

Original Research Paper

Fatal Dextropropoxyphene Poisoning An Autopsy Study of 11 Cases

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Abstract

Dextropropoxyphene is an opioid analogue with antitussive and analgesic action. The drug is available widely in the market under various trade names and even without prescriptions. Its abuse is well known and deaths due to its use have been reported. A few fatal cases have been reported from India as well. We hereby describe 11 cases of death due to Dextropropoxyphene poisoning reported in the Department of Forensic Medicine and Toxicology, All India Institute of Medical Sciences, New Delhi during the period from March 2011 to August 2012. The majority of cases were males (90.9%) predominantly of the young adult age group. Six (54.5%) of those deceased, were belonging to North Eastern part of India, staying at Delhi. All were unemployed and majority of them were addicted to multiple drugs. In all the cases, cyanosis of finger nails, congestion of organs and pulmonary edema were observed. The details of the autopsy along with histopathological findings and its preventive measures are briefly discussed in this paper.

Key Words: Dextropropoxyphene addiction; Drug abuse; Death; Autopsy; Prevention

Introduction:

The increasing trend of drug abuse is a global concern, as the most productive age group of a population is affected by this social evil. Abuse of drugs meant for medical purposes makes it more challenging problem to tackle.

Developing countries like India forms one of the major pharmaceutical markets of the world. There are loopholes in law to regulate the restriction of availability of such drugs for other than medical uses. Many such drugs which are banned in developed countries due to their toxicity are still openly marketed. All these factors in combination are costing thousands of lives; Dextropropoxyphene/Propoxyphene is one such commonly abused drug in India. [1]

Dextropropoxyphene and its various combinations are over the counter available drugs in India in the trade name of **Spasmaproxyvon, Spasmocip Plus and Relipen** etc. [2]

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Dextropropoxyphene is an opioid analogue structurally related to methadone. Its L-isomers is responsible for antitussive actions whereas analgesic effect resides in the D-isomers by actions on 'mu'-receptors but less selective than morphine. Due to the selective action on the 'mu'-receptor, it has high addictive potential. Serum peak level is reached within one hour following rapid oral absorption.

It is metabolized in liver by N-demethylation to produce a more active metabolite nor-propoxyphene. The half-life of propoxyphene is 6 to 12 hours whereas nor-propoxyphene is 37 hours. Due to prolonged half-life, nor-propoxyphene is believed to play a role in the prolonged clinical course following an overdose. [3-5]

The authors studied deaths in which associations with drugs containing Dextropropoxyphene were strongly established after considering the history, histopathological and autopsy findings of cases.

Case Series:

We studied 11 cases of death, over a period from March 2011 to August 2012, with alleged history of propoxyphene poisoning; the autopsies of all such cases were conducted at the Department of Forensic Medicine and Toxicology, All India Institute of Medical Sciences, New Delhi.

History and relevant facts were collected from the submitted inquest papers and by

questionnaires to the relatives, which are documented in a tabular form. (Table 1)

The cases with definite history of addiction to propoxyphene containing drugs and cases in which empty foils of propoxyphene containing drugs are found in the crime scene or in the deceased's clothing/ pocket are included in the study. Causes of death other than poisoning were ruled out in autopsy.

In our study we observed that, 10 out of 11 victims were of the age group between 20-30 years. Only one of the 11 victims was a female. Six out of the eleven victims were from the North eastern region of India.

All the victims were found to be unemployed except the female victim who was a housewife. In five cases, there was a definite history of addiction to propoxyphene containing tablets. In eight cases empty wrappers of propoxyphene containing tablets were recovered either from the crime scene or from the clothing/pockets of the deceased.

In three cases (3, 4, 5) the body of the deceased were found in various stages of decomposition. In all other cases the deceased were brought dead to the hospital. In two cases (6, 10) the deceased had previously attended the de-addiction centers multiple times and were discharged after improvement. In seven cases (2, 4, 5, 6, 8, 10 & 11) along with propoxyphene there was definite history of addiction to multiple agents including alcohol.

Autopsy Findings:

On autopsy, in all the eleven cases cyanosis of finger nails, congestion of organs and pulmonary edema were observed. (Fig.1-4) In 4 cases (1, 3, 6, and 7) minor injuries like small contusions, abrasion and cut were found on the extremities of the body.

On histopathology examination, kidneys showed Medullary congestion and lungs showed edema and congestion. (Fig 5, 6) Histology of other organs was within normal limits.

