

Response, Addiction to Cocaine Hinge on Gender

BY ERIK GOLDMAN
Contributing Writer

NEW YORK — Men and women respond very differently to cocaine, and these differences have important clinical implications, Scott Lukas, Ph.D., reported at the annual conference of the Association for Research in Nervous and Mental Disease.

Men tend to obtain higher plasma cocaine levels from a given dose of inhaled substance, and they tend to experience more euphoria. They are more likely to become addicted and have a far more difficult time shaking cocaine addiction. On average, women absorb less cocaine from a given intranasal dose and experience much less euphoria. This is especially true during the luteal phase of the menstrual cycle.

Women who do use cocaine, however, are much more likely than men to experience cardiotoxic effects. At any given inhaled dose, women absorb less, but they have heart rate changes that are nearly identical to those seen in men, said Dr. Lukas, professor of psychiatry and pharmacology at Harvard Medical School, Boston.

Tachycardia, sometimes life threatening, is a very common effect of cocaine use in women. "Emergency room admissions for cocaine-related heart palpitations are on the order of six females for every one male," he said.

He and other researchers studying gender response to illicit drugs believe that these differences are largely influenced by sex hormones. In 1971, pioneering stress physiologist Hans Selye suggested that hormones regulate resistance to various drugs and toxins. The hormonal effects, however, can cut both ways.

Dr. Lukas explained that the nasal mucosa is under sex hormone control, just as the uterine mucosa is. Estrogen increases nasal mucosal thickness, as well as the vis-

cosity of nasal mucosal secretions. Presumably, this would lower intranasal absorption of cocaine.

A study published in 1999 by other investigators documented gender-based differences in response to 0.9-mg/kg doses of intranasal cocaine. The data showed that men consistently had higher plasma levels and reported more intense subjective experiences of the cocaine high.

At the 0.9-mg/kg dose, men showed plasma levels of 150 ng/mL at 30-40 minutes, while women in the follicular phase had plasma levels of only 70 ng/mL from the same intranasal dose.

Women who were in the luteal phase had even lower plasma concentrations. The men and women had equivalent changes in heart rate.

"Men have a pretty immediate euphoric response to cocaine, and then an hour later they have a marked crash characterized by a lot of dysphoria. Women get a

lot less euphoria, especially during the luteal phase," he said at the meeting cosponsored by the New York Academy of Medicine

Given this differential in dose absorption, it is fairly easy to understand how this

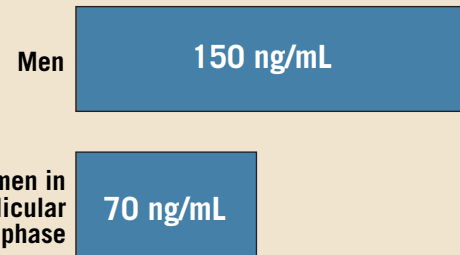
translates into cardiac problems for women who use cocaine. Dr. Lukas asked attendees to imagine a young couple out on a date.

"He wants to do some coke, and he's very excited about it. He snorts a line or two and gives the same to his girlfriend. He's immediately revved up, while she's not feeling very much. So he keeps giving her more and more, hoping she'll reach his level of euphoria." All too often, though, the young woman ends up reaching a frightening level of tachycardia and has to go to the hospital, he said.

Progesterone appears to exacerbate the cardiotoxic effects of cocaine. This has been shown in rodent experiments and in studies of pregnant women using cocaine. Dr. Lukas said the progesterone effect

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Women Absorb Cocaine More Slowly Than Men



might account in part for the observation that women have heart rate changes similar to those in men despite having lower plasma levels.

Because men are more likely to have immediate euphoric responses to cocaine, they are naturally more inclined to repeat an initial positive experience, leading to an increased risk of addiction.

According to James Anthony, Ph.D., chairman of epidemiology at Michigan State University, East Lansing, national statistics show that men are far more likely to become cocaine dependent, and they are also more likely than women to try crack cocaine.

