Original Paper

Histopathological Study in Fatal Aluminium Phosphide Poisoning Victims in Relation to Survival Period

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ABSTRACT

In this study, a histopathological examination of lungs, liver and kidneys in aluminium phosphide poisoning cases was done, and demonstrated significant pathological features in the form of fatty infiltration and hepatocyte necrosis in the liver, tubular necrosis in the kidneys with intra-tubular haemorrhages in a few cases, and pulmonary oedema, alveolar septal thickening, intra-alveolar haemorrhages and disruption of inter-alveolar septa in the lungs.

On correlating these histopathological features in the tissues with the survival period of the cases, it was observed that the liver was affected among only those cases surviving for more than 24 hrs following the intake of aluminium phosphide, while features of pathology in the lungs and kidneys were noted in general among all the cases.

Key Words: Aluminium phosphide; ALP; Autopsy; Histopathology; Survival period

INTRODUCTION

In India, aluminium phosphide (ALP) poisoning was first reported in 1981 from MGM Medical College, Indore.[1] Since then, cases of ALP poisoning has become a common occurrence particularly in Northern and Central India.[2] The fatal dose of ALP ranges from 150 to 500 mg, and its poisoning results in high fatality (37–100%).[1–4] The mechanism of ALP toxicity is not well understood, but it is attributed to phosphine, a byproduct generated when ALP comes in contact with moisture/water or acid. This engenders non-competitive inhibition of the respiratory chain enzyme cytochrome oxidase of mitochondria, which blocks the electron transfer chain and oxidative phosphorylation and produces an energy crisis in the cells. Furthermore, it is proposed that phosphine also inhibits catalase and peroxidase enzymes leading to free radicals stress damage to the cells.[5–8] Common causes of death in ALP poisoning cases include ventricular fibrillation, acute respiratory distress syndrome (ARDS), hepatic failure, acidosis, and dyselectrolytaemia.[9] The time of death following ALP consumption has been reported to range from 1 to 48 hrs in a number of studies.[5,10]

This study attempts to find some correlation with regard to histopathological features in the lungs, liver and kidneys with the survival period amongst ALP poisoning cases, which might help to understand the progression of toxic effects of ALP in the tissues.

MATERIALS AND METHODS

The study was carried out in the Departments of Forensic Medicine and Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, UP, India.

From a total of 164 suspected cases of ALP poisoning, 45 cases were included for the study.

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Inclusion criteria:
- Confirmed cases of ALP poisoning from positive history.
- Evidences produced confirming ALP poisoning.
- Cases with positive silver nitrate paper test of the gastric contents.

Exclusion criteria:
- Doubtful cases.
- Cases associated with known pathology of lungs, liver and kidneys or inherent organ pathology.
- Advanced decomposition.

All the included cases were categorized into different groups of survival period **(Table 1)**. The survival period was estimated from the time of intake of poison to the fatal outcome (death) of the victims in hours. Tissue samples of about 2 x 2 cm size from representative area of lungs, liver and kidneys were taken and processed for histopathological examination by conventional techniques. Routine haematoxylin and eosin (H&E) staining was done on all the processed tissue sections. Noted histopathological findings in the tissues were reviewed with survival period of the victims.

Furthermore, in this study, epidemiological data such as age, gender, seasonal occurrence, marital status of the victim, dose of poison consumed, etc, were also analyzed.

Table 1 Number of ALP Cases in Different Survival Period Groups

Survival period (in hrs)	No. of cases (n=45)	Percentage (%)
≤6	8	17.80
>6–24	18	40.00
>24–48	10	22.20
>48–72	6	13.40
>72	3	06.60
Total	**45**	**100**

RESULTS

The intention in all the cases of ALP poisoning was suicidal. Most of the cases, i.e., 84.60% (n=28) were between the age of 15 and 45 years. 60% (n=27) of the cases were unmarried and gender-wise 69% (n=31) of the cases were male. 55.60% (n=25) of the cases were from rural area, while the remaining 44.40% (n=20) cases from urban area. In the study, maximum number of ALP poisoning cases, i.e., 64.5% (n=29) was noted during the period between March and June (summer).

