

Retrospective Investigation of Intoxication Cases That Require Mechanical Ventilation

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Abstract

Aim: Intoxication cases are hospitalized in intensive care units not for intervention but for close observation and monitoring. Endotracheal intubation and mechanical ventilation may sometimes be required.

Materials and Methods: In total, 2118 intoxication cases have been hospitalized in our toxicology intensive care unit sequentially between March 2011 and March 2013. Of these patients, 23 cases that required endotracheal intubation and mechanical ventilation were included in this retrospective study; data was obtained by screening the patient files.

Results: Twenty-three cases (1.1%) required mechanical ventilation, and only 7 cases (0.33%) died. The most common reasons for requiring mechanical ventilation were unconsciousness and respiratory failure. During hospitalization, they were attached to mechanical ventilator for a mean of 4.17 days. While the mean duration of mechanical ventilation of patients with organophosphate intoxication was 6.92 days, the other non-organophosphate intoxication group was 1.18 days. There is significant statistical difference between two groups ($p < 0.01$). We compared the organophosphate intoxication group with other non-organophosphate intoxication group for Glasgow Coma Scale, arterial blood gas, C-reactive protein, and pro-calcitonin and troponin levels at initial admission. Pro-calcitonin levels were significantly high in the organophosphate group.

Conclusion: Intoxication cases that require mechanical ventilation can differ from classical intoxication epidemiology for age and sex. Organophosphate intoxications are one of the intoxication types that require mechanical ventilation and have the highest mortality. (*JAEM 2015; 14: 2-7*)

Key words: Intoxication, respiratory failure, mechanical ventilation

Introduction

Intoxications have been one of the major problems in closely related societies since ancient times (1). Intoxication is the emergence of some unwanted symptoms and signs in the organism by a toxic or non-toxic substance consumed in toxic dose (2).

Intoxication is the most common reason of non-traumatic coma under 35 years and comprises approximately 7%-10% of acute medical applications (3, 4). In United States, intoxications comprises 5%-10% of intensive care unit patients, and approximately 5%-30% of the multidisciplinary intensive care units are used for intoxication cases (5). Some of these cases require hospitalization in intensive care units because they are life-threatening intoxications and require continuous monitoring and follow-up (6). Critical intoxication cases are reversible patients that could clearly benefit from interventions in the intensive care. However, there is no commonly known course or predictable complications for intoxication cases. Accurate information cannot be often obtained about the type of toxic subject,

time of taking, and amount. Therefore, it is very difficult to accurately decide the follow-up of these patients. Intoxication cases are commonly hospitalized to intensive care units not for intervention but for close observation and monitoring. Thus, reduction in mortality and morbidity rates can be achieved. Furthermore, rarely endotracheal intubation and mechanical ventilation support can be required (7).

In this study, we aimed to evaluate the patients who are treated in Konya Training and Research Hospital, Department of Emergency Medicine Toxicology Intensive Care Unit for the last two years and required retrospective endotracheal intubation and mechanical ventilation.

Materials and Methods

Study design and population

In our emergency medicine clinic, there is a toxicology intensive care unit and the patients who apply because of non-intended or suicidal attempt intoxication and require hospitalization are



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followed up in this unit. The patients are evaluated by emergency medicine specialists and assistant physicians. In this unit, there are secondary health care intensive care beds for patients requiring mechanical ventilation and primary care intensive care unit beds for patients not requiring intensive mechanical ventilation. A total of 2118 intoxication cases have been hospitalized in our toxicology intensive care unit sequentially between March 2011 and March 2013. Of these patients, 23 cases requiring endotracheal intubation and mechanical ventilation were included in this retrospective study; data were obtained by screening the patient files.

Inclusion criteria of the study:

- All patients between 16 and 80 years requiring endotracheal intubation and invasive mechanical ventilation
- Patients that are followed up for examination and treatment and spend at least 24 h in the toxicology intensive care unit

The study protocol was approved by the local ethics committee (Necmettin Erbakan University, Faculty of Medicine Ethics Committee) and conducted in accordance with the Declaration of Helsinki and Good Clinical Practices.

