Thinner Ingestion Causes Hyperthermia

Tiner Zehirlenmesi ve Yüksek Ateş İlişkisi

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ABSTRACT Objective: Acute thinner intoxication is unusual and its clinical effects after ingestion are relatively unknown although, its physical features as a clear, colorless liquid with a sweet, pungent odor makes it a potential agent for household accidents and an ingestible poison especially for infants. Herein, we would like to draw attention to a previously unrecognized feature of thinner. **Material and Methods:** A total of 32 patients admitted with thinner ingestion between 1984 and 2006 were included in the study. Demographic specifications, amount of toxin ingested, body temperature, hyperthermia timing, accompanying infections, antibiotic use, vomiting, cough, level of consciousness, serum liver and renal function tests, urine analysis, and length of stay data were investigated retrospectively. **Results:** This study presents the clinical features of 32 children with thinner ingestion. The most impressive finding was the presence of hyperthermia (axillary body temperature >37.2°C) in 66% of the patients. Besides, 50% of the patients who received antibiotics had no accompanying evidence of infection except fever. **Conclusion:** The current study well demonstrates the clinical relationship between thinner ingestion and fever. We suggest that acute thinner ingestion may cause fever via increased lipid peroxidation products in the brain; however, this hypothesis needs further investigations for clarification. The knowledge that thinner itself plays a role on fever generation may decrease the gratuitous use of antibiotics in thinner ingestion.

Key Words: Toluene; poisoning; hyperthermia

ÖZET Amaç: Oral yoldan akut tiner zehirlenmesi nadir görüldüğü için kronik tiner zehirlenmesine göre daha az bilinir. Oysa, tiner hoş kokulu, renksiz ve berrak görünümüyle, çocuklar için ağızdan alımı kolay bir zehirdir. Bu makale ile tiner zehirlenmelerinde daha önce fark edilmemiş olan bir klinik özelliğe dikkat çekmek istedik. **Gereç ve Yöntemler:** Tiner zehirlenmesi sebebiyle 1984-2006 yılları arasında çocuk yoğun bakım ünitesine yatırılarak izlenen 32 hastanın dosya kayıtları geriye dönük olarak incelendi. Demografik özellikler ile birlikte alınan tiner miktarı, vücut sıcaklığı, ilk yüksek ateş zamanlaması, eşlik eden enfeksiyon varlığı, antibiyotik kullanımı, kusma veya öksürük varlığı, bilinç düzeyi, karaciğer ve böbrek fonksiyon testleri, idrar tahlili sonuçları ve hastanede kalış süreleriyle ilgili veriler analiz edildi. **Bulgular:** Oral tiner zehirlenmesi sebebiyle izlenen 32 olgunun klinik bulguları ortaya konmuştur. En çarpıcı bulgu, hastaların %66'sında yüksek ateş (koltuk altı vücut sıcaklığı >37.2°C) varlığıdır. Tedavi sürecinde antibiyotik kullanılan hastaların %50'sinde yüksek ateş dışında enfeksiyon lehine kanıt bulunamamıştır. **Sonuç:** Bu çalışma ile tiner zehirlenmesi ve yüksek ateş ilişkisi ortaya konmuştur. Tiner zehirlenmelerinde gözlemlediğimiz yüksek ateş reaksiyonunun beyinde ortaya çıkan lipid peroksidayon ürünlerine bağlı olabileceğini düşünmekteyiz; ancak, bu hipotezin ispatlanabilmesi için yeni deneysel çalışmalara ihtiyaç vardır. Tiner zehirlenmesinin kendi başına yüksek ateş sebebi olabileceğinin bilinmesi bu olgularda gereksiz antibiyotik kullanılmasını azaltabilir.

Anahtar Kelimeler: Tiner; zehirlenme; yüksek ateş

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Thinner is a chemical mixture that contains toluene, frequently concomitant with xylene, benzene, acetone, methanol, hexane, n-butyl acetate, ethanol and other substances. They are widely used as aromatic industrial solvents in textiles, paints, lacquers, glues, gasoline additives and solvent-based cleaning fluids. They are also used in rubber and plastic industries. The main agent in thinner compound is a neurotoxin called toluene, which constitutes approximately 60-70% of thinner ingredient.[1,2] It is a clear, colorless liquid at room temperature which gives it an appearance of water in pellucid bottles creating a drinkable image for children. Toluene has a sweet, pungent odor like benzene.

