

DEPRESSIVE DISORDERS IN SCHIZOPHRENIA

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SUMMARY

146 cases of schizophrenia, fulfilling Research Diagnostic Criteria and a regular followup of 6 months or more, were studied concerning depressive mood disorders at the onset of illness and over a period of time following neuroleptic treatment. There was no significant difference in the total number of cases depressed at the onset of illness (49) and at final followup (56). Following 8 weeks of neuroleptic treatment, depressive symptoms disappeared in 47 per cent of the depressed schizophrenics and these cases did not evince depression subsequently. However, 53 per cent of schizophrenics manifesting depression at final followup had no depressive symptoms at the onset of illness and in these cases depression occurred following neuroleptic treatment. It is contended that depression may be intrinsic of schizophrenia and neuroleptics may have a role in the causation of depressive disorders in schizophrenia.

The occurrence of depressive symptoms in the course of schizophrenia was recognized by Bleuler (1911) and Kraepelin (1919). Mayor-Gross (1920) found that some patients emerged from psychosis into a state of despair, which he regarded as a mode of reacting to a psychotic experience.

Depressive mood disorders associated with schizophrenia have received considerable attention in the recent years; however, the etiology of such depressive states has remained a persistent enigma. Depressive symptoms have been encountered in schizophrenia at the very onset of psychotic symptoms (Planansky and Johnston 1978) and during acute exacerbations of psychotic symptoms (Knights and Hirsch 1981). Depressive disorders have been reported in the course of chronic schizophrenia (Roy et al 1983). A serious depression in the aftermath of a schizophrenic episode has been described by several authors (Steinberg et al 1967, Bowers and Astrachan 1967, Roth 1970, Stern et al 1972, McGlashan and Carpenter 1976a, 1976b, Mackinnon 1977, Das and Kapur 1980 & Mandel et al 1982).

Depressive syndrome that follows the resolution of flagrant psychotic symptoms in schizophrenia has often been described

as postpsychotic depression (McGlashan and Carpenter 1976a), characterized symptomatically by sadness, suicidal ideas, massive inertia, neurasthenic complaints, feelings of emptiness or absence of feelings, striking passivity and impairment of interpersonal relations.

Postpsychotic depression has been regarded as a serious clinical entity requiring the institution of appropriate psychological or somatic treatments. Another related decision concerning management regards that the extent to which a patient with postpsychotic depression should be urged to resume premorbid functioning. Vigorous efforts at rehabilitation during this time may constitute a negative force (Miller and Sonnenberg 1973) and as the anergia is transient (may last from weeks to more than a year), patient should be urged to assume only those responsibilities that he can shoulder with comfort (Dette and Jarecki 1971).

The incidence of suicide is high in schizophrenia (Warnes 1968, Planansky and Johnston 1971) and it is estimated that about 10 per cent of all schizophrenics kill themselves (Miles 1977). An impending depressive state may still further increase the risk of suicide in schizophrenics recovering

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from psychotic symptoms, as they must contend with unalterable reality of their illness, their problems and their uncertain future (McGlashan and Carpenter 1976a). A substantial percentage of chronic schizophrenics also attempt suicide at sometime in their illness and the suicide risk is greater in those who develop a major depressive episode (Roy et al 1984).

Despite the importance of recognition of depressive states in schizophrenia, there has been a curious dearth of data in the Indian set up. In this study an attempt has been made to study the frequency and nature of depressive disorders in schizophrenia.

Material and Methods

All the adult new cases seen at the psychiatric out-patient department of Kasturba Medical College Hospital, Manipal, Karnataka from January 1978 to December 1979 constituted the material. ICD-9 (WHO 1978) criteria were used for diagnosis of schizophrenia. 2,179 adult new cases (15 years and above) were seen during this period and 529 cases (24%) constituted schizophrenia, as per ICD-9 criteria. The following were excluded from the study:

1. Patients with major physical illness.
2. Evidence of organicity, even if organic disorder could not be identified.
3. Evidence of alcohol or drug abuse or their withdrawal.
4. Latent schizophrenia.
5. Schizo-affective schizophrenia (schizophrenia with pronounced affective symptoms, depressive or manic).
6. Doubtful diagnoses of schizophrenia.
7. Schizophrenia-like psychoses, with antecedent stressful life events.