Study protocol

The patients will be evaluated for age, sex, exposed to or taken drugs, serum drug levels, reason and way of exposure, clinical characteristics, methods of treatment, complications, duration of hospitalization, and mortality. Further, the reasons for endotracheal intubation and mechanical ventilation should be evaluated and recorded.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences 15.0 (SPSS Inc., Chicago, Illinois, USA) software program. Quantitative variables were presented as mean \pm standard deviation, and categorical variables were presented as number of cases (percentage). Differences between the groups were compared using the Mann-Whitney U test for quantitative variables and using chi-square and Fischer exact tests for categorical variables.

Results

Demographic data

The mean age of the 23 cases included in the study was 43.8 years and was detected as minimum 16 years and maximum 80 years. Of these cases, 15 were males (65.2%), 8 (34.8%) were females, and M:F ratio was approximately 2:1. When we look at the reasons of intoxication; we detected that 19 (82%) cases were taken overdose drugs for suicide, 2 (8.7%) were addicted, 1 (4.3%) case was intoxicated accidentally, and 1 (4.3%) case was intoxicated as a result of side effects of the regularly used medication.

Twenty (87%) cases were orally exposed to the toxic substance, 2 (8.7%) were intravenously exposed, and 1 case (4.3%) was intoxicated by inhalation. All the orally intoxicated cases were treated by gastric lavage and administered active carbon. Twelve (52.2%) reported cases were of organophosphate intoxication. Demographic data are summarized in Table 1, and distributions of the toxic substances causing intoxication are summarized in Table 2.

Primary results

In two years, of the total 2118 intoxication cases, 23 cases (1.1%) required mechanical ventilation, and only 7 cases (0.33%) died. The most common reasons for requiring mechanical ventilation were un-

Table 1. Distribution of cases by sex and age group

| | Cases | Number | % |
|------------|--------|--------|------|
| | | 23 | 100 |
| Sex | | | |
| | Male | 15 | 65.2 |
| | Female | 8 | 34.8 |
| Age groups | | | |
| | 16-20 | 5 | 21.7 |
| | 21-40 | 7 | 34.4 |
| | 41-60 | 5 | 21.7 |
| | 61-80 | 6 | 26.1 |

Table 2. Distribution of toxic substances in patients

| Substance that causes intoxication | n | % |
|------------------------------------|----|------|
| Organophosphates | 12 | 52.2 |
| Other group | 11 | 47.8 |
| Bupropion | 1 | 4.3 |
| Citalopram+Risperidone | 1 | 4.3 |
| Digoxin | 1 | 4.3 |
| Propranolol+Amitriptyline | 1 | 4.3 |
| Carbon monoxide | 1 | 4.3 |
| Carbamazepine+Quetiapine | 1 | 4.3 |
| Eroin | 2 | 8.7 |
| Quinapril+Salicylates | 1 | 4.3 |
| Clozapine | 1 | 4.3 |
| Quetiapine+Olanzapine | 1 | 4.3 |
| Total | 23 | 100 |

consciousness and respiratory failure. Only 2 cases were connected to mechanical ventilators because of cardiopulmonary arrest. Of the 23 cases that required mechanical ventilation, 7 (30.4%) of them died and 16 cases (69.6%) were discharged after treatment. The characteristics of dead and discharged after treatment patients are summarized in Table 3 and Table 4.

The cases were followed up for a mean of 7.95 days in the toxicology intensive care unit, at least hospitalized for 1 day or maximum 29 days. During hospitalization, they were connected to mechanical ventilator for a mean of 4.17 days, at least 1 day or maximum 23 days. While the mean duration of mechanical ventilation of patients with organophosphate intoxication was 6.92 days, the other non-organophosphate intoxication group was 1.18 days. There was significant difference between the two groups ($p < 0.01$; Table 5). We also compared the organophosphate intoxication group with other non-organophosphate intoxication group for Glasgow Coma Scale (GCS), arterial blood gas, C-reactive protein, and pro-calcitonin and troponin levels at initial admission. Pro-calcitonin levels were significantly high in the organophosphate group ($p = 0.003$; Table 6).