The role of oxygen radicals, like malondialdehyde, on fever mediation have been recently demonstrated.[3,4] After being exposed to thinner, significantly increased levels of lipid peroxidation products like malondialdehyde have previously been shown in hippocampus, cortex and cerebellum of animal models.[1,5] Considering these data in the literature, we suggest that acute thinner ingestion may play a pyrogenic role via increased lipid peroxidation products in the brain. Our experience of 32 pediatric patients with acute thinner ingestion between 1984 and 2006 revealed a clinical realization of hyperthermia with a 66% frequency.

Acute intoxication via ingestion is rare and the clinical effects after acute thinner ingestion are relatively unknown.[6,7] Its physical features make it a potential agent for household accidents and an ingestible poison especially for infants. Herein, we would like to draw attention to a previously unrecognized feature of acute thinner intoxication.

MATERIAL AND METHODS

A total of 32 patients admitted to the hospital with thinner ingestion between 1984 and 2006 were included in the study. A retrospective investigation was performed trough their charts. The time from exposure to admission, gender, age, amount of toxin ingested, maximum body temperature, first hyperthermia time, accompanying infections, antibiotic use, vomiting, cough, level of consciousness, serum liver and renal function tests, urine analysis, and length of stay in the hospital data were all gathered. Hyperthermia was defined as axillary body temperature above 37.2°C.[8] The results were analyzed by Statistical Package for Social Science (SPSS) software version 11.5. The Mann-Whitney U test was used to compute comparisons to determine differences between the groups. As being a retrospective one, this study does not conflict with the Declaration of Helsinki.

RESULTS

Totally 32 patients were admitted to the hospital with thinner ingestion between 1984 and 2006. Twenty-five were males (78%) and 7 were females (22%) with a mean age of 2.1 years (1-5 years) (Table 1). This difference in gender correlates well to the general accident incidence in children under five. Ingested amount of the thinner ranged from a sip to 150 mL (estimated mean 25 mL). Mean interval from exposure to admission was 1.8 hours (0-11 hours). Temporarily depressed consciousness was a common feature (28%) on admission. Seventeen patients suffered from vomiting and 5 patients had coughing episodes. Most common feature observed throughout the admission period was fever. Twenty one (66%) patients presented with hyperthermia (Table 2). The mean highest body temperature was 38.5 ± 0.7°C (37.4-39.9°C) (Table 1). The first rise of the body temperature took a mean time interval of 13.3 ± 9.4 hours (3-36 hours) (Table 1). Neither vomiting and coughing nor depressed consciousness had a significant correlation with fever. Fourteen (44%) patients received antibiotics, while only seven had a documented infection: one concomitant urinary tract infection, one preseptal cellulites, one perianal abscess and 3 with emerging pneumonitis. The

TABLE 1: Characteristics of fever in thinner ingested patients.

	n	Min	Max	Mean	Std. Deviation
Age (year)	32	1.0	5.0	2.1	.952
Fever onset time (hours)	21	3	36	13.3	9.380
Body temperature (°C)	21	37.4	39.9	38.5	.714

TABLE 2: Rate of fever in thinner ingested patients.

	n	%
Total patients	32	100
No fever	11	34
With fever	21	66
Fever with concomitant infection + antibiotic use	7	22
Fever without infectious evidence + antibiotic use	7	22
Fever without infectious evidence + no antibiotic use	7	22

remaining (50%) antibacterial treatment applied patients did not carry a strong evidence of any infectious process except hyperthermia (Table 2). The mean time for hospital stay was 2.9 ± 2.8 days (1-15 days). Presence of high fever did not prolong the length of stay in hospital in patients who did not have a concomitant infectious process (p: 0.294). No relationship was demonstrated between the amount of toxin ingested and fever (p: 0.442). Liver and renal function test results revealed normal.