In relation to survival period, the maximum number of cases, i.e., 40% (n=18) survived for more than 6–24 hrs, followed by 22.2% (n=10) who survived for more than 24–48 hrs, 17.8% (n=8) who survived for less than 6 hrs, 13.4% (n=6) who survived beyond 48–72 hrs and the least number, 6.6% (n=3) cases survived for a longer period of more than 72 hrs following ALP intake **(Table 1)**. As per the information obtained from the police, history of victims, and their family members, the physical form of ALP consumed was tablet, and the number of ALP tablet intake among the cases ranged from one to four. The time of consumption was generally during late evening and night hours in most of the cases.

Autopsy Findings: Externally, bluish hue was predominant in 80% (n=36) of cases. Features of jaundice (presence of icterus and/or yellow discolouration of skin) were noted in 20% of the cases. Internally, all the organs were found congested. The stomach mucosa was congested, inflamed and bore haemorrhagic spots in 53.34% (n=24) cases. Stomach contained grayish-brown fluid or pasty material in 17.78% (n=8) of cases, and had a distinct odour of phosphine, which was perceived in 24.45% (n=11) victims. In the lungs, surface haemorrhagic spots were noted in 24.5% (n=11) cases, mainly present over interlobular spaces. Similar haemorrhagic spots were present in the liver in 11.2% (n=5) cases, and in the kidneys in 20% (n=9) of the cases. Furthermore, liver showed fatty changes in 11.2% (n=5) cases and features of jaundice in 6.7% (n=3) cases (**Table 2**).

Histopathological Study: Congestion was a common histopathological finding in all the tissues, whereas oedema was noted in 62.22% (n=28) cases in lungs, 60% (n=27) cases in kidneys and 57.78% (n=26) cases in liver. Furthermore, in the lungs, thickening of alveolar septa with congested intra-septal vessels were noted in 53.34% (n=24) cases, and in 20% (n=9) cases, disruption of alveolar septa was noted with extravasation of RBC in alveoli in 13.34% (n=6) cases (**Fig 1**). In the kidneys, tubular necrosis of varying degree was noted in 44.5% (n=20) cases **(Fig 2)**. Intratubular haemorrhage was noted in 8.8% (n=4) cases. In the liver, hepatocyte necrosis was noted in 31.12% (n=14) of the cases, predominantly around the congested central vein of liver. Fatty degeneration of hepatocytes was present in 24.44%

Table 2 External Autopsy Findings of Liver, Lungs and Kidneys in ALP Poisoning (n = 45)

Organs	Autopsy findings	Number of cases	Percentage (%)
Lungs	Hyperaemia/congestion	45	100.00
	Surface haemorrhagic spots	5	11.20
	Jaundice	3	06.70
	Fatty changes	5	11.20
Liver	Hyperaemia/congestion	45	100.00
	Surface haemorrhagic spots	11	24.50
	Pneumonic lung	24	53.40
Kidneys	Hyperaemia/congestion	45	100.00
	Surface haemorrhagic spots	9	20.00

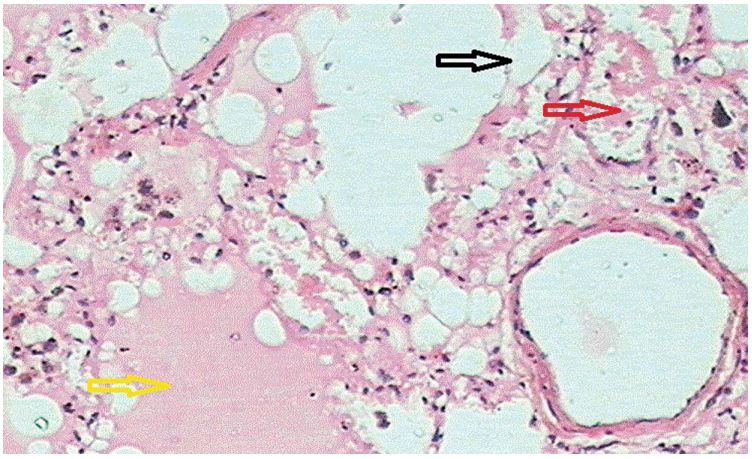

Fig 1 H & E Stained Histology of Lung (40X) Showing Congestion and Pulmonary Oedema (*yellow arrow*), Disrupted Alveoli (*black arrow*) and Intra-alveolar RBC (*red arrow*)

(n=11) cases, which was more markedly noted around portal triad (**Figs 3 & 4**). Biliary stasis within hepatocytes and kupffer cells was also seen in 8.8% (n=4) of the cases.