Viscera of all the cases were sent for chemical analysis and dextropropoxyphene came as positive in one case, whereas the reports of other cases are awaited.

Causes of death other than poisoning had been ruled out by autopsy. Manner of death could not be determined with absolute certainty in our cases but accidental overdose was strongly suspected on the basis of police inquest papers and history.

Discussion:

Propoxyphene was first marketed in 1959 and the first death due to its toxicity was reported in 1964. [6] There after numerous

studies regarding its toxicity were reported from different parts of the globe. The first hundred fatal poisoning due to propoxyphene were reported from North Carolina. 65% of such deaths were due to suicide and the ratio of deaths of women to men was more than two (45 out of 65 suicidal deaths). [7] In India, deaths due to propoxyphene abuse are rarely reported and literature in this regard is scarce. Kaur N et al conducted a review study in which three cases of fatal propoxyphene poisoning were reported. [8]

We have found that majority of the victims were of the age group 20-30 years. This observation may be due to the higher peer group influence in this group of population, who turn into victims of drug abuse. This is in accordance with the study conducted by Birgitta Jonasson et al who observed that "age to be an important characteristic regarding the choice of drug and found that younger people predominantly died of Dextropropoxyphene abuse". [9] Similar finding was observed among the treatment seekers who reported for treatment were youngsters and were more often abusers of drugs like propoxyphene. [1]

The observation that "abuse of drugs was a predominantly male phenomenon" was established by a Focused Thematic study, based on interviews of subjects across multiple sites in India. In our study male victims (90.9%) outnumbered significantly to those of the females (9.1%). This finding further strengthens the above fact. [1] Unemployment, poor education, corruption and organized crime have a vicious relation with drug abuse. [10]

In our study, ten out of eleven victims were unemployed and one was a housewife. This significant finding is in lieu with the above observation. In three cases, the bodies were found in various stages of decomposition in their residence. This observation highlights the social detachment of the victims as well as secluding themselves during the use of such drugs.

In two of our cases (18.1%), the victims had previously attended the de-addiction centre multiple times and were discharged. But they resumed the use of contraband drugs which demands the need of continuous long term support as well as rehabilitation.

In seven cases (63.6%), there were history of addiction to multiple agents, like Diazepam, Ketamine, alcohol and other I.V drugs though many of them started abusing a single drug for recreational purposes, they gradually developed addiction to multiple drugs because of peer groups and other social activities. This observation highlights the

propensity in addicts for multiple drug abuse and proves drug abuse as a psycho-socio-medical problem. In our study 6 out of 11 (54.5%) victims were from North Eastern region of India. In Delhi, the populations of North Eastern origin are meager as compared to total population. So finding of 54.5 % of victims being from the North-eastern region is significant.

Spasmodoxyvon and other similar compositions are one of the most abused drugs in the North Eastern region of India. [1] Probably, the migrated population of these region have carried this particular trend to the study region (South Delhi) and thus showed increase number of death in that ethnic group.

In propoxyphene intoxication, respiratory and the cardiovascular system are most adversely affected. Propoxyphene is responsible for both Central Nervous System and Cardiac toxicity, whereas the major metabolite Nor-propoxyphene contributes only to the cardiac toxicity. This is manifested as dysarrhythmias along with prolongation of QT interval and PR-interval in ECG. These signs and symptoms are developed within 1 hour of intake. [11] This explains the asphyxial signs observed in the victims at autopsy and the sudden nature of death of the victims.

Hudson Page et al found at autopsy that lungs were heavy, edematous and congested with abundant white froth in respiratory tract in their cases. [7] The findings, we observed at autopsy in our cases are in agreement and additional to that observed by them.

Weighing overall balance between risk and benefit, FDA (Food and Drug Association) recommended removing all the products of propoxyphene from the US market. [12] Similarly, European Commission has banned the use of Dextropropoxyphene since 2011. [13, 14] Dextropropoxyphene is listed as a controlled substance in India also under the NDPS Act. [15] Though the drug has been listed in the controlled substances under NDPS act in India, yet it is been widely sold and purchased over the counter leading to unrestrained use by individuals. In this context, the International Narcotics Control Board has urged the Government of India to strengthen measures to ensure that pharmacists comply with prescription requirements and ensure that over the counter pharmaceutical preparations are not diverted to be used for non medical purposes. [10]

The authors observed that there are plenty of pharmaceutical preparations that can substitute the use of propoxyphene and its combinations. These drugs are addictive and

have narrow therapeutic range which creates drug abusers and causes sudden death in victims. After evaluating the present scenario and keeping in view of poor compliance to laws by pharmacies and general population in India, we suggest a complete ban and withdrawal of these drugs from the market, in lieu with United States and European commission guidelines.