When the dead and survived patient groups were compared, no significance was observed between both groups for age, sex, ini-

Table 3. Characteristics of the patients who died

| Poisoning agents | GCS score | Length of stay in ICU | MV time | Why was the need of MV | Applied special treatments | Causes of death |
|------------------------------|-----------|-----------------------|---------|---|-----------------------------|---|
| OP - 1 | 3 point | 5 days | 4 days | GCS:3, Respiratory failure | Atropine and PAM | Respiratory failure and VT |
| OP - 2 | 15 point | 17 days | 13 days | Respiratory failure and Pneumonia | Atropine and PAM | Respiratory failure and Pneumonia |
| OP - 3 | 7 point | 2 days | 2 days | Respiratory failure, Disorders of Consciousness | Atropine and PAM | Respiratory failure and Pulmonary edema |
| Bupropion | 5 point | 1 days | 1 days | Disorders of Consciousness | - | VT vs. VF |
| Digoxin | 15 point | 4 days | 1 days | Cardiopulmonary Arrest | Dialysis/atropine | Digoxin Overdose |
| Propranolol Amitriptyline | 5 point | 1 days | 1 days | Disorders of Consciousness | Dialysis/NaHCO ₃ | Bradycardia, Hypotension |
| Quinapril Salicylate | 15 point | 3 days | 1 days | Cardiac arrest, Disorders of Consciousness | Dialysis/NaHCO ₃ | Bradycardia, Hypotension, Acidosis |

OP: Organophosphate; MV: mechanical ventilation; GCS: Glasgow Coma Scale; ICU: intensive care unit; VT/VF: ventricular tachycardia/fibrillation; PAM: pralidoxime

Table 4. Characteristics of the patients who were discharged after treatment

| Poisoning agents | GCS score | Length of stay in ICU | MV time | Why was the need of MV | Applied special treatments |
|------------------------------|-----------|-----------------------|---------|--|------------------------------|
| OP - 4 | 3 point | 8 days | 5 days | GKS:3, Respiratory failure | Atropine and PAM |
| OP - 5 | 6 point | 16 days | 6 days | Disorders of Consciousness, Intermediate syndrome | Atropine and PAM |
| OP - 6 | 8 point | 29 days | 23 days | Respiratory failure, Disorders of Consciousness, Intermediate syndrome | Atropine and PAM |
| OP - 7 | 9 point | 11 days | 8 days | Respiratory failure | Atropine and PAM |
| OP - 8 | 15 point | 7 days | 1 days | Respiratory failure, Excessive secretion | Atropine and PAM |
| OP - 9 | 15 point | 7 days | 1 days | Respiratory failure, Excessive secretion | Atropine and PAM |
| OP - 10 | 6 point | 15 days | 6 days | Respiratory failure, Disorders of Consciousness, Intermediate syndrome | Atropine and PAM |
| OP - 11 | 6 point | 21 days | 11 days | Respiratory failure, Disorders of Consciousness, Intermediate syndrome | Atropine and PAM |
| OP - 12 | 13 point | 6 days | 3 days | Disorders of Consciousness | Atropine and PAM |
| Citalopram, Risperidone | 13 point | 3 days | 1 days | Disorders of Consciousness | - |
| Carbon monoxide | 5 point | 3 days | 2 days | Disorders of Consciousness | High Pressure O ₂ |
| Quetiapine, Carbamazepine | 3 point | 6 days | 2 days | Disorders of Consciousness | Dialysis and IV lipid |
| Quetiapine, Olanzapine | 3 point | 3 days | 1 days | Disorders of Consciousness | - |
| Clozapine | 15 point | 5 days | 1 days | Respiratory failure, Disorders of Consciousness | - |
| Heroin - 1 | 5 point | 5 days | 1 days | Disorders of Consciousness | Naloxone |
| Heroin - 2 | 8 point | 3 days | 1 days | Respiratory failure, Disorders of Consciousness | Naloxone |

