medical/illness explanation.
where taking treatment and medicines becomes more meaningful and practical. Another factor which plays an important part in enhancing compliance is the nature and quality of the relationship between the mental health professional and the patient. The chances of patient remaining compliant are greater in a trusting doctor-patient relationship environment.

In our culture where remedial measures other than medical treatment are often sought for the patient, the issue of compliance assumes larger meaning. At times the caregivers take patients off medicines to seek magico-religious and other forms of non-medical treatments such as ayurvedic, homeopathic etc. In such a situation, educating the caregivers about the virtues of medical treatment with a view to have the patient in the follow-up net is an urgent and rewarding task.

Studies have shown compliance enhancing effects of counselling and psychoeducation to the patients and family members. Kemp et al. (1996) have recently shown promising results of their method of "motivational interviewing" in enhancing compliance.

b. Psychotherapies: Cognitive Behavioural Therapy (CBT):

Many researchers have developed treatment approaches based on general principals of cognitive behaviour therapy. According to Kuipers (1996) CBT has the following main goals:

1) To reduce the distress and interference that arises from the experience of persistent psychotic symptoms such as delusions and hallucinations.
2) To increase the individual's understanding of psychotic disorders and to foster motivation to engage in self-regulation behaviour.
3) To reduce the occurrence of dysfunctional emotions and self-defeating behaviour arising from feelings of hopelessness, negative self-image or perceived psychological threat.

In recent years, CBT has emerged to be beneficial in a variety of contexts in schizophrenia ranging from promotion of insight (Kingdon & Turkington, 1991), modifications of hallucinations and delusions (Fowler et al., 1995; Chadwick et al., 1996; Haddock & Slade, 1996; Chadwick & Birchwood, 1994; Kingdon et al., 1994; Persaud & Marks, 1995; Kuipers et al., 1997; Garety et al., 1997). The CBT techniques used in dealing with drug resistant hallucinations in schizophrenia patients include pragmatic and practical suggestions, use of ear plugs or diversional activities such as listening to music (Nelson et al., 1991; Fowler et al., 1995; Nelson, 1995). In a randomised controlled trial, Kuipers et al. (1997) and Garety et al. (1997) have shown that individual CBT on a weekly or fortnightly basis was effective in reducing distressing impact of psychotic symptoms and helped in improving mood and engagement in activities. It was also shown that good outcome is strongly predicted in patients with persistent delusions by cognitive measures. Garety et al. (1997) identified cognitive flexibility and number of recent hospital admissions as predictors of good outcome in patients receiving CBT.

Subsumed under the broad label of CBT are various approaches targeted at all or any of the goals as mentioned above by Kuipers (1996). Cognitive coping behavioural strategies attempt to equip the clients and their caregivers with adaptive ways of dealing with distress due to psychotic symptoms. Relabelling and psychoeducation strategies help the individual patient to relabel psychotic experiences such that the patient is able to accept that the experiences that he has are not unique to him alone but occur to other patients. Some work has been done in evolving techniques for modification of delusional beliefs by Shapiro & Ravenette (1959), Watts et al. (1973) and Chadwick & Lowe (1990). Other strategies that are being developed are the techniques of CBT that help to reduce or modify dysfunctional assumptions on the part of the patients and their caregivers. However, these are innovative research ideas and not a great
deal of data about their efficacy are available.

2. Family Interventions: Psycho-educational intervention with families of schizophrenia patients has a well-established literature. Family-based interventions focus on information, communication, support and problem solving with a view to ward off relapse. Pioneering work by Vaughn & Leff (1976, 1981) clearly showed that the patients' survival outside the hospital without relapse was closely related to attitudes and behaviour of the family members towards the patient. Anderson (1983), Falloon et al. (1982) and Falloon & Shanahan (1990) showed that behavioural family management was effective in reducing readmission rates in discharged schizophrenia patients. Studies with "high risk" families by Leff et al. (1989, 1990) and Hogarty et al. (1986, 1989) show that family intervention is effective in reducing relapse rates in such patients. Family interventions have also been shown to reduce burden of care, improve patients' functioning in social areas and are cost effective to the extent that these are less expensive than conventional therapies (Falloon et al., 1982, 1985; Tarrier et al., 1988, 1989, 1991, 1994). In more striking studies, Telles et al. (1995) and McFaren et al. (1985) have shown the beneficial effects of family interventions in managing difficult patients in the setting of the community. In recent reviews of family intervention studies, Mari & Streiner (1994), Dixon & Lehman (1995), Schooler (1995), Penn & Mueser (1996) and Anderson & Adams (1996) concluded that such interventions are beneficial in most cases and though these strategies are effective, these are underused. John (1997) reviewed family intervention work done in India and opined that psychosocial inputs in the management of schizophrenia are important and integral components of the care of the patients.