All the cases received conventional neuroleptic treatment and antiparkinsonian

medication (benzhexol) was routinely given concomitantly (electroconvulsive therapy was used in some cases of catatonic schizophrenia and in a few cases of other types of schizophrenia with little response to drugs, at the discretion of treating consultant). Cases with diagnostic or management problems received in-patient observation and treatment, ranging from 3 to 6 weeks.

The cases were followed up fortnightly in the first month and monthly or bimonthly afterwards, depending on the severity. A register of these cases and their follow up was maintained and if any case had not turned up for follow up as advised, a letter was despatched requesting for a followup. The followup period ranged from a minimum of 6 months to a maximum of 48 months from first visit.

The patients who were considered definite cases of schizophrenia were studied concerning symptomatology at first visit, and at each followup. At the first visit, symptoms noted at a thorough clinical mental status examination and/or during preceding one week were coded in the case record, that had a structured list of 93 symptoms, covering 15 major aspects of psychiatric phenomenology: general appearance, behaviour, psychomotor activity, speech, affect, thought disorder, delusions, hallucinations, catatonic features, neurotic symptoms, sexual disturbances, memory, orientation, appetite and sleep. At each followup, symptoms noted at a detailed mental status examination were recorded in the case-sheets. The cases, even the ones with indubitable diagnosis of schizophrenia, that had not a minimum regular followup of 6 months were excluded from the study, as this much duration was thought necessary for a clear-cut picture to emerge, and to study the phenomenology over a course of time.

As the criteria for the diagnosis of schizophrenia in ICD-9 were not very specific, Research Diagnostic Criteria (Spitzer et al 1978) were applied retrospectively to these cases, at the time of final assessment done in December 1981. The cases that satisfied the RDC criteria for definite schizophrenia and a minimum regular followup of 6 months or more were only considered for final analysis. Schizophrenics were not categorized into RDC sub-types for this study. The depressive symptoms recorded in the files were scrutinised and analysed as per the RDC criteria for different types of depressive syndromes.

Results

Out of 529 cases of schizophrenia 146 cases satisfied the criteria laid down in this study.

At first presentation, out of 146 schizophrenics, 49 cases (34%) showed noticeable depressive symptoms, which as defined in this study were: One or more distinct periods with dysphoric mood (depressed, sad, hopeless) or pervasive loss of interest or pleasure that lasted at least one week from the onset of a noticeable change in the patient's usual condition, associated with at least 2 of the following symptoms: poor appetite; sleep difficulty; loss of interest or pleasure in usual activities, including social contact or sex; feelings of self-reproach or excessive or inappropriate guilt; slowed thinking or indecisiveness; recurrent thoughts of death or suicide or any suicidal behaviour. These symptoms represented A and only 2 symptoms of B of RDC criteria for a definite diagnosis of schizo-affective disorder, depressed type and these were not sufficient for a schizo-affective diagnosis. Schizophrenics showing momentary shifts from one dysphoric mood to another dysphoric mood, e.g. anxiety to depression to anger, or those manifesting fleeting depressive symptomatology (that

were insufficient to meet the specified criteria) were disregarded.

After 8 weeks of neuroleptic treatment (no antidepressants were given), it was found that, out of 49 cases of schizophrenia who had manifested depressive symptomatology at first visit, in 23 cases (47%) depressive symptoms had abated and they did not manifest depression subsequently; still, in 26 cases depressive symptoms persisted and these formed part of the cases who evinced depression at final assessment.

Followup: Out of 146 cases of schizophrenia, 15 cases could be followed up for 6 months only and these warranted description separately from the remaining 131 cases who were followed for more than 6 months.

Out of 15 cases of schizophrenia who could be followed for 6 months only, depressive symptoms were persisting in 2 cases at the end of 8 weeks of neuroleptic treatment and subsequently these 2 cases (13%) progressed to develop major depressive disorder superimposed on residual schizophrenia; and the other 13 cases (87%) showed no evidence of depression.

In 131 cases, where followup exceeded 6 months, the last visit the patients had made prior to the end of December 1981 was taken as the final followup visit. However, the duration of followup, from first visit to 'final' visit, was not uniform in all the cases: 24 cases had 7-12 months followup; 25 cases - 13-18 months; 32 cases - 19-24 months; 19 cases - 25-30 months; 12 cases - 31-36 months; 9 cases - 37-42 months; 10 cases - 43-48 months.

The entire followup period, commencing with the first followup visit after 8 weeks of neuroleptic therapy and extending upto the final followup visit was screened for depressive symptomatology.