In relation to survival period, it was observed that the features of liver pathology, viz., gross (icterus, fatty changes) and histopathological findings of fatty degeneration and hepatocyte necrosis, were noted mainly among victims surviving for 24 hrs and/or more following ALP consumption. But the pathological findings in lungs and kidneys did not show any significant association with survival period, except for the fact that they were the only features noted among the cases with survival period of less than 24 hrs, but were also in general, noted in cases surviving for more than 24 hrs (**Fig 5**).

DISCUSSION

In this study, 80% of cases died within 48 hrs following ALP consumption. In their study, Jain et al reported survival time varying between 1 and 47 hrs.[5] In the study by Ranga et al, the average time interval between poisoning and death is 3 hrs, with a range of 1–48 hrs, and as many as 95% of fatalities occur within first 24 hrs.[9]

Histopathological findings in this study indicate that ALP causes damage to vital organs such as lungs, liver and kidneys, and that features of liver injury by the poison are found only among the victims who survive for more than 24 hrs following ALP intake. Karanth et al also reported that features of hepatotoxicity usually develop 72 hrs after ALP poisoning.[7] But Arora et al report liver injury in all severe intoxication cases.[10] This capacity of

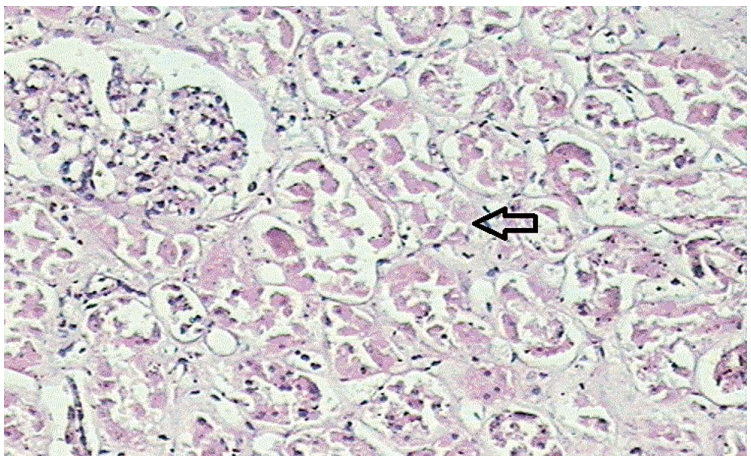

Fig 2 H & E Stained Histology of Kidney (100X) Showing Extensive Tubular Necrosis (*arrow*), with Occasional Viable Tubules and Normal Glomeruli

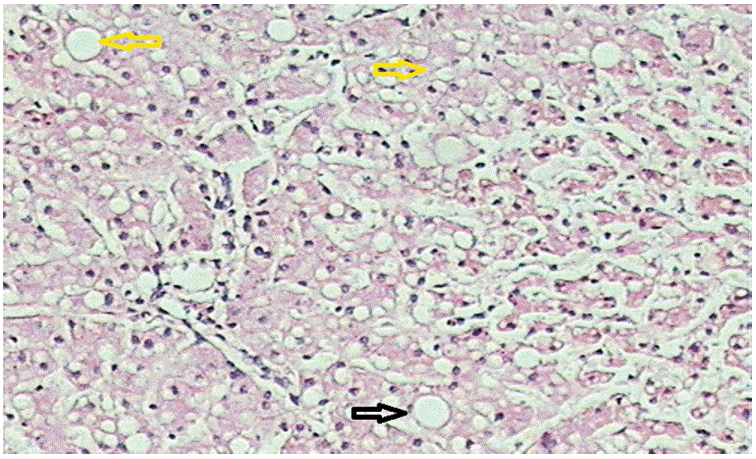

Fig 3 H & E Stained Histology of Liver (100X) Showing Fatty Infiltration within Hepatocytes of Both Macro and Micro Vesicular Type (yellow arrow), with Signet Ring Sign (black arrow)

