CASE REPORTS

Cognitive Deterioration from Long-Term Abuse of Dextromethorphan: A Case Report

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Submitted: May 10, 1993
Accepted: January 18, 1994

Dextromethorphan (DM), the dextrorotatory isomer of 3-hydroxy-N-methylmorphinan, is the main ingredient in a number of widely available, over-the-counter antitussives. Initial studies (Bornstein 1968) showed that it possessed no respiratory suppressant effects and no addiction liability. Subsequently, however, several articles reporting abuse of this drug have appeared in the literature. The drug is known to cause a variety of acute toxic effects, ranging from nausea, restlessness, insomnia, ataxia, slurred speech and nystagmus to mood changes, perceptual alterations, inattention, disorientation and aggressive behavior (Rammer et al 1988; Katona and Watson 1986; Isbell and Fraser 1953; Devlin et al 1985; McCarthy 1971; Dodds and Revai 1967; Degkwitz 1964; Hildebrand et al 1989). There have also been two reported fatalities from DM overdoses (Fleming 1986). However, there are no reports describing the effects of chronic abuse. This report describes a case of cognitive deterioration resulting from prolonged use of DM.

Key Words: dextromethorphan, abuse, toxicity, cognitive decline

CASE REPORT

A 39-year-old insurance salesman was hospitalized in an acute manic state. His level of functioning had deteriorated gradually over the preceding year and he had quit his job. During the lengthy hospitalization he was usually in a depressed state characterized by intense suicidal ideation. He also experienced restlessness and insomnia that was refractory to various sedative-hypnotics. Although he was preoccupied with religious matters during his depressive states, this rarely reached delusional proportions and he had no other evidence of psychosis while depressed.

Less frequently, he experienced brief manic-like episodes characterized by euphoric mood, aggressive and disruptive behavior, poor attention span, copious note-writing and frequent religious experiences such as communication with God, along with grandiose delusional ideas that he was chosen by God for a special purpose. These manic episodes lasted only a few days and were followed by prolonged depressive periods.

The frequency of his mood fluctuations gradually increased. There was no history of any mood disorder prior to one year before presentation, although he had a past history of alcohol dependence and had abused Gravol on a few occasions in the past. Since the onset of his mood disorder, he had been virtually abstinent from alcohol and there was neither alcohol nor Gravol detected on repeated drug screen-

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ing. His family history was negative for mood disorders but almost all his immediate family members abused alcohol. His past medical history was unremarkable.

Clinical observation of his behavior on the ward and informal assessment suggested some degree of cognitive impairment in both mood states, particularly with respect to recent memory and problem-solving ability. On the basis of these observations it was felt that a formal, quantitative assessment of cognitive functioning was warranted. This testing was conducted four months after admission. The initial testing revealed intellectual functioning in the low average to average range (Wechsler Adult Intelligence Scale – Revised (WAIS-R) full scale IQ = 89; verbal IQ = 94; performance = 84). The difference between the verbal IQ and performance IQ was significant at the five percent confidence level. Scaled scores ranged from five (object assembly) to ten (vocabulary, arithmetic). The Trail Making Test was completed in 41 seconds (Part A) and 62 seconds (Part B; approximately the 25th and 50th percentiles, respectively). While these times were not particularly suggestive of organic involvement, the performance on Part A was somewhat poorer than would be expected in relation to the patient's IQ. The bicycle drawing was extremely crude and lacked detail. A follow-up assessment was conducted 12 months later but the patient's deteriorated state prevented completion of many of the tests. He had become increasingly irritable and failed to arrive for numerous appointments. Whenever test procedures became challenging or required effort, the patient would become angry and leave the office saying "I can't do this stuff". Of the six WAIS-R subtests completed on this second occasion, scores on three (digit span, vocabulary, picture arrangement) did not change, one improved (picture completion) and two decreased (information, block design). Only two memory subtests (logical memory I and II) from the Wechsler Memory Scale – Revised (WMS-R) were completed. He scored in the tenth percentile (immediate recall) and second percentile (delayed recall). Although no previous WMS-R scores were available for comparison, these scores are significantly lower than would be predicted on the basis of the patient's IQ.

A computed tomography (CT) scan of the head several months after admission showed no abnormalities. A single photon emission computed tomography (SPECT) scan showed diffuse patchy uptake in the bilateral cerebral hemispheres suggesting a nonspecific widespread dysfunction. Electroencephalogram (EEG) did not show seizure activity but quantitative EEG mapping showed excessive central alpha activity, especially on the right side. The possibility of a concurrent diagnosis of temporal lobe epilepsy was considered in view of his episodic religiosity and hypergraphia. However, he continued to deteriorate clinically despite an adequate trial of carbamazepine.

His manic states became more severe and suggestive of an organic confusional state, including features such as visual hallucinations, slurred speech, ataxia, bilateral nystagmus in all directions, urinary retention, dysnomia, subjective feelings of brief severe muscle weakness and trance-like spells lasting up to two minutes. Although numerous previous broad drug screens had been negative, a more extensive drug screening was conducted during one of these spells. Both blood and urine testing showed the presence of guafenesin and DM. He confessed to frequent consumption of cough syrup, one bottle at a time, each bottle containing 1500 mg DM hydrobromide, 5000 mg guafenesin and 3.5 mg alcohol.