Depressive symptoms, which were

present at first visit, were persisting in 24 cases after 8 weeks of neuroleptic treatment. Depressive symptoms emerged for the first time in 7 cases between 2 and 6 months of followup; in 12 cases, between 7 and 12 months; 4 cases, between 13 and 18 months; 3 cases, between 19 and 24 months; 2 cases, between 31 and 36 months; 2 cases between 37 and 42 months.

Thus out of 131 cases of schizophrenia, in the follow up period, 77 cases (59%) did not manifest 'noticeable' depressive symptoms and 54 cases (41%) manifested varying degrees of depression, the nature of which was assessed as per the RDC criteria for different types of depressive syndromes.

14 cases of schizophrenia (10%), in whom prominent psychotic symptoms had abated, yet residual symptoms like emotional blunting, extreme social withdrawal, eccentric behaviour or mild formal thought disorder persisted, developed pronounced depressive symptoms, that persisted for more than 2 weeks without any activation of psychotic schizophrenic features. The depressive symptoms were sufficiently severe to qualify for the full depressive syndrome (A & B of major depressive disorder in RDC). These cases were labelled as "depressive syndrome superimposed on residual schizophrenia (secondary depression)", as per RDC criteria.

33 cases (25%) in whom residual schizophrenic symptoms had persisted, revealed 'noticeable' depressive symptoms which were not sufficiently severe to qualify for major depressive disorder. However, the depressive symptoms noted in these cases were sufficient to meet the criteria A, B & C (but not D, E & F) of minor depressive disorder in RDC.

4 cases (3%) developed schizo-affective disorder - depressed type i.e. symptoms of

major depressive disorder overlapped temporally with active period of schizophrenic symptoms (delusions, hallucinations, formal thought disorder or grossly disorganised behaviour).

3 cases (2%) in whom schizophrenic symptoms had fully remitted, developed a depressive syndrome that met the criteria (A, B, C, D, E & F) of definite major depressive disorder in RDC. These were given the RDC label of "secondary major depressive disorder".

Discussion

Schizophrenic patients, in the present study, manifested depressive symptomatology at first presentation and over a course of time following treatment.

At first presentation, depressive symptoms were evident in 34 per cent of the untreated schizophrenics in this study. A large number of reports are now available concerning the frequency of depressive symptoms in Schizophrenia and some of the recent studies reported higher prevalence of depression in acutely admitted schizophrenia, nearly 50 per cent of cases or more (Knights and Hirsch 1981, Johnson 1981). The estimate of the frequency of depression in the present study can be regarded as conservative, as schizophrenics manifesting depressive symptoms insufficient to meet the specified criteria were disregarded. Depression may be a ubiquitous concomitant of schizophrenia, that gets overlooked clinically because of other more florid psychotic symptoms and when the psychosis remits depression becomes evident (McGlashan and Carpenter 1976, Moller and Zerssen 1982). From the present study, it appears that depressive symptoms may be integral of schizophrenia as these symptoms have occurred at the very onset of schizophrenia. However, depressive symptoms, in the present study, have not been found to be invariably associated with the

onset of schizophrenia.

It is notable that in 47 percent of schizophrenics with 'noticeable' depressive symptoms, the depressive symptoms had abated following 8 weeks of neuroleptic therapy. It has been pointed out that some neuroleptics have antidepressant properties (Robertson and Trimble 1983, Becker 1983). However, it is also quite possible that antipsychotic drugs, at least some of the commonly used ones, have, in fact, no distinct antidepressant properties and that depression integral of schizophrenia disappears in some cases following neuroleptic-induced improvement in schizophrenia.

In this study, out of 15 cases of schizophrenia who could be followed for 6 months only, only 2 cases developed major depressive disorder superimposed on residual schizophrenia and both these cases had 'noticeable' depressive symptoms at the onset, whereas at followup the depression was more pronounced and conspicuous.

In the present study, out of 131 cases of schizophrenia in which the followup exceeded 6 months, 41 per cent of the cases manifested varying degrees of depression. Other studies revealed that the frequency of depression occurring in schizophrenia, following abatement of psychotic symptoms, ranged from 25 per cent of cases (McGlashan and Carpenter 1976a, Mandal et al 1982) to about 50 per cent of cases (Knights et al 1979, Johnson 1981).

