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Current Trends in the Abuse of Pentazocine and Tripelennamine: The Metropolitan St. Louis Experience

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ABSTRACT: A discussion of the intravenous use by narcotic addicts in metropolitan St. Louis of a combination of pentazocine and tripelennamine, known as "T's and blues," is presented. The folklore and ritual of "T's and blues" use were gleaned from interviews with addicts. The cause of, possible adverse reactions to, and medical examiners' experience with this new mode of drug abuse are discussed. Pharmacology relative to the abuse of pentazocine and tripelennamine is reviewed.

KEY WORDS: toxicology, pentazocine, tripelennamine

Pentazocine is a potent analgesic indicated for the relief of moderate to severe pain. In 1965, the World Health Organization Expert Committee on Dependence-Producing Drugs [*1*] concluded that there was little likelihood of pentazocine being abused, that it presented no significant risk to public health, and that there was no need for narcotic controls of pentazocine either internationally or nationally.

In July 1967, permission was granted by the Food and Drug Administration to market the drug in the United States. At that time, the drug was heralded as a nonaddicting potent analgesic [*2*] ushering in "a new era in analgesia" [*3*]. One year later the manufacturer received the first case report of dependence to parenteral pentazocine [*4*]. Since then, the ability of pentazocine to produce psychic craving, euphoria, tolerance, and physical dependence has been well documented [*5-7*]. However, abuse of pentazocine has generally been within the medical-medicine context, that is, the "therapeutic community." As stated by Inciardi and Chambers [*8*] in 1971, "Abuse or dependence ... [is] associated with physicians overprescribing, pharmacists overfilling prescriptions, and inadequate internal controls of institutional drug supplies." Pentazocine abuse was not associated with the "heroin addict" and was seldom encountered on the illicit drug market.

This communication concerns the abuse of pentazocine as a street drug and its present

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popularity on the illicit drug market in metropolitan St. Louis, Mo. The drug is generally used in combination with tripelennamine, an antihistamine occasionally used by heroin addicts in illicit narcotic preparations [9]. The mixture of pentazocine and tripelennamine is known as "T's and blues." "T's" refers to the trade name of pentazocine, Talwin®, and "blues" is slang derived from the light blue color of the 50-mg tripelennamine tablets marketed under the trade name Pyribenzamine®. Portions of the information presented here are derived from interviews with area drug counseling and law enforcement personnel, cases from the toxicology laboratory of St. Louis University, and personal interviews with area drug addicts.

Use of the Drugs

Widespread use of the combination of pentazocine and tripelennamine among narcotic addicts in St. Louis apparently began in the summer of 1977. Pentazocine was represented on the illicit drug market as "synthetic morphine." The mixture was well known in Chicago and use in St. Louis probably developed because of the geographic proximity of the two cities and close ties between the two within the illicit drug market. At the time of the appearance of abuse of the combination in St. Louis, illicit heroin mixtures were of a poor quality, some mixtures containing less than a half percent of heroin.[3] Until 1979, when the Drug Enforcement Administration added pentazocine to Schedule IV of the Controlled Substance Act, the sale of the drug did not carry the strict legal penalty associated with the sale of heroin under the Missouri Controlled Substance Act. The compounds were illegal to sell without prescription under federal law; however, the offense was only a misdemeanor. Since pentazocine was sold to addicts as synthetic morphine, and illicit sales were not a felony, the trade in T's and blues became a profitable business. Within months after their introduction, a "drug war" erupted over their distribution rights, resulting in several homicides.

The drugs are sold in their legitimate commercial solid dosage forms, 50 mg pentazocine (Talwin) and 50 mg tripelennamine (Pyribenzamine) tablets. Pentazocine may be used alone, but generally various ratios of pentazocine to tripelennamine tablets are used at one time. Addicts refer to "doing 6/2 or 8/3 tablets." Users titrate themselves, varying the tablet ratios upward until the desired subjective or euphoric state is obtained. Conversations with T's and blues users do not reveal hard-and-fast rules regarding combination usage; for example, extremely high doses of pentazocine will be used with or without appropriate ratios of the antihistamine. Users are well aware of the ability of the antihistamine alone to produce convulsions. Users will often increase the dose of tripelennamine in combination with pentazocine until convulsions occur; after that point the dose is reduced.

