

ACUTE SEVERE SUICIDAL POISONING BY HERBICIDE PENDIMETHALIN; A RARE CASE REPORT FROM RURAL INDIA

Alok Kumar¹, Archana Verma²

*¹Department of Forensic Medicine & Toxicology, ²Department of Neurology
Rural Institute of Medical Sciences and Research, Saifai, Etawah – 206301 (U.P.), India.*

INTRODUCTION

In India, an agricultural country with a predominance of rural population (60-80%), acute agrochemical toxicity is a major health problem as they are freely available and extensively used. Agrochemical compounds pose an important community health hazard throughout the world, particularly in the Asia-pacific region. Due to their severe intrinsic toxicity, new compounds of low toxicity and high potency are continuously being developed to replace them.

Pendimethalin is such a compound which is widely-used as herbicide for the control of annual grasses and certain broadleaf weeds in commercial crops¹. It claims to exhibit least human toxicity and has been classified as a group C possible human carcinogen by the United States environmental protection agency². Only a very few cases of its toxicity have been reported till date around the world, invariably due to its deliberate ingestion³. Its toxicity is mainly manifested by head ache, drowsiness, nausea, vomiting, sore throat, retching and haematemesis etc. Here we report a patient who suffered gastro duodenal injury along with significant neurological manifestation after its deliberate self ingestion. This case is being reported on account of its rarity and significance for community health.

Case report

A young male farmer aged 25 years, was brought to emergency at 7.30 pm with an acute episodes of intractable vomiting which was watery in nature, and altered sensorium. He had no previous history of any premorbid illness. According to the history given by the

relatives, the patient was completely alright at 4.00 PM when he told his wife that he had consumed some chemical to end his life. The amount taken was around 50 ml. Since then he was having recurrent episodes of vomiting along with other features like headache, burning sensation and pain in throat and stomach. Later on he became drowsy followed by altered sensorium. He was taken to some local hospital but could not be relieved and referred to U.P. RIMS & R, Saifai.

At hospitalization, he was restless, confused, and delirious. Relatives denied consumption of any drug, poison or medications except the deliberate ingestion of some liquid which was later on found to be the herbicide GADAR (P 30% E.C.). Vital signs revealed temp 98 F, pulse rate of 74/ minute, blood pressure of 122/80 mmHg, respiratory rate of 21 per minute. Neurological examination revealed GCS of 9 /15 (E2V3M 4) with reduced movements of all four limbs. Pupils were normal size and reacting to light. Examination of chest revealed bilateral vesicular breathing. The examination of other systems was within normal limit.

The laboratory investigations included complete blood count, GBP, erythrocyte sedimentation rate, routine chemistries, liver and renal function test were within the normal limits.

In this case the diagnosis of Pendimethiline poisoning was made by reliable information from the victim, his relatives, used containers of the poison brought by them and the clinical findings. This was later on confirmed by the lab investigations.

Empirically, he was treated symptomatically with IV fluid, Omeprazole, and Antacids along with broad spectrum antibiotics and showed dramatic response. On the next day he regained consciousness, and there were no sensory motor deficit noticed. He was irritable and having burning sensation in throat and epigastrium. On the third day his psychiatric reference was done for his irritable behavior and found to be suffering from depressive symptoms with impulsive personality and advised Tab. Escitalopam 10 mg HS and Tab. Zolpidum 10 mg SOS.

After talking to relatives as well as the patient, this unfortunate incidence was found to be purely suicidal in nature. All the legal protocols were done as per the institutional rules.

What is pendimethalin?

pendimethalin ($C_{13}H_{19}N_3O_4$) is a dinitroaniline herbicide, its chemical name is n-(1-ethylpropyl) - 2,6-dinitro-3,4-xylidine and cas no. is 40487-42-1. It is a yellowish orange crystal-like solid with a faint nutty or fruit-like odor⁴. Pendimethalin is available in emulsifiable concentrate, wettable powder, or dispersible granule formulations.

A - Trade and Other Names: in India it is available as Gadar, Panda, Pendi etc in other countries its trade names include AC 92553, Accotab, Go-Go-San, Herbadox, Penoxalin, Prowl, Sipaxol, Stomp and Way-Up⁵.

B - Regulatory Status: Pendimethalin is a slightly toxic compound in EPA toxicity class III. Its products must bear the Signal Word CAUTION or WARNING, depending on the formulation. Pendimethalin is listed in the K1-group according to the HRAC classification and is approved in Europe, North America, South America, Africa, Asia and Oceania for different crops including cereals (wheat, barley, rye, triticale), corn, soybeans, rice, cotton, potato, tobacco, legumes, fruits, vegetables, nuts as well as lawns and ornamental plants.

Mode of Action

Pendimethalin acts during both pre & early post-emergence phase. It controls the weed population and prevents weeds from emerging, particularly during the crucial development phase of the crop. It is absorbed by plant roots and shoots and hampers their growth by inhibiting cell division and cell elongation⁶. Once absorbed into plant tissues, its translocation (move throughout to other plant parts) is limited and it breaks down by sunlight, microbes and oxidation⁶.

