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CINNAMEDRINE: POTENTIAL FOR ABUSE

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ABSTRACT

Three cases of psychological dependence upon the over-the-counter preparation of cinnamedryl, caffeine and aspirin (Midol®) are reviewed. The relationship between cinnamedryl, amphetamine and other sympathomimetics is discussed. Similarities are noted in symptomatic response and chemical structure.

INTRODUCTION

Midol, a nonprescription preparation of caffeine (32.4 mg), aspirin (454 mg) and cinnamedrine hydrochloride (14.9 mg), is widely used for the treatment of dysmenorrhea. According to the manufacturer, aspirin and caffeine provide analgesia while the cinnamedrine acts as a smooth muscle relaxant presumably in the uterus.⁽¹⁾

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In 1982 Babington and Monson described a case of dependence on Midol in a thirty-seven year old woman who abused the drug for sympathomimetic-like effects.⁽²⁾ Due to the patient's drug history, it was felt that the abuse potential was a result of the effects of cinnamedrine rather than the aspirin or caffeine.

We describe below three additional cases of Midol abuse.

Case Reports

All three patients presented below were examined by the senior author (K.F.) at a tennis camp in upstate New York and all lived in a large Southern city and attended the same high school there. They had been introduced to the Midol habit at school where due to relative availability and inexpense of the tablets this sort of abuse was rather common. All three patients refused to even consider discontinuing their Midol consumption.

<u>Case 1</u>

This patient was a 15-year-old girl who had consumed twenty to thirty Midol tablets per day on a regular basis. She gave no history of dysmenorrhea. She stated her only reason for consumption was the "buzz" it gave her. She denied ever abusing alcohol, drugs of abuse, or caffeine products. She gave a history of diminished appetite without weight loss, difficulty falling asleep, and nocturnal sleep disorder. Most recently she complained of depression when once she was unable to obtain Midol for an

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eight-day period. Her academic performance declined steadily during this period.

Physical examination showed bilateral mydriasis, a pulse rate of eighty, increased motor activity, and no other positive findings. Mental status examination revealed a thin and tense adolescent white female oriented to person, place and time. Speech was mildly pressured but content and associations were unremarkable. The mental status examination was otherwise unremarkable.

Case 2

The second patient was another 15-year-old girl who consumed approximately twenty tablets per day for over one year. She also had no history of dysmenorrhea and reported Midol abuse for a "lift". She denied any changes in appetite or academic performance and also denied drug, caffeine, or alcohol abuse. Her need for sleep had declined by one hour nightly since beginning her Midol habit.

Physical examination was entirely within normal limits except for increased motor activity. Mental status examination revealed a thin white adolescent female with no remarkable findings.

<u>Case 3</u>

The last patient seen was a 14-year-old girl whose daily consumption of Midol had been approximately twenty tablets over a one-year period. Again there was no history of dysmenorrhea. Her sole self-stated reason for the abuse was a "chance to buzz". She also denied abuse of caffeine products, alcohol or other drugs. There was no history of academic decline though she did report nervousness and recurring intermittent nausea.

Physical examination revealed a fine resting tremor, increased deep tendon reflexed and bilateral mydriasis. Mental status examination was remarkable only for mildly pressured speech.

DISCUSSION

The description of symptomatology in the above patients is similar to Babington's and Monson's description of their patient. The presentation is also similar to that of sympathomimetic agents.

The relationship between the reported effects and clinical signs and cinnamedrine is, however, somewhat unclear. Cinnamedrine has been variously classified as a sympatholytic $^{(3)}$ or sympathomimetic agent.⁽⁴⁾ In the other reported case the authors were able to rule out caffeinism due to the relatively small amount ingested, approximately 65 to 250 mg per day, and lack of previous similar response to proprietary caffeine tablets. In our report the higher rate of daily caffeine ingestion, approximately 600 to 1000 mg per day, meets the definition of caffeinism.⁽⁵⁾ However, not all effects can be attributed to the caffeine. Caffeine has not been shown to be an anorectic and, in fact, can cause a hyperphagia.⁽⁶⁾ In addition, while the effects of caffeine may be subjectively pleasant, they do not produce a "buzz" in any dosage.

The chemical structure of cinnamedrine is related to that of three sympathomimetics including amphetamine which are illustrated in Figure 1. All

amphetamine



(-) $-\alpha$ - aminopropiophenone

(+) - norpseudoephedrine

$$\bigcirc \stackrel{\mathsf{OH}}{\longrightarrow} \stackrel{\mathsf{CH}}{\longrightarrow} \stackrel{\mathsf{CH}}{\rightarrow} \stackrel{\mathsf{CH}}{\rightarrow} \stackrel{\mathsf{CH}}{\rightarrow} \stackrel{\mathsf{CH}}{\rightarrow} \stackrel{\mathsf{CH}_3}{\longrightarrow} \stackrel{\mathsf{CH}_3}{\rightarrow} \stackrel{\mathsf{CH}_3$$

cinnamedrine (N - cinnamylephedrine)

FIGURE 1. Structural formulae of amphetamine, aminopropiophenone, norpseudoephedrine and cinnamedrine.

of these compounds produce anorexia⁽⁷⁾ and increased motor activity.^(8,9) Further, these three compounds have high abuse potential. Amphetamine is a worldwide drug of abuse from its sympathomimetic effects. Norpseudoephedrine and d-aminopropiophenone are constituents of the plant, "Khat", which is widely abused in the Arabian peninsula for effects similar to that of Midol.⁽¹⁰⁾

An interesting observation is that the few cases reported or cited in the literature involve Southern patients. This may suggest a, thus far, regional pattern. As with other regionally abused drugs such as pentazocine/pyribenzamine⁽¹¹⁾ in St. Louis, metronidazole/alcohol⁽¹²⁾ in the Great Lakes area and phencyclidine⁽¹³⁾ in San Francisco, this pattern cannot be expected to remain static.⁽¹⁴⁾ Since all three patients attended the same school, it is possible, however, that unique social factors may have reinforced this. Because of its ease of purchase as a nonregulated drug and its relatively low price, it may soon be another major drug of abuse. The inability or refusal of our three patients and that of the previously cited patient⁽²⁾ to discontinue the drug indicates that its potential for psychological dependence is quite high.

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