The tablets are placed in a vial and allowed to dissolve in a small quantity of water. Disintegration of the pentazocine tablets is rapid and the hydrochloride salt quickly dissolves. The tripelennamine tablets resist disintegration somewhat, and usually need to be ground into a powder that is then added to the vial. The resultant solution is then drawn through cotton into a 3.0-ml syringe and injected intravenously. Addicts using only pentazocine reported "soaking" 60 to 90 tablets a day and injecting themselves three or four times daily with this solution. Although there is a wide variation, estimates of the dose of pentazocine used range from 200 to 600 mg per injection This accounts for statements by addicts that the commercially available parenteral ampules of pentazocine do not produce the euphoria of the tablets. The commercial product contains only 30 mg/ml. Tripelennamine doses vary from 100 to 250 mg per injection.

[3]Harold Messler, chief criminalist, St. Louis Police Department, St. Louis, Mo., personal communication.

Adverse Effects of Abuse

The most often reported adverse effects of the intravenous use of pentazocine and tripelennamine together are nausea, vomiting, and headache, all well-recognized side effects of large doses of pentazocine alone [*10*]. More serious adverse reactions reported were convulsions and loss of consciousness, particularly following rapid injection of high doses of the mixture. Tonic-clonic seizures and central nervous system excitation are well-recognized side effects of large doses of antihistamines [*11*], and in T's and blues users are probably due to the tripelennamine. In this regard, addicts interviewed indicated that they did not inject tripelennamine alone because "everyone knows blues alone cause convulsions." The subjective effects of the drugs, like all psychoactive agents, may vary with the mood of the user. Although sedation and a dreamlike euphoria are the predominant effects, several users were reported to be highly excited or stimulated at times. This may be related to an increase in the tripelennamine dose administered.

Dysphoria and a feeling of paranoia occasionally occur with use of the drugs. Addicts indicated that while the mixture is not preferred to heroin, it is, at the doses administered, an acceptable alternative. Asked if T's and blues were as good as, or better than, heroin, one addict typified the response of those interviewed by replying, "There ain't nothing in the world better than good smack." However, one addict was extremely enthusiastic about the combination and stated that "after T's and blues, heroin is a thing of the past."

Immediately following intravenous injection of the mixture, addicts often lose consciousness and, upon regaining their senses, are unable to recall the events surrounding the injection. This loss of short-term memory appears to be a common experience. Addicts indicated that persons using the drugs regularly for several months often had lapses in memory and at times a diminution of long-term memory. Disorientation following intravenous administration of pentazocine is a known side effect of the drug [*10,12*]; however, at present the literature contains no mention of possible memory impairment. Pentazocine, at therapeutic doses, has been reported to occasionally produce visual hallucinations [*10*]; however, users of T's and blues, even those with prior experience with hallucinogenic agents, did not report hallucinating effects.

A burning sensation and irritation at the site of injection is another common complaint. Local irritation and narcotic tissue damage are known to occur following intravenous use of pentazocine in hospitalized patients [*10*].

Perhaps the greatest damages associated with T's and blues abuse are those of any form of intravenous drug addiction involving nonsterile injections and intravenous injections of insoluble tablet particle matter. The development of infections, both local and systemic, and the transmission of disease (hepatitis, venereal disease, and others) are well-documented entities of intravenous drug abuse [*13-15*]. Talwin and Pyribenzamine tablets both contain insoluble materials. The development of pulmonary occlusion disease resulting from drug abuse, and in particular from the intravenous injection of tablet material, is well recognized [*16-18*]. Insoluble tablet materials carried to the lungs are known to cause thrombosis and occlusion of arterioles and capillaries and elicit granuloma formation with parenchymal fibrosis [*19,20*]. The physiologic end result of these processes may include restrictive ventilatory disturbances, impairment of oxygen transfer across the alveolar-capillary membrane, and pulmonary hypertension.

Medical Examiners' Cases

In postmortem toxicological analyses for the Medical Examiners Offices of St. Louis County and the City of St. Louis, T's and blues have been identified in ten cases (Table 1). No death was attributed to a fatal intoxication from the drugs. With the exception of one carbon monoxide suicide, all deaths were homicides. Toxicological drug screening

TABLE 1—*Medical examiners' cases positive for pentazocine and tripelennamine.*

Toxicology Case	Age	Sex	Race	Cause of Death	Verdict	Other Toxicologic Findings[a]
77-926	20	male	black	gunshot wound	homicide	ethanol, 146 mg/dl
77-1426	27	male	white	carbon monoxide poisoning	suicide	hemoglobin carbon monoxide, 78%; morphine
77-2117	29	male	black	gunshot wound	homicide	none
77-2912	34	male	black	gunshot wound	homicide	none
78-1849	34	male	black	gunshot wound	homicide	none
78-1893	33	male	black	gunshot wound	homicide	chlordiazepoxide
78-2239	29	female	black	gunshot wound	homicide	none
78-2328	30	male	black	stab wound	homicide	ethanol, 22 mg/dl; diazepam; meprobamate
78-2549	29	male	black	gunshot wound	homicide	ethanol, 43 mg/dl; phenobarbital
78-2843	36	female	black	gunshot wound	homicide	morphine