At final assessment, in cases where followup exceeded 6 months, superimposed on residual schizophrenia 10 percent of the cases developed major depressive disorder and 25 percent of the cases showed 'noticeable' depressive symptoms (that would meet the criteria for minor depressive disorder if 'nonpsychotic' dimension was ignored-minor depressive disorder in RDC is meant for nonpsychotic episodes only). For depression occurring in schizophrenics fol-

lowing abatement of psychotic symptoms, the term postpsychotic depression is often used (McGlashan and Carpenter 1976a). However, the term postpsychotic appears ambiguous and could be erroneously interpreted as following any psychosis, that could be organic, reactive, epileptic, alcohol or drug-induced, or even manic. 'Post-psychotic' also implies that the patient is no longer actively psychotic but the depression manifested by some of the cases, in this study, was undoubtedly of psychotic intensity. It would be more appropriate to say that such cases were no longer actively schizophrenic. In the Research Diagnostic Criteria, the afore-mentioned depressive syndrome has been designated as "depressive syndrome superimposed on residual schizophrenia (secondary depression)", which is too elaborate for routine labelling. It does not encompass cases that develop depressive symptoms, not sufficient to meet the criteria for major depression disorder and there is no appropriate RDC category for such cases as have been encountered in this study.

The author suggests that the depressive syndrome superimposed on residual schizophrenia could be conveniently and more precisely labelled as post-schizophrenic depression (PSD). The term post-schizophrenic depression denotes that the patient is no longer actively schizophrenic and the depressive syndrome has superimposed on residual schizophrenia, without any activation of schizophrenic symptoms and the cases that develop a major depression could be labelled as PSD-Major and those with minor depression, PSD-Minor (based upon the severity of depression and not the causality).

Post-schizophrenic depressive disorders, in particular some of the minor depressive states, might be reactive in nature manifesting as the patients recover insight into

their illness and life situation. Such depressive states might also result from guilt or shame patients feel in relation to their having become psychotic (Wildroe 1966). However, depression occurring in a manic following recovery could also be construed as reactive in a similar fashion whereas we find this is not the case. In schizophrenia, following improvement when there is every reason to be happy, for major depressive disorder to supervene cannot be merely passed off as reactive and endogenous factors seem to be operating.

As encountered in this study, post-schizophrenic major depression was quite severe and stable and was often incapacitating in that the patients were unable to carry out any relatively complex goal directed activity such as work, taking care of the house or participation in social and recreational activities. It, not infrequently, resembled a retarded major depressive disorder with pervasive loss of interest or pleasure and absence of reactivity of mood to changes in environment was conspicuous. The patients often harboured delusions of self-reproach and guilt and suicidal preoccupation was prominent.

Neuroleptic drugs have long been implicated in the causation of post-schizophrenic depression i.e. the PSD is pharmacogenic (De Alarcon and Carney 1969, Ayd 1975, Falloon et al 1978). In the present study, there was no significant difference ($P < 0.05$) between the number of schizophrenics depressed before neuroleptic treatment (49) and those that manifested depression at follow-up (56). It would thus appear that neuroleptics play no role in the causation of depressive symptoms. However, further analysis showed that neuroleptics might have prominent depressogenic effects. In 23 out of 49 depressed schizophrenics, depressive symptoms had abated at the end of 8 weeks of neuroleptic treatment, and the initial depression persisted in only 26 cases at final followup. Out of 56 cases manifesting de-

pression at followup, 30 cases (53%) had no depressive symptoms at first presentation and they revealed depression following neuroleptic treatment. These findings indicate that depression might develop de novo following neuroleptic treatment of schizophrenia in some cases and depression in such cases does not represent an already existing symptom complex. None of the schizophrenics, in this study, had major depressive disorder at the beginning of treatment (since a prominent affective syndrome was an exclusion criterion for diagnosis of schizophrenia), whereas following neuroleptic treatment, superimposed on residual schizophrenia, 16 cases manifested major depressive disorder. It is probable that neuroleptics also cause aggravation of existing depressive symptomatology. However, this is unlikely to be a simple relationship, since in some double-blind trials, the placebo group has experienced an identical frequency of depression as the active drug recipients (Leff and Wing 1971, Hirsch et al 1973). Some studies have refuted the concept of 'pharmacogenic' depression in schizophrenia (Strain et al 1982, Roy et al 1984). The occurrence of depressive symptoms in the course of schizophrenia was also sporadically noted even before the introduction of neuroleptics (Mayer-Gross 1920, Lewis and Hubbard 1931, Eissler 1951, Lewis and Piotrowski 1954). These findings suggest that depression could be an inherent part of schizophrenia, though neuroleptics may have a role in precipitating depressive disorders in schizophrenia.

