

## CASE REPORT

## Antidepressant Induced Suicidal Ideation

W. CREANEY, I. MURRAY and D. HEALY\*  
*Academic Unit, North Wales Hospital, Denbigh, Clwyd LL16 5SS*

KEY WORDS—Fluoxetine, fluvoxamine, suicidal ideation, akathisia, dissociation.

There has long been a view that patients who are recovering from depression are at greater risk of killing themselves than patients who are severely depressed. This paradoxical response has been attributed to a quicker resolution of depressive retardation than of accompanying suicidal ideation. This supposedly leaves subjects who are suicidal with more energy and drive to set about effecting their own demise (Kendall and Zealley, 1988; Gelder *et al.*, 1989). This explanation has a certain *ad hoc* quality to it. While it may account for some suicides in individuals recently put on antidepressants, it seems unlikely to be the only mechanism that might lead to suicide.

A recent report by Teicher *et al.* (1990) of prominent suicidal ideation commencing several days after starting fluoxetine suggests a quite different picture. Describing six cases, they reported that while the depressed mood of subjects began to lift on fluoxetine, they *became* suicidal, where they had not been before, and in a manner that suggested they had become obsessed with the idea of suicide. In attempting to account for their findings, Teicher *et al.* (1990) noted that all subjects became akathisic and postulated that the development of akathisia might be in some way related to the development of suicidal ideation.

There are a number of difficulties with this report. One is the fact that all the subjects involved had rather complicated clinical pictures with some being diagnosed as having borderline personality problems. A second is that the dose of fluoxetine used was higher than is now generally recommended. A third is that many of the subjects were taking concurrent psychotropic medication and hence ascribing the problem solely to fluoxetine seems unwarranted.

We report on two subjects. One had a reaction

somewhat similar to that of the Teicher *et al* subjects and another had one that was quite different. These reactions we believe shed further light on the issue of possible antidepressant induced suicidality.

## CASE A

Mr. A, a university lecturer was 48 when seen by us. He had been treated previously for depression on three occasions, one of which involved a notable fugue state. On each occasion there had been marked side effects to all psychotropic drugs he had been given except for benzodiazepines. In August of 1990, he was seen for complaints of depression, anxiety and increasing obsessionality. He was assessed at length on two occasions. Even so it was not possible to decide conclusively whether there was a major depressive disorder present. A trial of antidepressants was decided on for diagnostic purposes. In view of his obsessionality and his history of difficulties with other antidepressants, he was put on fluoxetine.

He took fluoxetine 20 mg for five days. On day 3 he felt 'wonderful' but could not sleep that night. It felt as though his mind was 'like a video on fast forward'. This was extremely frightening. The following day he felt 'miserable and helpless'. He found that it was 'increasingly difficult to focus on things'. He also felt that he could not stop thinking. There was no particular content to his thoughts. The quality about them that impressed him the most was how out of control they were. There was no akathisia.

He thought this state was most likely caused by the drugs but he feared they might have induced permanent damage as his misery continued after he discontinued the drug. He contacted the clinical service in considerable distress, two days after discontinuing treatment, to find out whether the

\* Author to whom correspondence should be addressed.

effects were likely to be reversible or not. He was first seen at length five days after discontinuing fluoxetine. At this point he was still feeling unwell but he had amnesia for the details of his experience.

He agreed to take fluvoxamine, having been reassured beforehand that there had been no reports of such reactions on fluvoxamine. He waited a month before starting fluvoxamine. While taking fluvoxamine he kept notes.

He took fluvoxamine 50 mg one evening and went to bed. The following day he felt agitated and was slightly nauseated but was still able to function. Later in the evening he became somewhat 'elated'. He took a second and final dose of fluvoxamine that night and found himself unable to sleep. He felt dangerous, wanting, for example, 'to get into his car and drive a long distance at high speed, while sorting out the problems of western civilisation as I went'. He had the same reaction as on fluoxetine of feeling that his mind was 'like a video on fast forward'. He had 'a distinct feeling of my brain and my body being separated, with my body tired and my brain over active'.

He was unable to sleep and got up at 6.30 am, when he felt 'dreadful and unable to do anything'. He was extremely nauseated and remained so all week, eating only one meal that week. He was dysphoric all week and found himself 'more obsessive and bothered about things'. During the course of the week, on several occasions, he noticed a distinct confusion about time—'I looked at the clock frequently that night and found that it appeared repeatedly to show the same time'. He found it difficult 'to gauge the passage of time'. He felt 'helpless, ill, mentally restless, beyond despair and suicidal'—but with no consistent thoughts of a single method of effecting his own demise.