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Fig. 1: Cyanosis of Nail Beds



Fig. 2: Congestion of Kidney, Spleen



Fig. 3: Congestion of Brain

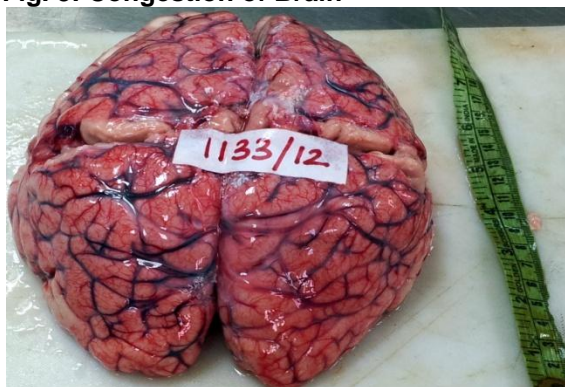


Fig. 4: Pulmonary edema and Congestion in Lungs



Fig. 5: Medullary congestion in Kidney on HPE

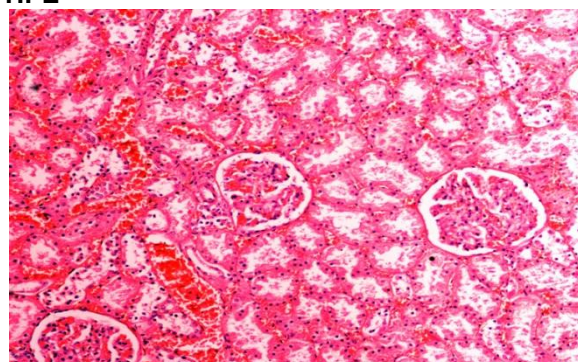


Fig. 6: Edema and Congestion in Lungs on HPE

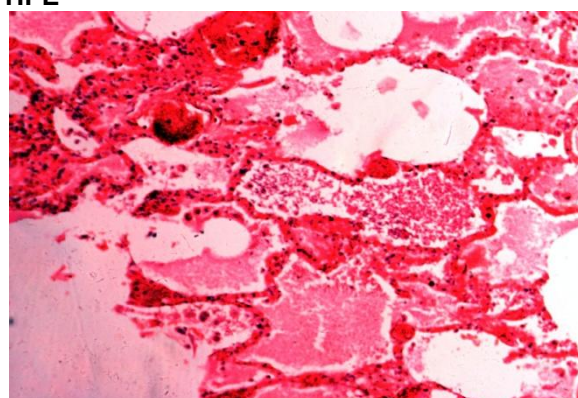


Table 1

History and Relevant Facts obtained through Questionnaires and Inquest Papers

S.N.	Age(yrs)	Sex	Staying at	State of origin	Occupation	Scene of occurrence
1	30	Male	Fatepur beri	Manipur	Unemployed	History of addiction to Spasmoproxyvon tablets
2	25	Male	K.M Pur	West Bengal	Unemployed	Spasmocip plus tablets recovered from home
3	31	Male	K.M Pur,	NE	Unemployed	History of addiction to Spasmoproxyvon tablets
4	28	Male	N.F Colony	Delhi	Unemployed	Empty wrappers of Spasmoproxyvon found in home
5	25	Male	Munirka,	NE	Unemployed	Strips of Spasmocip plus tablets
6	22	Male	Dakshinpuri	Delhi	Unemployed	Empty wrappers of Spasmocip was recovered from the site
7	28	Male	Manipur	Manipur	Unemployed	History of addiction to Spasmoproxyvon since many months.
8	23	Female	S. Vihar,	Delhi	House wife	Three empty wrappers of Spasmocip plus recovered from scene.
9	34	Male	Vasant vihar	Manipur	Unemployed	Empty wrappers of relipen recovered from pocket.
10	22	Male	Bihar	Bihar	Unemployed	History of addiction to Spasmoproxyvon with recovery of empty wrappers from scene.
11	30	Male	Delhi	Delhi	Unemployed	Empty wrappers of Spasmocip was recovered from the site