EARLY DEPRESSIVE STUPOR RESPONSIVE TO MOCLOBEMIDE

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ABSTRACT

The clinical application of moclobemide, a new reversible monoamine oxidase type A inhibitor is being extended within the depressive group of disorders. The following case history describes its successful use in the early stage of depressive stupor.

Keywords: *Depressive Disorder; Moclobemide; Stupor*

INTRODUCTION

The antidepressant moclobemide, chemically a benzamide derivative, is the first short-acting reversible inhibitor of monoamine oxidase (MAO) type A (Freeman, 1993). It affects noradrenalin, serotonin and, to a lesser degree, dopamine neurotransmission in the central nervous system (Nair *et al.,* 1993). Unlike traditional, irreversible MAO inhibitors (e.g. phelzine), moclobemide has negligable hepatic toxicity, a very short half-life (two hours) and does not require a tyramine-restricted diet up to a dosage of 600 mg/day (Gieschke *et al.,* 1987; Nair *et al.,* 1993). Due to the favourable side effect profile, the full therapeutic dose can be given from the start of treatment resulting in rapid onset of its clinical action. Moclobemide has been proven to be as effective as tricyclic antidepressants in controlled trials (Freeman, 1993; Angst *et al.,* 1995).

Although moclobamide is reported to be effective in depression accompanied by psychomotor retardation, to the best of our knowledge no case reports or controlled trials have been published on its efficacy in depressive stupor. Spear *et al.* (1997) reported a case of a 72-year-old woman whose stupor resolved after two days of treatment with moclobemide 300 mg/day and diazepam 10 mg/day. However, the case description clearly suggests that the suspension of stupor was largely due to the administration of diazepam.

CASE REPORT

This paper reports on a 73-year-old woman who was admitted for assessment following inability to cope at home and complaints of poor sleep. On specific inquiry she gave a five-month history of uncharacteristic anhedonia, social isolation, somatic preoccupation, poor sleep, and poor appetite. She was not suicidal. No other complaints were elicited, in particular, there were no features of a dementing illness, psychotic process, or anxiety-based disorder. On examination, she was appropriately dressed and maintained eye contact as she smiled and readily explained the above changes in terms of her poor hearing, eye sight, and persistent tremor following an earlier cerebrovascular accident.

Although there was mild agitation present, careful observation over the next eight days failed to confirm any other features of a suspected depressive illness or of any other disorder. In particular, she slept and ate well, was noted to be conversing with others and seemed to enjoy being on the ward. A Hamilton Rating Scale for Depression score of 13 and Mini-Mental State Examination score of 23 were recorded. Discharge planning included multiple offers of support and help with meals-on-wheels, district nursing and home-help, all of which were declined. The patient was discharged home. 10 days later she was readmitted. She had been found at home lying in bed motionless except for her eyes, which followed the author across the room. After considerable coaxing, she uttered a single phrase saying that she wanted to die. She had not eaten since the previous day and repeatedly refused to take any fluid despite poor tissue turgor. Unable to consent to admission, she was brought in as an involuntary patient.

The patient's past psychiatric history included a course of ECT 30 years previously, notes of which were no longer available. Her past medical history included hypertension, angina, and a minor cerebrovascular accident eight months earlier resulting in a right-sided tremor that had been unresponsive to antiparkinsonian medication. A computed tomograpy (CT) scan of the brain three months prior to this admission was suggestive of multiple infarcts, with damage being reported particularly in the frontal lobes. There was no known family history of psychiatric illness. Her personality was independently described as having always been dramatic, attention-seeking, and manipulative, and only one of her four children maintained any contact.

Because of the diagnostic uncertainties and the ever-changing clinical presentation, it was decided to observe her before treatment. Her vital signs were within normal range and her mobility and nutritional status were satisfactory enough to allow drug-free observation in the hospital environment. A physical examination, including neurological status, did not show any changes compared with her previous admission and to repeat the organic work-up was considered unnecessary.