## CASE B

Mr. B, a former manager of a large public utility, was 67 when first seen by us. He had recurrent episodes of depression over 30 years, with a history of responding better to MAOI than to tricyclic antidepressants.

His first admission to hospital for depression was in 1987. He was subsequently seen in outpatients regularly with his antidepressants being changed frequently. During 1988 and 1989, he was given flupenthixol, Parstelin (tranylcypromine with trifluoperazine), alprazolam, thioridazine, viloxazine, dothiepin, maprotiline as well as having a constant supply of either diazepam or clobazam. These were

all given in adequate doses and for reasonable periods of time but none seemed to work well. During this period, there was no hint of suicidal thoughts or gestures.

He had a second admission to hospital in January of 1990 following an overdose with nitrazepam tablets. He appeared to have sunk into a depressive state during the previous three weeks, with early morning wakening, diurnal variation of mood, poor concentration, loss of appetite and loss of interest. Eight days before admission, he was changed from the non-5HT re-uptake inhibiting, maprotiline, to dothiepin, which has 5HT re-uptake inhibiting properties (Healy *et al.*, 1985).

He failed to respond to amoxapine 10 mg bd, clobazam 10 mg tds and nitrazepam 5 mg nocte and was given 6 ECT, to which he responded. He was discharged home on thioridazine, nitrazepam, clobazam and amoxapine 15 mg tds. He did well until the end of August, when early morning wakening, diurnal variation in mood, poor concentration and loss of interest recurred.

Amoxapine was changed to trazodone with no effect. On Sept 13th, his trazodone and clobazam were replaced with fluoxetine 20 mg mane and alprazolam 250 mcg tds. According to his wife, there appeared to be a definite lightening of his spirits, increase in his sociability and decrease in the level of his retardation. But he also appeared to become more tense and restless.

Sixteen days after commencing fluoxetine, he got out of bed at 0500 hours and went out walking in the rain. He came back five hours later, with sand on his shoes but seemingly unable to give an account of where he had been. Subsequent anamnesis revealed that he had awoken intensely preoccupied by suicidal thoughts and had set off determined to kill himself. His first plan had been to throw himself into a quarry. He is insistent that the only thing that prevented this happening was his inability to find a suitable location.

Five days later, he again awoke early, left the house and went into the sea, fully clothed. In the area, the sea is shallow and he had to walk out several hundred yards to get to neck depth. At this point he had second thoughts and retraced his steps, with considerable difficulty sustaining extensive lacerations of both feet and arms in the process.

In hospital all drugs were discontinued. He had a clear major depressive disorder. A subsequent systematic set of interviews, two of which were conducted with Mr. B sedated with diazepam, revealed that there had been recurrent but not constant

images of self-harm during the five days between the two episodes. These were of a violent nature, such as cutting his wrists with a serrated carving knife or inserting a metal scissors into the electric mains with one hand while holding on to an earthed metal tap with another. He could give no good reason why he had such thoughts.

Five weeks after the last dose of fluoxetine, he was commenced on imipramine 75 mg nocte, increasing to 125 mg nocte after seven days. There was no improvement in his condition during the first week of treatment. After that he became more tense, restless and anxious. He appeared unable to sit still, stand in one place or hold a coherent conversation. There was no apparent suicidal ideation—he put this down, however, to being safe while he was in hospital.

Imipramine, which of course is a 5HT re-uptake inhibitor (Todrick, 1991) was discontinued. After a week he was started on phenelzine. Three weeks later he was substantially better and took weekend leave. A fortnight later he was discharged fully recovered.

## DISCUSSION

These two cases suggest that the emergence of suicidal ideation on antidepressants cannot always be attributed to a lifting of psychomotor retardation but rather that the ideas may in some instances be produced by antidepressants.

There are some features of case B that resemble the phenomena reported by Teicher *et al.* (1990). However, in contrast to the American cases, both of our subjects developed symptoms when on fluoxetine 20 mg per day only. In both cases, there was a past history of substantial achievement and stable functioning. In Mr. B's case there was a clear history of major depressive disorder meeting DSM III-R criteria. The deteriorating course of his illness over the previous three years can perhaps retrospectively be attributed to a clinical failure to recognise that he had a previous history of prior response to MAOI's and a lack of response to tricyclics. Of note here is that a feature of the American cases was that three of them showed a good response to MAOI's after discontinuation of fluoxetine and that the MAOI's are among the few antidepressants to have no 5HT reuptake inhibiting properties.