Dr. Lukas cited a single-photon emission computed tomography study of brain changes in cocaine-dependent men and women. The study showed that men had far more detectable brain damage than the women.

"In effect, the men had lots of mini-strokes all over the brain. Women had some, but far [fewer] of them," Dr. Lukas said.

Men showed more cerebral vasoconstriction, compared with women, and overall, they were more sensitive to the brain-damaging effects of cocaine.

For reasons that are not entirely clear, men using cocaine have much greater difficulty with detoxification, he said, not that detoxification is easy for cocaine-dependent women. In general, however, women become drug free more quickly and have better long-term, drug-free response rates.

Dr. Lukas, who has conducted several studies of drug abuse among women, stressed the importance of doing this kind of research, while also acknowledging the considerable difficulties of doing drug studies in females.

"The female body is so much more complex than the male's. Men are far easier to study. With women, there are more hormonal cycles going on, menstrual cycle phases, and pregnancy, body mass, and dosing issues.

"And there are the issues related to prepubertal vs. childbearing age vs. menopausal stages of life. And of course, you have to take into account use of oral contraceptives or hormone replacement therapy," he said.

Drug research on women is expensive. He noted that it costs between \$1,200 and \$1,500 in pretrial blood work just to determine whether a woman can participate in a trial.

And there's the ongoing need for pregnancy testing.

"I can't say enough about this. Testing once at the beginning of a yearlong study is not sufficient. In our lab, we're doing cocaine and alcohol studies. Anytime a woman in one of our studies comes to my lab, she gets a pregnancy test. "In the last decade, I've detected six women who [came] to the lab to take cocaine or alcohol and did not know they were pregnant. Testing adds to the cost of a study, but it is money well spent. You don't want to unwittingly give cocaine to a woman who's pregnant," Dr. Lukas said. ■

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Nurse-Patient Interaction Helps Reduce Opioid Dependence

BY HEIDI SPLETE
Senior Writer

WASHINGTON — A team approach to managing opioid dependence with buprenorphine kept 32 of 37 patients (86%) on buprenorphine therapy at 4 months' follow-up, Daniel Alford, M.D., reported in a poster presented at the annual conference of the Association for Medical Education and Research in Substance Abuse.

The patients, who were aged 18-52 years, began treatment over a 6-month period. Most were male (62%) and white (92%). The treatment protocol included an

average of two in-person contacts and 15 phone contacts from a nurse care manager during the first 2 weeks, followed by one to four contacts per week. Follow-up visits included random urine samples, pill counts, and observations of dosing.

The team approach featured extensive interaction between patients and nurse care managers, with physician assessments and consultations.

The nurse care manager made the initial assessment of each patient's substance use, medical and

psychiatric history, and social support system by telephone, Dr. Alford said.

Physicians reviewed and fur-

Four months after patients started the program, only 13% of their opioid urine tests were positive, compared with 100% at baseline.

ther assessed the patients before enrolling them in the study and prescribing buprenorphine.

The physicians also performed physical exams at enrollment and 4 months after the start of treatment.

The nurse care manager also obtained initial lab tests, educated the patients about buprenorphine, and reviewed patient responsibilities.

The nurse case manager devised an induction schedule based on physician guidelines, and was in frequent contact with the patients until they reached their stable maintenance doses.

Patients had access to the nurse care managers by cell phone, Dr. Alford said at the conference, which was also sponsored by Brown Medical School.

After 4 months, only 13% of opioid urine tests were positive, compared with 100% at baseline, said Dr. Alford, who is with Boston Medical Center.

Ninety-two percent of the patients had social support for their treatment, and 56% were attending counseling sessions or mutual self-help meetings, he reported.

A majority of the patients (59%) had a medical comorbidity at baseline, but 68% had no usual source of primary care. Further, 54% reported psychiatric comorbidity, but only 20% had received psychiatric care prior to the study. ■