During the next two weeks, the patient presented a varied picture. At times she showed psychomotor retardation and had to be helped out of bed, dressed, and assisted to the lounge. She was mute or monosyllabic, with a blank face that failed to show any reaction. Occasionally she even refused food and required persistent encouragement to take any fluids, at times her only intake was from the nursing staff repeatedly syringing liquid into her mouth. She was, at times, incontinent of urine and occasionally of faeces. At other times she was hostile and resistive, shouting *'You're mad!'* when approached, and kept her eyes closed and resisted opening them. Otherwise she would eat, drink, and toilet herself independently.

Throughout the current hospital stay, her physical condition was unchanged from the earlier admission and a full blood count, erythrocyte sedimentation rate, vitamin B_{12}, folate, urea, creatinine, and electrolytes were within normal levels, although thyroid-stimulating hormone was low at 0.11 mIU/L (normal range, 0.17-3.5) and the free thyroxine marginally elevated at 33.2 pmol/L (normal range, 11.0-28.0).

As the patient did not improve significantly over the two-week assessment period, a decision was made to start antidepressant treatment with moclobemide 600 mg/day. Moclobemide was chosen because of its rapid onset of action and effect on psychomotor retardation. During the next five weeks, her strange behaviour slowly abated and her condition improved. During the second admission, the Hamilton Depression Rating Scale could not be administered due to her semi-stuporous condition. At discharge she was eating and drinking, getting herself up and dressed in the morning, conversing and laughing, and entertaining the staff with her often astute and quick-witted replies. 18 months later she leads an independent life, regularly attends the follow-up clinic, takes her medication, and remains free from depressive symptoms.

DISCUSSION

The clinical picture of stupor has been known since ancient Greek times; Hippocrates was probably the first author to describe a case of psychogenic stupor (Sennert, 1971; Johnson, 1993). Stupor has been difficult to define due to the lack of its conceptual framework (Berrios, 1981a). Neurologists emphasise the impairment of consciousness in conceptualising stupor: *"unresponsiveness from which the subject can be aroused only by vigorous and repeated stimuli"* (Plum & Posner, 1972). In psychiatry, stupor is defined as a complete absence, in clear consciousness, of any voluntary movements (Wing *et al.,* 1974). In Berrios' (1981b) succint definition, *"stupor names a symptom complex whose central feature is a reduction in, or absence of relational functions (i.e. action and speech)"*. In other words, stupor means the suspension of both expressive and reactive movements. The triad of akinetic mutism in clear consciousness remains a useful aide memoire, at least for clinical purposes (Berrios, 1981a).

Stupor is uncommon, or rarely reported (Johnson, 1984), with an annual prevalence of 1.34 per 100,000, a possible female predominance, and a mortality of 11% in an early series (Joyston-Bechal, 1966). Smith (1959) reported 27 cases of first-episode stupor from a large psychiatric hospital. The diagnostic distribution of the 27 cases was as follows: 12 depression, nine schizophrenia, four mixed neurotic states with both depressive and hysterical features, and two epilepsy. In the early Maudsley series, the aetiology was distributed between schizophrenia (35%), depression (27%), and those of organic origin (20%), while 10% of cases had mixed neuroses (Joyston-Bechal, 1966). In Johnson's (1984) more recent series of 25 stuporous patients observed over 15 years in a psychiatric teaching hospital, 10 suffered from depression, four had schizophrenia/schizoaffective disorder, 10 were diagnosed with organic stupor (e.g. brain stem encephalitis, parietal astrocytoma, basilar aneurysm, traumatic encephalopathy, craniopharyngoma, lithium and neuroleptic intoxication) and only one patient was thought to have 'psychogenic' stupor. Altshuler *et al.* (1986) found 27% of patients had schizophrenia, 32% had affective disorder, 18% had organic mental disorder and 27% had non-psychiatric diagnoses (cerebrovascular accident, post-encephalitic parkinsonism, and post-herpetic encephalitis) in their series of 22 mute stuporous subjects.