In our opinion, the suicidal ideas that developed in both men were out of character. Why should this have happened? Reviewing four cases of attempted suicide associated with akathisia conse-

quent on neuroleptic administration, two of which were successful, Drake and Ehrlich (1985) suggested that akathisia could lead to suicidal ideation, in patients who had had no previous suicidal thoughts.

Lipinski *et al.* (1989) noted the development of akathisia in subjects taking fluoxetine. There are physiological grounds to suspect that the 5HT system modulates the dopaminergic system in the brain (Tricklebank, 1989). Such an interaction might provide a basis for the development of effects such as akathisia. Given that most tricyclic antidepressants inhibit 5HT re-uptake, it is possible that akathisia may occur more often on other antidepressants. Lipinski *et al.* (1989), for example, noted a tricyclic antidepressant-induced 'jitteriness' which is being increasingly recognised. This may be related to akathisia. It appears to a particular risk in patients with panic-disorder.

Our first subject, however, was not akathisia. Enquiries from Eli Lilly brought the response that of 2.38 million scripts in the United States, there had been 51 cases of reported 'euphoria', 13 of 'CNS stimulation' and 11 of 'hyperkinesia'. It is not exactly clear what these terms mean as they have been applied by company medical officers attempting to categorise what may be a diverse range of reactions. As this 'euphoria' does not appear to develop into frank mania, an alternative explanation is that these are substance-induced dissociative reactions.

Substance-induced dissociation is a poorly categorised area that has recently been reviewed by Good (1989). He has pointed to the occurrence of amnesic states, depersonalisation, explosive reactions and automatisms that can all be termed dissociative; they follow the use of a wide variety of agents, including minor tranquillisers, anaesthetics and other drugs with central effects.

In case A, a good argument can be made for substance-induced dissociation, given the nature of the symptoms, the rapidity of their onset and their occurrence on small amounts of the drug. This patient's history suggested comparable prior responses to other antidepressants. A case can be made for dissociative effects in case B also, as in this case there was substantial amnesia for thoughts or feelings experienced while on fluoxetine.

A common feature of Drake and Ehrlich's and our cases was distress consequent on misattribution of drug-induced effects. Mr A, for instance, even though clear that the effects were likely to have been drug induced, suspected that the changes were

permanent, owing to their persistence after discontinuation of treatment. The emergence of suicidal ideation on antidepressants may highlight the fact that when given in clinical situations, there are potentially two sorts of side effects of psychotropic compounds. There are those that are clearly side effects, such as dry mouth or difficulties with micturition and those that may be interpreted as either side effects or as worsening of the illness. The latter include increased nervousness and restlessness and dissociative reactions such as depersonalisation, de-realisation and even hallucinations.

If suicidal ideation can arise consequent on a misattribution of drug induced changes, it should be possible to prevent all such suicides. But if such a mechanism is upheld, there may in the future be implications regarding potential medical negligence in the case of subjects committing suicide, while taking almost any currently available psychotropic compound.

#### ACKNOWLEDGEMENTS

The authors acknowledge the contributions of the nursing staff on Seiriol ward Ysbyty Gwynedd and of the patients who took an active part in the attempt to establish what was happening.

#### REFERENCES

- Drake, R. E. and Ehrlich, J. (1985). Suicide attempts associated with akathisia. *American Journal of Psychiatry*, **142**, 499–501.
- Gelder, M., Gath, D. and Mayou, R. (1989). *Oxford Textbook of Psychiatry*. Oxford Medical Publications.
- Good, M. I. (1989). Substance-induced dissociative disorders and psychiatric nosology. *Journal of Clinical Psychopharmacology*, **9**, 88–93.
- Healy, D., O'Halloran, A., Carney, P. A. and Leonard, B. E. (1986). Normal and abnormal variation in platelet 5HT uptake in control and depressed patients. *Journal of Psychiatric Research*, **20**, 345–354.
- Kendall, R. E. and Zealley, A. K. (1988). *Companion to Psychiatric Studies*. 4th edition, Churchill Livingstone.
- Teicher, M. H., Glod, C. and Cole, J. O. (1990). Emergence of intense suicidal preoccupation during fluoxetine treatment. *American Journal of Psychiatry*, **147**, 207–210.
- Todrick, A. (1991). Imipramine and 5-HT Reuptake Inhibition. *Journal of Psychopharmacology*, **5**, 263–267.
- Tricklebank, M. D. (1989). Interactions between dopamine and 5HT-3 receptors suggest new treatments for psychosis and drug addiction. *Trends in Pharmacological Sciences*, **10**, 127–129.