NASAL TOXICITY OF COCAINE: A HYPERCOAGULABLE EFFECT?

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Nasal insufflation of cocaine injures the nasal mucosa and can perforate the septum. Cocaine-induced vasoconstriction resulting in ischemia is one of the methods that may be responsible for this damage. We are determining whether cocaine also produces a hypercoagulable state that may compound factors which have been previously established to cause damage to the nasal mucosa and septum. This study uses Modified Recalcification Time (MRT), a test developed in our laboratory that has the ability to measure the overall coagulation process. Our study revealed no connection between cocaine and enhanced platelet function or monocyte-released tissue factor. The coagulation process was unaffected by the addition of the drug, so we conclude that cocaine does not cause a hypercoagulable state and cannot assist in the explanation regarding the ischemic changes of the nasal septum. (*J Natl Med Assoc.* 2000;92:39–41.)

Key words: cocaine ♦ coagulation ♦ ischemia

Nasal insufflation of cocaine (snorting) injures the nasal mucosa and can perforate the septum. Microvascular impairment by cocaine-induced vasoconstriction and/or bradycardia, and hypovolemic hypotension may explain the adverse effects of cocaine. However, it is unknown if cocaine acts in concert with these factors by accelerated coagulation. Platelet-activated aggregation and monocyte-activated tissue factor release are leading causes of accelerated coagulation. If either of these processes is affected by cocaine, the process of coagulation will be altered and may help to explain the injury to the nasal mucosa and septum. This study was facilitated by the availability of the Modified Recalcification Time (MRT) test developed in our laboratory. It has the unique capability of measuring the overall coagulation process rather than assessing coagulability by the determination of individual participants in the coagulation process.

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MATERIALS AND METHODS

The MRT test incorporates the contribution of all circulating cellular and chemical mediators, including the potent, but neglected monocyte-generated tissue factor, in coagulation. Most coagulation tests use plasma instead of whole blood, thereby neglecting to incorporate the influence of the cellular factors in the overall coagulation process. Also, no commonly used coagulation test assesses the vital role of tissue factor, previously referred to as thromboplastin and coagulation factor III, in clot formation in a similar manner. The MRT test will measure in part platelet function, thrombin formation, fibrinolytic changes, and, importantly, tissue factor release.

Platelet Function

Six (5 ml) samples of citrated blood were obtained from six volunteers. Aliquots (490 μl) were taken and randomly placed in seven different vials marked A, B, C, D, E, F, and G along with 10 μg of saline (Table 1). Then, A received 1 μg of cocaine,

Table 1. Platelet Function

Aliquot	MRT time
A	5.7 ± 1.6 : 1 μg cocaine
B	5.7 ± 1.6 : 0.1 μg cocaine
C	5.1 ± 1.5 : 0.01 μg cocaine
D	5.4 ± 1.5 : 1 μg cocaine
E	5.6 ± 1.5 : 1 μg cocaine + 0.01 μg epinephrine
F	5.3 ± 1.7 : 10 μl saline + 0.01 μg epinephrine

Table 2. Monocyte Tissue Factor Function

Aliquot	MRT time
A	6.5 ± 1.2 : 10 μl saline (10 min)
B	6.4 ± 1.5 : 10 μl saline (2 h)
C	4.4 ± 1.8 : 5 μg *E coli* (2 h)
D	6.6 ± 1.2 : 5 μg cocaine and 10 μl saline (10 min)
E	6.1 ± 1.5 : 5 μg cocaine and 10 μl saline (2 h)
F	4.4 ± 1.8 : 5 μg of cocaine and *E coli* (2 h)

B received 0.1 μg of cocaine, C received 0.01 μg of cocaine, D received 0.01 μg of epinephrine and 1 μg of cocaine, E received 0.01 μg of epinephrine, and F received only the 10 μl of saline. All aliquots were incubated at 37°C for 10 minutes. The MRT was determined using the Sonoclot coagulation analyzer by taking 300 μl of each aliquot and adding 40 μl of 1 mol/L $CaCl_2$ to initiate clotting.