Uses

Pendimethalin is a selective herbicide used to control most annual grasses and certain broadleaf weeds in fields which interfere with growth, development, yield and quality of agricultural and horticultural crops by competing on nutrients, water and light. Thereby it protects certain crops like wheat, corn, potatoes, rice, cotton, and other as mentioned earlier. Incorporation into the soil by cultivation or irrigation is recommended within 7 days following application⁵. Its application is highly valuable in areas where weed infestation is particularly high.

The health and Toxicological Effects

Pendimethalin has caused thyroid problems in rats. In addition, it has also been classified as a "possible human carcinogen" by U.S. EPA based on benign thyroid tumors⁵. In animal studies Pendimethalin is highly toxic to fish and aquatic invertebrates, slightly toxic to birds^{6,7} and nontoxic to bees⁴. It generally demonstrates low toxicity on ingestion and very low toxicity if it is inhaled or gets on the skin. It is also toxic if it gets in the eyes.

Fate in humans and animals

Pendimethalin is largely unabsorbed from the gastrointestinal tract, and excreted unchanged in the feces⁸ its absorbed part is also rapidly metabolized in the kidneys and liver and is then excreted via urine⁸. It does not bioaccumulate (build up) in mammals.

Harmful levels of exposure

Pendimethalin is said to be slightly to practically nontoxic by ingestion, or by skin exposure^{4,6}, with reported oral LD50 values of 1050 mg/kg to greater than 5000 mg/kg in rats^{4,6}.

DISCUSSION

Different compounds, developed to protect crops are now themselves causing significant health hazards. Acute agrochemical poisoning is a global public health problem and a leading cause of mortality and morbidity in the developing countries of Asia - Pacific region including India. This is mostly due to exposure to organophosphates (most common in India), organochlorines, and aluminium phosphide compounds which are an integral part of agriculture within this region and are readily available at very cheap rate. Due to their intrinsic toxicity, new chemicals of high potency and low toxicity continue to be developed e.g. Imidacloprid, Pendimethiline, and Pencycuron etc., but they are released to the market without appropriate data on direct human toxicity. Instead, human toxicity is often extrapolated from toxicological studies in animals, the relevance of which is poorly defined. They are classified as a "moderate toxic", and generally demonstrate low human lethality but at times they may be hazardous⁹.

Pendimethalin generally exhibits very low human toxicity even in large ingestions. However co-ingestions with other similar chemicals may be hazardous. There is dearth of literature on pendimethalin toxicity, and available reports indicate that the pendimethalin toxicity is invariably associated with oral ingestion.

A study of 71 cases identified only 2 incidences resulting from skin and eye contact and the rest from swallowing intentionally or accidentally. Among them, 20 remained asymptomatic, 38 had mild effects (nausea, vomiting and sore throat) and only 7 patients develop significant toxicity in the form of

severe retching, vomiting of blood etc. Four patients died as a result of also taking other herbicides and because of inadequate airway management³.

In another case, a 73-year-old man has been reported to develop nausea and epigastric pain and corrosive gastroduodenal injury after accidental ingestion of the diluted (300 times with water) pendimethalin formulation. As he was chronic alcoholic for years and had no history of gastro duodenal ulcer, the accidental ingestion was supposed to cause this injury¹⁰.

Poisoning in India

The exact incidence of poisoning is not known in India due to lack of central registry but approximately it accounts for 10% of admissions in medical emergency. Poisoning is typically suicidal in nature which is ranked as third leading cause of death in age group 15-44 years. It was responsible for around 600,000 deaths in 1990s¹¹. In the past 50 years suicide rates have increased by 60%¹². After accidents and maternal mortality; suicide is the leading cause of death among the young in India, with a high prevalence in rural areas. Suicide is second leading cause of death among young people and with the decline in maternal death rates; it could soon become the leading cause of death among young women in India. Ingestion of agrochemical compounds is the principle mode for suicide. Of the 1.87000 people who committed suicide in India in 2010, around half (49% men and 44% women) consumed poison, mainly pesticides¹³.

Most of these toxicities occur due to exposure to (OP), organochlorines and aluminium phosphide. Among them, organophosphates OP poisoning is most common in India and chiefly presents as deliberate self ingestion in young population (20 -30 yrs) for suicidal purpose and quite uncommon in aged people more than 50 yrs. A case of a 55 yrs old farmer has also been reported, who developed significant toxicity by accidental inhalational

exposure during handling of multiple OP pesticides¹⁴.

Acute poisoning is a medical emergency, which poses a major threat to life. Its type, associated morbidity and mortality varies from place to place and changes over a period of time. The incidence of poisoning is rising in India. More than 50,000 people die of poisoning every year¹⁵. In India, OP compounds are the commonest class of pesticides which have been implicated in cases of poisoning, as ours is an agriculture based society and pesticides are readily available at a cheap rate. The OP toxicity chiefly presents as suicidal attempt by oral ingestion other routes of administration and modes of poisoning are very uncommon.