The underlying pathogenetic basis of stupor remains uncertain and reflects its changing conceptual history (Berrios, 1981a). Psychological views were only developed this century, corresponding to the publication dates for suggested cases of hysteria, while current views are characterised by a revival of the notion that stupor may be a primary disorder of motility involving the basal ganglia (Berrios, 1981a; Altshuler *et al.,* 1986).

In depressive stupor, the patient gradually, almost imperceptibly, slips into an increasingly retarded state, eventually becoming, stuporous. Persistent catatonic signs such as mannerisms, stereotypes, and verbigerations are usually absent. The commonly accepted view is that depressive stupor is seldom complete and patients do respond to external stimuli (Johnson, 1984). Retrospectively, our patient's initial admission represented the onset of a depressive illness, although her symptoms and signs were limited. However she was discharged untreated, only to be found stuporous l0 days later. Following admission, intensive nursing care effectively rehydrated her and ensured that she was not left in bed. The stupor was interspersed with periods of excitement throughout the early days, with the patient suddenly becoming active and, at times, abusive.

In this case, clinical features of psychogenic unresponsiveness were largely absent. When present they included the observation that hysterical patients usually lie with their eyes closed or actively resist having them opened (Plum & Posner, 1972), the very brief duration of the unresponsiveness, usually hours (Garmany, 1955), the rarity of complete dependence on staff for feeding and toileting, and the ability to stimulate a response to emotionally relevant topics (Lishman,1998). There is a preponderance of anxious,

cyclothymic and obsessional personality traits in stuporous patients (Berrios, 1981b). Although our patient had her eyes closed and was dehydrated at admission, her clinical condition remained unchanged throughout a two-week assessment period, she was occasionally incontinent of urine and faeces, and failed to demonstrate any response to topics that the daughter had suggested would be relevant. The possibility of an organic explanation for her stupor was pursued, including the mildly abnormal thyroid function tests, but was eventually excluded. It was felt that a previous, mild and non-progressive stroke confirmed by a recent CT scan could not explain the psychiatric presentation.

The treatment of stupor reflects the nature of the underlying cause. In the Maudsley series (Joyston-Bechal, 1966) almost half of the cases resolved within one week and only one-fifth lasted for more than one month. One-third resolved spontaneously, but of the physical treatments employed, ECT was regarded as the most effective. All but two of Johnson's depressive and schizophrenic patients received a course of ECT; the two depressive patients, as in our case, were treated with supportive measures and antidepressants. After a failure to improve spontaneously, our patient started moclobemide and returned to her usual self five weeks later. The justification for choosing moclobemide was manifold. Firstly, moclobemide is known to have a fast action, particularly in depression associated with psychomotor retardation, accompanied by excellent tolerability. Secondly, the patient was unable to give informed consent for ECT and her next-of-kin was reluctant to consent. Thirdly, intensive nursing care maintained the patient's vital parameters within the normal range, making sure that the principal risks to stuporous patients — dehydration, pulmonary embolism, and chest infection — were safely avoided (Johnson, 1993).

This case of early depressive stupor is important for a number of reasons. Firstly, it demonstrates a convincing response to moclobemide, a reversible MAO-A inhibitor Secondly, it serves to remind clinicians that depressive stupor is typically partial in its presentation and is therefore likely to show outbursts of excitement and intermittent preservation of feeding and toileting. Finally, and perhaps most importantly, this case report emphasises the need for careful assessment prior to treatment. Our patient was found motionless and almost mute in her home. This clinical picture, perhaps commonly assumed to be the only description of stupor, was not seen again once she was admitted to hospital. That is, skilled nursing care that repeatedly and persistently encouraged her to mobilise and accept fluids effectively masked both the signs and confirmatory electrolyte abnormalities expected with stupor. Unwittingly therefore, treatment had already been initiated during what had been an assessment period. It may be for similar reasons that stupor is seemingly an uncommon occurrence today (Johnson, 1984).

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