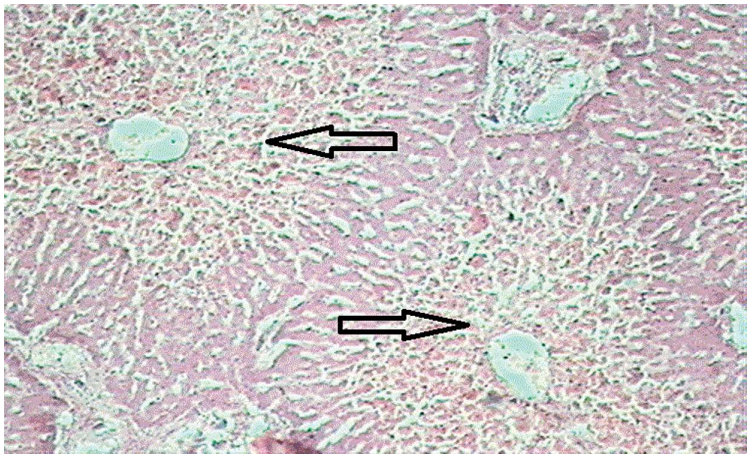

Fig 4 H & E Stained Histology of Liver (100X) Showing Marked Centrilobular Hepatocyte Necrosis (*arrow*), around Congested Central Vein and Small Area of Viable Hepatocytes around Portal Triad

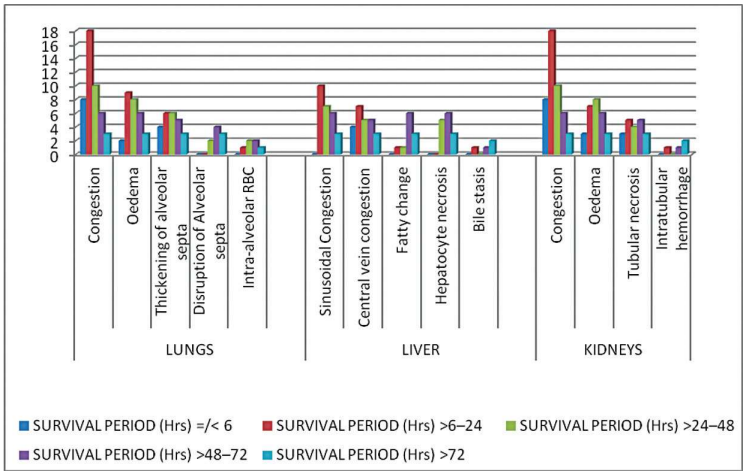

Fig 5 Histopathological Changes in Lungs, Liver & Kidneys in Relation to Survival Period in ALP Poisoning

the liver to resist ALP injury compared to kidneys and lungs could be due to the inherent function of the liver as a detoxification organ, and the capacity for regeneration in response to injury.[11]

These findings of tissue injuries suggest that the immediate risk following ALP poisoning seems to rest in cellular hypoxic event leading to critical dysfunction of vital organs. Anger et al in their autopsy study found "asphyxia syndrome" with major visceral congestion as the main finding in ALP poisoning cases.[12] Furthermore, Sinha et al reported that in their study, microscopy of the lungs revealed alveolar thickening, oedema, dilated capillaries, collapsed alveoli and haemorrhage.[13]

These results call for the need for fast cardio-pulmonary support and measures to counter cellular hypoxia in such cases as life saving measures. Subsequently, the need to monitor kidney and liver function tests on regular basis is essential to provide better management of such poisoning cases in the form of damage control measures, as well as early identification and management of organ failure.

This study demonstrates that the younger age group (between 15 and 30 years) is the most affected, i.e., 62%, which is a concern as they represent the productive members of the country. Similarly, studies by Misra et al, Chugh et al, and Singh et al have reported that ALP poisoning is more common among younger age groups.[14–16]

CONCLUSION

ALP is a time-tested popular rodenticide indispensable in agrarian and developing countries such as India. In this study, the nature of ALP fatality and its toxicity to tissues through histopathological examination could help provide information about the broad sequence of tentative intoxication events in lungs, liver and kidneys following poisoning.

The results of this study emphasize the need of care centers with critical care management resources for fast and prompt management in ALP poisoning cases, especially because the poison has high fatality rate, non-availability of antidote and affects all the vital organs eventually. The study also reflects the great loss of life for a developing country such as India, especially the younger productive population in a very preventable situation. Given the fact that the poisoning incidence of ALP among both rural and urban populations is very high, and especially the vulnerability of young population to poisoning, there is not only a need for awareness to be generated, but also the need for improvement of regulatory bodies in the control of dispensation and use of ALP among the public.

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