There is dearth of literature on pendimethalin toxicity, it is a urea derivative fungicide of very low toxicity. However co-ingestions with other similar chemicals may be hazardous. In case of Systemic poisoning the treatment is principally symptomatic as there is no specific antidote.

Emergence of such entirely new poisoning by the so called non toxic compounds is a big challenge to community health especially in rural population. Their clinical outcomes rely on early recognition, prompt referral and aggressive treatment in collaboration with different specialties. Awareness programs about such new toxicities should be implemented at different levels. This article illustrates that ingestion of these so called non toxic and safe compounds may also lead to significant toxicity which has not been reported earlier. The treating physicians should have a close watch and pay more attention to these patients⁹.

Such incidences are alarming as the clinical consequences of poisoning with such relatively newer and nontoxic compounds are not very well described, therefore such information / case reports are valuable for clinicians and concerned authorities and may help to save a number of precious lives⁹.

CONCLUSION

Substitution of existing highly toxic agrochemical compounds by the newer non/less toxic compounds in affected areas may help to save a number of precious lives. But such occurrence by these so called non toxic compounds is a big challenge to the community health. Their clinical consequences are not very well described and outcomes rely on early recognition, prompt referral and aggressive treatment in collaboration with different specialties. Therefore such information / case reports may help to improve clinical management and inform pesticide regulators of their relative toxicity. Awareness programs about such new toxicities are also highly valuable.

Though the appropriate and timely management has vital role, the importance of preventive measures and public awareness can not be ignored in saving precious lives and should be implemented at different levels.

Key message

The exposure of so called non toxic compound should not be ignored as this case illustrates that they may also be hazardous. The treating physicians should be vigilant and must have a close till full recovery of these patients.

ACKNOWLEDGMENTS

Authors are thankful to Dr. Atul Mishra (CMO), Mr. Kailash Srivastava and Ms. Deepa Sahu of Medical Record Section of UP RIMS and R, Saifai, Etawah., for their contribution and support.

REFERENCE

1. Engebretson J, Hall G, Hengel M, Shibamoto T. Analysis of pendimethalin residues in fruit, nuts, vegetables, grass, and mint by gas chromatography. *J Agric Food Chem* 2001; 49:2198-206.
2. US Environmental Protection Agency. R.E.D. Facts: Pendimethalin. Washington, DC: US EPA; 1997.
3. Chuang CC, Wang ST, Yang CC, Deng JF. Clinical experience with pendimethalin (STOMP) poisoning in Taiwan. *Vet Hum Toxicol* 1998; 40:149-50.
4. Kidd, H. and James, D. R., Eds. *The Agrochemicals Handbook*, Third Edition. Royal Society of Chemistry Information Services, Cambridge, UK, 1991 (As Updated).10-2].
5. Pendimethalin Roadside Vegetation Management Herbicide Fact Sheet. Available at - <http://www.wsdot.wa.gov/NR/rdonlyres/5D42BF92-F25F-4FBE-A486-E25F2FBB23E3/0/pendimethalin.pdf>
6. Weed Science Society of America. *Herbicide Handbook*, Seventh Edition. Champaign, IL, 1994.10-59].
7. U.S. Environmental Protection Agency. Pesticide Fact Sheet Number 50: Pendimethalin. Office of Pesticides and Toxic Substances, Washington, DC, 1985.10-116.
8. Zulalian, J. Study of the absorption, excretion, metabolism, and residues in tissues of rats treated with carbon 14 labeled pendimethalin, Prowl herbicide. *J. 118*].
9. Kumar A, Verma A, Jaiswal K, Kumar S, Prasad R. Emergence of entirely new poisoning in rural India; an upcoming health hazard to the community health. *Ind. J. of Community Health*, 2012;24(3): 248-251.
10. Acute gastroduodenal injury after ingestion of diluted herbicide pendimethalin *Singapore Med J* 2009; 50(3): e105-e106]
11. Eddleston M. Patterns and problems of deliberate self poisoning in the developing world *QJM* 2000;93:715-31.
12. Krishnaswamy Sampathkumar, Sooraj Yesudas. Hair dye poisoning and the developing world. *J Emerg Trauma Shock*. 2009 May-April; 2 (2): 129-131.
13. 40% of India's suicides in four southern states; an article in *The Times of India*, 23 June, 2012.
14. Kumar A, Pathak A, Verma A, Kumar S. Accidental Inhalational Poisoning by Multiple Pesticides of Organophosphorus Group in An Aged Person; An Uncommon Occurrence. *J. of Forensic Medicine & Toxicology* Vol. 29 No. 2, July - December 2012. 78-83.
15. Aggarwal P, Handa R, Walia JP. Common poisoning in India. *JFMT* 1998; 15 (1): 73.