Monocyte Tissue Factor Function

Aliquots (500 μl) of citrated blood taken out of 5-ml samples from 15 subjects were placed into six categories of vials: A, B, C, D, E, and F (Table 2). Prior to this, categories A and B received 10 μl of saline, C received 5 μg of *Escherichia coli* endotoxin (a monocyte activator), D and E received 5 μg of cocaine and saline, and F received 5 μg of cocaine and 5 μg of *E coli* endotoxin. Vials A and D were incubated for 10 min at 37°C, whereas vials B, C, E, and F were incubated for 2 h to increase monocyte-generated tissue factor. After adding 40 μl of 0.1 mol/L $CaCl_2$ to 300 μl of each aliquot, the MRT was determined instrumentally as previously described. The aliquots incubated for 10 min represent resting values; the others incubated for 2 h were used to activate monocytes and to allow sufficient time for the generation of tissue factor or other procoagulants or anticoagulants to be generated.

DISCUSSION

From the data of the experiment "Platelet Function," on comparing A, B, C, and D with G and E, and with F, no statistically significant changes in the coagulation of blood were noted. Different amounts of cocaine in the blood (10, 0.1, and 0.01 μg; in 500 μl of blood) did not result in a significant change in MRT values after comparing it with blood without the addition of any cocaine. Also, comparing the MRT values of the sample's aliquots E with F, cocaine with epinephrine in the blood did not change the coagulation. These observations suggest that cocaine does not cause a platelet-induced prothrombic state alone, or in the presence of epinephrine.

In the "Monocyte Tissue Factor Function" experiment, the data suggest that there was no change related to monocyte-generated tissue factor release when samples were intubated for different times and cocaine amounts, by comparing A with D, and B with E. Results from this experiment imply that cocaine (10 μg/ml), in vitro, does not activate monocyte release of tissue factor.

It is known that "snorting" pure or adulterated cocaine may cause nasal mucoperichondrial effects and necrosis with resultant septal perforation, sinusitis with osteitis, and loss of smell and taste. The hydrochloride portion of the molecule makes it water-soluble, acidic (pH 4.0), and topically irritating. Cocaine is a powerful vasoconstrictor and causes an effect on the microvascular circulation. Evaluation of our relevant data (in vitro) reveals no effect of cocaine on platelet function and monocyte-released tissue factor. Other hypotheses should be pursued to unravel additional factors behind the occlusion of the microvascular circulation. Future investigations should be directed toward the effects of cocaine on the endothelial lining, because it is believed that cocaine possesses characteristics that would complement its vasoconstrictive properties. Until other microvascular effects of cocaine are known, the extent and pathophysiology of the otolaryngologic complications of cocaine abuse, such as total nasal septal bony and cartilaginous necrosis with resultant saddle-nose deformity and osteolytic sinusitis secondary to chronic "snorting," will be incompletely explained.

CONCLUSION

It is believed that perforation of the nasal septum in cocaine users is a result of ischemia and may be secondary to bacterial infection. The study showed the following effects in vitro:

1. Different cocaine concentrations do not effect platelet function in platelet-activated aggregation.
2. Cocaine (10 μg/ml) does not activate monocyte release of tissue factor.

After looking at all the data, we conclude that cocaine does not cause a hypercoagulable state, which may lead to microvascular impairment and ischemia. In addition to vasoconstriction, other alternative effects of cocaine should be investigated to resolve the pathophysiologic explanation of the ischemic changes of the nasal septum in the cocaine user. One possible approach could be studying the endothelial cells. Endothelial cells that line the capillaries also release tissue factor. Cocaine might enhance tissue factor release by acting on the endothelial cells. Only future studies will give better insight on how cocaine further induces ischemic changes by affecting the hypercoagulable state.