Many manuals on psychoeducational techniques have been published (Falloon et al., 1985; Barrowclough & Tarrier, 1992; Kuipers et al., 1992). Psychoeducational techniques are geared towards educating the patients and the caregivers, problems solving by the patients and family member and emotional processing. These are in conjunction with medication.

Another important aspect of working with the families is using techniques for fostering better relationships between the consumers i.e. the patients and their caregiver and the mental health staff engaged in therapy. The need for acquiring skills (by the mental health team) for promoting positive staff attitude towards the patients and caregiver is crucial for the success of any family intervention. It is well recognised that the caregivers carry a great deal of burden of care, are often under tremendous stress due to the sick member of the family and have often been given negative signals in terms of being blamed for the misfortune of the patients. They may also have frustrations, despair and a fear that things will not work out well. Working with such families is not easy. It may be difficult to engage them in any therapeutic plans as they may be pessimistic about the outcome or may perceive the therapeutic process and their involvement too demanding. The attitude adopted by the staff influences the cooperation one gets from the family members. Display of patience, tolerance, willingness to persist and flexibility in approach by the staff towards the caregivers leads to better response from the family and encourages a mutually trusting partnership between the family and the staff (Kuipers & Bebbington, 1990; Birchwood & Smith, 1990; Kuipers et al., 1992).

3. Community based Interventions: For diverse reason, both in the developed and developing countries, community care of schizophrenia patients has become a dire necessity. In this context, management of treatment refractory schizophrenia cases in the community poses certain challenges and problems. The broad aims of community based interventions are to improve the quality of life of the patients, improve or stabilise mental health of the patients and minimise relapses and rehospitalisations. In addition to such general measures as good community
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Psychiatry outreach programme and active multi-disciplinary team of mental health professionals, some specific measures of community based interventions are as follows:

Psychiatric research has clearly established that relapse in stable schizophrenia patients is often preceded by prodromal symptoms for weeks and in many cases for months. Careful monitoring of the patients in follow-up studies has indicated that in the weeks before a relapse increase in life stresses occurs (Das et al., 1997). Therefore, a strategy of “early symptoms and signs monitoring” of the patients in the community is likely to pay rich dividends. Common prodromal symptoms of relapse are insomnia, tension, poor appetite, difficulties in concentration, restlessness or increasing listlessness, depression, irritability, aggression etc. It is also recognised that many patients have a set pattern of emergence of symptoms before relapse, some thing which has been termed “relapse signature” (Birchwood & Shepherd, 1992; Birchwood et al., 1992). Prompt psychiatric help to the patients and the caregivers in such situations can often abort a relapse.

Another community based intervention strategy which has significant impact on the rate of rehospitalisation in those at greatest risk of relapse requiring hospitalisation is described as “assertive outreach programme”. Prevention of crisis and prompt crisis intervention by trained mental health professionals are the main techniques used and all help/intervention is provided in the patient’s home. The programme of “assertive outreach” is a staff intensive programme i.e. the ratio of staff to patient is quite high and staff involved in the delivery of services in this programme aggressively and assertively pursue the welfare of the patient (Witteridge, 1991; Muijen, 1994; Marks et al., 1994; Wykes, 1994; Wykes & Carson, 1996).

“Crisis intervention” is another alternative which can reduce rehospitalisations and clinically and socially benefit the patient (Muijen et al., 1992).

CONCLUSIONS

Considerable advances have been made in the management of treatment resistant schizophrenia patients. The whole phenomenon of treatment refractoriness is now better understood and refinement in management techniques have occurred. These refinements include judicious use of conventional and atypical antipsychotics coupled with a wide array of psychosocial intervention strategies. Further, it is now apparent that these newer drugs and psychosocial interventions are beneficial to the treatment resistant patients and the caregivers in effecting symptomatic improvement, reducing chronicity and disability, minimising and preventing relapse, averting the necessity of rehospitalisations, reducing the burden of care and improving the quality of life of the patients and their long suffering families. Strategies aimed at early intervention in the setting of the home of the patients are likely to play increasing role in decreasing treatment resistant, preventing relapses and minimising rehospitalisations.

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