DISCUSSION

Toluene belongs to a group of organic compounds known as alkyl benzenes. Toluene toxicity commonly presents as inhalant abuse. Clinical effects of chronic abuse are well described and include cardiac, renal, pulmonary, hepatic and neurologic damage.[6,9] This product was been shown to cause functional and structural changes in the central nervous system. Acute and chronic effects of toluene on neurons have been previously documented.[10] Acute toluene intoxication via ingestion is unusual and its clinical effects after acute ingestion are relatively unknown. Acute poisoning may be fatal with high doses. Fatal dose is considered 45-50 mL.[11] Toluene is readily absorbed by ingestion of thinner and may cause hepatic, renal, cardiac insufficiency, pneumopleurisy, rhabdomyolysis and fulminant polymyositis as a wide impact poison.[2,11,12]

The current study presents the clinical features of acute toluene ingestion in a relatively large study group. Temporary loss of consciousness, vomiting and cough seems to be the frequent clinical features of oral toluene intake. One of the main aims of this study was to draw attention to a particular clinical feature of toluene ingestion, hyperthermia. Current medical literature lacks the evidence on the pyrogenic effect of toluene. This may be due to the clinicians' lack of awareness about the recent theories on fever generation.

Recently it has been suggested that nitric oxide (NO) and oxygen radicals, but not prostaglandins, modulated fever.[3] Fever originates from central nervous system; however, neither exogenous nor endogenous pyrogens are able to cross the blood-brain barrier and the true signal-transmitting pathway through the blood-brain barrier structures is still unknown.[4] Immediately pursuing a pyrogenic stimulus like bacterial endotoxins, there exists an increased production of free oxygen radicals in the circulation by cells of the reticuloendothelial system, followed by the release of cytokines considered as putative endogenous pyrogens. Enhanced formation of NO lowers the thermoregulatory set point.[4] Malondialdehyde level measurement provides an estimation of free oxygen radical production.[3] Investigations on rats pretreated with methylene blue, an inhibitor of superoxide and hydroxyl radical production, revealed a diminished febrile response to lipopolysaccaride (LPS) implementation. Methylene blue lowered the levels of malondialdehyde formation (as an index of lipid peroxidation) in rats representing the role of oxygen radicals in fever formation.[4] Another similar vivisect on rabbits demonstrated that intravenous administration of the NO synthase inhibitor (N-nitro-L-arginine) could reduce the LPS-induced rise in body temperature.[13] Even aspirin which has well known antipyretic action through inhibition of cyclooxygenase activity, also acts as an oxygen radical scavenger. This knowledge high-rises a suspicion of its true effect on fever.[3] Riedel et al has recently reported that inhibition of oxygen radical formation by methylene blue, aspirin or α-lipoic acid prevented bacterial-lipopolysaccharide-induced fever in rabbits.[14]

Thinner exposure causes a significant rise in malondialdehyde in all brain regions. After being exposed to thinner, levels of lipid peroxidation products like malondialdehyde in hippocampus, cor-

tex and cerebellum have previously been shown to be significantly increased compared to those in control rats.[1] A similar investigation also demonstrated that intraperitoneal injection of toluene caused significant elevation in the rate of reactive oxygen species generation in the brain.[5] Toluene generates reactive oxygen species and the toxic effects associated with these reactants.

Accordingly, one may easily suggest that malondialdehyde formation in the brain secondary to toluene ingestion may play a role on fever formation.

There exists very little clue about fever and toluene in the literature, such as a pediatric case of toluene ingestion who presented with fever in the first day of admission with concomitant severe toxic features.[6] Although the authors suggested an intercourse with chemical pneumonia for fever, the presence of fever itself may be meaningful for that case. Although 43% of our cases received antibiotics, only 21% had a documented infectious etiology. Fever following thinner ingestion may easily be misdiagnosed as developing chemical pneumonia.

Although it was previously postulated that oral intake of thinner might increase serum transaminase and urate levels, we did not observe renal or hepatic impairments in our patients.[2] Similarly, changes in blood chemistry like increase in creatinin and blood urea nitrogen and acidosis had also been reported in inhalation abuse of toluene; however, in our series we did not observe such deviations.[2]

Regarding the recent knowledge from the literature about the role of oxygen radicals in fever formation and the effect of toluene on oxygen radical formation in the brain tissue, we may conclude that acute thinner ingestion may cause fever via lipid peroxidation products in the brain. This clue may prevent clinicians from misinterpreting of fever as a sign of infection and irrational use of antibiotics in case of thinner ingestion. Further investigations are needed to elucidate the pyrogenic effect of toluene in man.

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