Some authors (Rifkin et al 1975, Van Putten and May 1978) have advanced the concept of 'akinetic depression' in schizophrenia, to refer to a syndrome resembling depressive illness, which occurs in association with drug-induced Parkinsonism. Van Putten and May (1978) reported that anticholinergic drugs were beneficial in al-

leviating such depression, while Quitkin et al (1978) pointed out that those symptoms which respond to anticholinergics were part of drug-induced Parkinsonism. Moller and Zerssen (1981) found that depressive symptoms were as common in schizophrenics on anticholinergics as in those who were not. In the present study, antiparkinsonian drugs were routinely used along with neuroleptics and drug induced akinesia appeared less likely as a source of observed depressive states. Hirsch (1982) concluded that there was little reason to regard the akinetic syndrome as a form of depression, though the concept had heuristic value to remind us that apparently anergic depressed schizophrenics might have drug-induced Parkinsonism.

It has to be noted that certain "negative symptoms" described in schizophrenia seem to have semblance to some of the depressive symptoms described here. The negative symptoms of schizophrenia include impoverished speech, affective flattening, avolition apathy, loss of libido, anhedonia, social withdrawal and attentional impairment (Andreasen 1982, Andreasen-Olsen 1982, Lewine et al 1983). However, many of the individual negative symptoms such as poverty of speech, physical anergia, anhedonia-asociality complex, also occur, in depressive illness (Andreasen 1982). A sharp demarcation between negative schizophrenic symptoms and postschizophrenic depressive symptoms does not exist and attempts directed at this are bound to be controversial. As assessed in this study, the depressive manifestations included a painful depressive affect rather than a blunted affect and a constellation of other affective symptoms including pervasive loss of interest or pleasure, feelings of self-reproach or guilt, recurrent thoughts of death or suicide or any suicidal behaviour, which reflect more a depressed state than a negative schizophrenia. Moreover, some of the residual symptoms such as emotional blunting and ex-

treme social withdrawal were prerequisites for a diagnosis of residual schizophrenia in this study, and the depressive states noted in such cases were in addition to the negative symptoms of schizophrenia. Negative schizophrenia is similar to the concept of simple schizophrenia (Andreasen and Olsen 1982), negative symptoms in schizophrenia do not appear to be related to a possible postpsychotic depression, the latter being relatively time-limited (Pogue-Geile and Harrow 1984).

4 cases (3%) in whom schizophrenic symptoms were still active, developed superimposed major depressive disorder in the course of time and it appears that some cases presenting as schizophrenia later progress to schizo-affective disorder. 3 cases (2%) in whom schizophrenic symptoms remitted totally, thereafter developed major depressive disorder. In the absence of residual schizophrenic symptoms, these cases cannot be equated with postschizophrenic depression and the RDC label of secondary major depressive disorder seems appropriate for such cases. In these cases the initial diagnosis of schizophrenia was not in doubt and only one of them manifested 'noticeable' depressive symptoms at first presentation. It is not clear how such a transformation could take place; nevertheless, some studies in the past revealed that some cases of schizophrenia later develop manic-depressive illness (Ziskind et al 1971, Sheldrick et al 1977, Sartorius et al 1977, Mellor et al 1981).

Thus, it is clear that depressive symptoms occur in schizophrenia at the onset of illness and over a course of time with or without treatment; hence, depression must be intrinsic of schizophrenia. It could be that schizophrenia shares a common pathophysiological mechanism with depression and neuroleptic-induced improvement in schizophrenia might thus unmask or precipit-

ate depression. Hirsch (1982, 1983) refutes the concept of neuroleptic-induced depression and proposes that depressive symptoms are an integral part of schizophrenic symptoms and must, therefore, share with schizophrenia common pathophysiological processes. Galdi (1983), while disagreeing with the views expressed by Hirsch (1982), advances the concept of 'pharmacogenetic depression' which occurs in genetically predisposed schizophrenic patients following neuroleptic treatment. Though, the views of Galdi and Hirsch look apparently dissimilar, it is evident that both of them emphasize intrinsic mechanisms.

The patients included in this report can be regarded as definitive cases of schizophrenia in view of the exclusion criteria. However, the retrospective application of RDC criteria and lack of uniformity in the duration of followup pose certain limitations. Prospective studies using operationally defined criteria for the diagnosis of schizophrenia and objective methods of evaluation for assessment of depressive syndromes in such cases are in order and the causality of depressive mood disorders in schizophrenia, which may well be heterogeneous, needs to be re-examined.

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