Intermittent Neuroleptic Treatment of Therapy-resistant Schizophrenic Psychoses

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ABSTRACT – Discontinuing anti-psychotic medication sometimes leads to substantial improvements in therapy-resistant schizophrenics. This phenomenon warrants systematic study, as it might serve as a fruitful element in the treatment of this category of patients.

It is well-known that a subgroup of schizophrenic patients do not profit from the use of regular antipsychotic medication. In fact, between 5 and 25% of all schizophrenics do not benefit from any neuroleptic medication (Brenner, Denker, Goldstein et al. 1990). There is, as yet, no generally accepted protocol on how to act in these cases. Often the psychiatrist will administer a series of antipsychotics in a trial error fashion, hoping that eventually one of these remedies will be effective. Repeatedly, a particular medication having little or no effect is stopped after a short while just to prepare the patient for the next type of medication.

In this connection, we have noticed that some schizophrenic patients, known as therapy-resistant, notably improve in the period immediately after discontinuing a seemingly ineffective antipsychotic. That is to say, the severity of psychotic symptoms declines, independent of the side effects of the medication. Some time after the patient has, again, adjusted him-or herself to a new medication (which, because of the observed improvement of the patient in the build-up phase, looks promising), a gradual exacerbation of symptoms occurs, eventually ta-
king the patient back to his starting-point in most cases. An illustration of this is Mr. A., a 46-year-old chronically schizophrenic patient who changed medication in the context of an “international multi-center trial” study on the efficacy of a relatively new neuroleptic. As part of that study the “positive and negative syndrome scales for schizophrenia” (PANSS) of Kay, Opler & Fiszbein (1986) were completed at fixed points in time. During the initial treatment with a classical neuroleptic medication (i.e. Zuclopentixol, 3 dd 25 mg), Mr. A. had a total PANSS score of 133. A week after the old medication had been stopped and new medication had been given (i.e., remoxipride 2 dd 150 mg), Mr. A. had a PANSS score of 75. After two weeks, there was a further improvement; the PANMS score being 70 points. The improvement was maintained until four weeks after the beginning of the new medication (PANSS score 73). As late as four weeks after the beginning the patient still scored 73 points. At that point Mr. A’s condition became rapidly worse. Thus, after six weeks, the score on the PANSS had risen to 106. And although no further PANSS data were obtained beyons this point, we know that the symptomatology of the patient has in every respect returned to the starting level previous to the investigation.

With this type of experiences in mind, the question arises whether therapy-resistant schizophrenies, are, at the receptor level, characterized by a continual tuning in to an “inadequate” or “schizophrenic” homeostasis. This would imply that a temporary disruption of this (inadequate) homeostasis, as is the case with abruptly stopping medication after prolonged use, could offer them temporarily relief. Possibly, a disruption of the inadequate balance can be brought about in various ways. The literature suggests that remissions occur when using a wide range of medications, whether with or whithout regular neuroleptics. For instance, in his survey on the treatment of therapy-resistant schizophrenia, Meltzer (1992) mentions benzodiazepines, carbamazepine, reserpine, lithium, tricyclic antidepressants, L-dopa and d-amphetamine, verapamil, and even opioid drugs. More invasive methods such as electroconvulsive therapy and psychosurgery are also discussed. Furthermore, bromocriptine is mentioned in the literature (Gattaz & Kollisch 1986). These diverse medications and treatment methods cast doubt on the idea that a specific (chemically) effective mechanism is responsible for the observed remission effects. Rather, it appears that the effects are due to a non-specific disruption of an existing “inadequate” balance. If it is, indeed, true that therapy-resistant patients temporarily improve after stopping medication, then this phenomenon could be used as an element in the treatment of therapy-resistant schizophrenia. An “intermittent” neuroleptic treatment, that is to say, neuroleptics stopped at fixed intervals, could possibly prove to be beneficial for therapy-resistant schizophrenics who can make no lasting improvement by having various antipsychotics administered to them over long periods. Clearly, then, the beneficial effects of intermittent neuroleptic treatment warrants systematic research. At a more theoretical level, such research could bring to light whether the results of an intermittent medication regime are, indeed, based on a repeated and non-specific disruption of an inadequate homeostasis. Admittedly, the concept of homeostasis is vague. However, Pavlovian conditioning processes involved in the behavioural effects of repeated drug intake may provide a further specification of this concept. Thus, Siegel (1983) has shown that with prolonged and intensive drug intake, compensatory-conditioning effects emerge which neutralize the primary effects of a
specific drug. For example, animals repeatedly injected with epinephrine, initially react to this drug with a marked tachycardia. However, in due time the animals exhibit a preparatory bradycardia that will cancel tachycardia responses elicited by epinephrine. Such a counterregulation might also occur with neuroleptic drugs and possibly therapy-resistant schizophrenic patients are extremely sensitive to these compensatory processes. Withdrawal of neuroleptics would undermine these compensatory processes and might contribute to an improvement in symptomatology. While these formulations are highly speculative, they are testable.

References


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