He continued to consume the cough syrup at the rate of approximately one bottle every week for several months despite advice to the contrary. Shortly after ingestion he would develop a toxic, manic-like psychosis lasting 24 to 48 hours followed by depressed mood, intense suicidal ideation and insomnia. His cognitive deterioration persisted despite periods of abstinence of several weeks when he had no access to cough syrup. Mood instability continued to be a problem as well and he remained in hospital for almost another year. Trials at rehabilitation, including a residential drug and alcohol treatment program, were all unsuccessful. He continued his abuse of cough syrup whenever he had the opportunity, despite much encouragement to abstain. His serum bromide level was 3.4 mmol/L with the therapeutic range being 9.4 mmol/L to 18.7 mmol/L and the toxic range being 12.5 mmol/L to 25 mmol/L.

DISCUSSION

There are reports in the literature of DM abuse cases similar to this one resulting in acute symptoms of euphoria, decreased attention and concentration, ataxia, nystagmus, restlessness, lethargy, tactile and visual hallucinations, confusion, depression, synaesthesias, insomnia, dilated pupils, slurred speech and aggressive behavior (Bornstein et al 1968; Katona 1986; Devlin et al 1985; McCarthy 1971; Dodds and Revai 1967; Degkwitz 1964; Fleming 1986; Orrell 1986; Helfer and Kim 1990). However, in our patient there was significant progressive deterioration in his cognitive state that was present even during periods of abstinence. We are unaware of any reports in the literature of either longstanding cognitive decline secondary to DM abuse or associated changes on brain imaging. There are reported cases of bromide toxicity, especially organic bromide, causing an irreversible cerebello-bulbar syndrome with cerebellar atrophy on CT and EEG changes (Van Balkom et al 1985). However, our patient had a low bromide level and it is unlikely that bromide toxicity is responsible for his deterioration.

Some of his symptoms might possibly be the result of an underlying temporal lobe seizure disorder, especially since DM has been known to increase the frequency of complex

partial seizures in epileptics by 25% compared to placebo (Fisher et al 1990). This could explain why the DM abuse was associated with an abnormal quantitative EEG in our patient. However, it is important to note that none of his symptoms responded to carbamazepine.

It is interesting that our patient had prolonged cognitive effects from DM toxicity while the cases reported in the literature showed only short-lived changes. It is known that five to ten percent of caucasians are slow metabolizers of DM (Hildebrand 1989) and perhaps our patient cleared the drug more slowly which resulted in greater accumulation and toxicity. While this is only speculation, it is clear that DM is not as safe a medication as was originally believed.

REFERENCES

Bornstein S, Czermak M, Postel J (1968) A propos d'un cas d'intoxication médicamenteuse volontaire au bromhydrate de dextromethorphane. Ann Med Psychol 1:447-451.

Degkwitz R (1964) Dextromethorphan (Romilor) als rauschmittel. Nervenarzt 35:412.

Devlin K, Hall A, Smolinske S, Wruk K, Kulig K, Rumack B (1985) Toxicity from long-acting dextromethorphan preparations. Vet Hum Toxicol 28:296.

Dodds A, Revai E (1967) Toxic psychosis due to dextromethorphan. Med J Aust 2:231.

Fisher R, Cysyk B, Lesser R, Pontecorvo M, Ferkany J, Schwerdt P, Hart J, Gordon B (1990) Dextromethorphan for treatment of complex partial seizures. Neurology 40:547-549.

Fleming P (1986) Dependence on dextromethorphan hydrobromide. Brit Med J 293:597.

Helfer J, Kim O (1990) Psychoactive abuse potential of Robitussin – DM. Am J Psychiatry 147(5):672-673.

Hildebrand M, Seifert W, Reichenberger A (1989) Determination of dextromethorphan metabolizer phenotype in healthy volunteers. Eur J Clin Pharmacol 36:315-318.

Isbell H, Fraser H (1953) Actions and addiction liabilities of dromoran derivatives in man. J Pharmacol Exp Ther 107:524-530.

Katona B, Watson S (1986) Dextromethorphan danger. N Eng J Med 314(15):993.

McCarthy J (1971) Some less familiar drugs of abuse. Med J Aust 2:1078-1081.

Orrell M (1986) Dependence on dextromethorphan hydrobromide. Br Med J 293:1242-1243.

Rammer L, Holmgren P, Sandler H (1988) Fatal intoxication by dextromethorphan: a report on two cases. Forensic Sci Int 37:233-236.

Van Balkom A, Van de Wetering B, Tavy D, Hekster R, Van Woerkom T (1985) Cerebellar atrophy due to chronic bromisovalum abuse demonstrated by computed tomography. J Neurol Neurosurg Psychiatry 48:342-347.