[a] Carbon monoxide and ethanol are reported as concentrations in blood; all other drugs are reported as qualitative urine results.

for the presence of pentazocine and tripelennamine was initially performed on urine by the thin-layer chromatographic (TLC) method of Davidow et al [*21*]. This procedure does not separate pentazocine and tripelennamine (System A, Table 2). However, acid hydrolysis of urine results in partial conversion of pentazocine to its alcohol metabolite [*22*], which is then easily distinguished from tripelennamine, nicotine, and narcotics such as methadone or morphine that may also be present. An alternative TLC system [*23,24*] can be used to separate the urinary products resulting from T's and blues use (pentazocine, pentazocine-*trans*-acid, pentazocine-*trans*-alcohol, and tripelennamine) as well as other commonly occurring drugs (System B, Table 2).

Discussion

The pharmacological rationale behind the use of combinations of pentazocine and antihistamines is open to speculation. Pentazocine is an effective narcotic agonist and a weak antagonist. It is not surprising that the extremely large doses of pentazocine used by addicts produce heroin-like effects. Therefore, molecular mechanisms to explain the effects desired by addicts have included actions on physiological disposition of the classical neurotransmitters such as norepinephrine, serotonin (5-hydroxytryptamine), and dopamine [*25*]. It is intriguing to speculate that pentazocine, acting as a narcotic agonist, might also alter the physiological disposition of the newly postulated neurotransmitters, such as the enkephalins and endorphins, that have morphine-like effects. Tripelennamine has also been reported to potentiate catecholamines and other neurotransmitters [*26*]. The mechanism of this effect is thought to be a cocaine-like action on sympathetic nerves, that is, tripelennamine blocks re-uptake of neurotransmitters into the nerve endings [*27*]. Furthermore, if a similar mechanism operates within the central nervous system and involves such powerful pharmacological agents as the endorphins, then the combined effects of large doses of pentazocine and tripelennamine in producing the drug "rush" could be understood.

Additionally, tripelennamine is a potent local anesthetic (having greater potency than procaine) and the well-known effect of large doses of tripelennamine to produce convulsions is due to alteration of sodium/calcium composition and membrane permeabilities. Recent work by Snyder [*28*] on the ionic composition of the opiate receptor has shown that sodium fluxes dictate agonist or antagonist activity. It is interesting to speculate that tripelennamine could alter the sodium balance within the opiate receptor, thus enhancing the agonistic activity of the pentazocine.

TABLE 2—*Thin-layer chromatographic systems used to identify drugs in urine.*[a]

Compound	System A,[b] R_f	System B,[c] R_f
Methadone	0.84	0.33
Methapyrilene	0.74	0.31
Morphine	0.15	0.21
Nicotine	0.68	0.21
Phencyclidine	0.86	0.46
Pentazocine	0.70	0.65
Pentazocine-*trans*-alcohol	0.61	0.47
Pentazocine-*trans*-acid	0.26	0.39
Tripennamine	0.72	0.26

[a] All drugs chromatographed on precoated silica gel, 250 μm thick, on 20- by 20-cm glass (Whatmann LK5D). All runs, 15 cm. Drugs/metabolites were detected by spraying the thin-layer chromatograms with iodoplatinate.

[b] Ethylacetate/methanol/ammonia (85:10:5) [*21*].

[c] Dioxane/72% acetic acid solution (94:6) [*22,23*].

Conclusion

It is now over a year since the first reports appeared in the literature on the abuse of pentazocine and tripelennamine [*29,30*]. There seems to be no indication that the use of T's and blues is decreasing, even though pentazocine has been placed by Illinois into Schedule II and by the Drug Enforcement Administration into Schedule IV. It is well known that street drug use is very faddish, and it remains to be seen whether T's and blues are destined for years of abuse. Reports are already being received of pentazocine/tripelennamine use in other cities[4] (New Orleans, Buffalo, New York) and, perhaps more alarmingly, the use of pentazocine in combination with other more potent pharmacologic agents such as Ritalin®.

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