OP: organophosphate; MV: mechanical ventilation; GCS: Glasgow Coma Scale; ICU: intensive care unit

tial GCS, and the duration of connection to mechanical ventilators ($p=0.300$, $p=0.657$, $p=0.497$, and $p=0.524$, respectively). Further, there no significant association was detected between initial admission lactate levels, saturation, and pH values ($p=0.920$, $p=0.349$, and $p=0.592$, respectively) (Table 7).

Secondary results

We also evaluated organophosphate intoxications that comprise approximately half of the cases. Within the study period, a total of 97 organophosphate cases were followed up in our toxicology unit. Of these cases, 55 (56.7%) were males and 42 (43.3%) were females. The mean age was 38.6 years. Twelve (12.3%) of them required mechanical ventilation; 3 (3.1%) of these 12 cases died.

No significant association was detected between initial cholinesterase levels of organophosphate intoxication cases with mortality rates ($p=0.326$; Table 8). Moreover, no significant correlation was observed between cholinesterase levels and the duration of connection to mechanic ventilators ($p=0.238$).

Discussion

In all, 95% all the intoxication cases are suicidal attempts, and this is more frequent in women. Intoxication cases are also more frequent between the ages of 20–35 years (3). However, in our findings, the number of male cases that required mechanical ventilation was approximately twice that of female cases. Further, the mean age of the cases was higher than that in other studies. This can possibly be because of the inclusion of only mechanical ventilation requiring cases in the study.

It has been previously reported that while in developed countries the most common medications consumed for suicidal attempts are analgesics and antidepressants and mortality is approximately 0.5% in these cases, in developing countries, common agricultural pesticides are used and mortality can reach to 20% in these cases. A great proportion of these cases are young and healthy, increasing the importance of the issue (8).

The mortality rate of intoxications differs between 0.3% and 27% (9–11). Although the general mortality rates of acute intoxication cases are low, they consists a large proportion of hospitalization to intensive care units and because of this they are a patient group using the resources of intensive care units; therefore, they are a patient group using the resources of intensive care units (12, 13). The unpredictability of the course of these patients is a major problem, and the mortality rate because of intoxications, such as organophosphate and aluminum phosphate, is high. While mortality rates of intoxication cases as a result of suicidal attempt is 0.5% in advanced centers, this ratio is detected between 10%–20% in countries wherein intensive care resources are inadequate (14). In Western countries, mortalities because of analgesics, sedatives, and antidepressants are common, while in India, mortalities because of pesticides is more common (15, 16). In our study, the general mortality rate is 0.33%. In the study conducted by Şencan et al. (17), 21% of the 55 organophosphate cases died, and the highest rate was methanol intoxication with 54.5% of the 11 cases. Furthermore, in the study conducted by Lam et al. (18), 5 of the 8 patients died in the intensive care unit; of these, 1 died because of multiple organ failure developed as a result of thinner + paracetamol intoxications, 1 died because of brain death developed as a result of carbon monoxide intoxication, 1 died because of cardiac arrest developed as

Table 5. Comparison of mechanical ventilation times

| Poisoning agents | Number | Average duration of MV |
|---------------------------|--------|------------------------|
| Organophosphate Poisoning | 12 | 6.92±6.30 days |
| Other poisonings | 11 | 1.18±0.40 days |

MV: mechanical ventilation; Mann-Whitney U test ($p=0.001$)

Table 6. Organophosphate group comparison with the other group

| | Organophosphate group (n=12) | Other group (n=11) | p value |
|--------------------|------------------------------|--------------------|---------|
| pO ₂ | 72.2±26.2 | 61.3±21.2 | 0.218 |
| pCO ₂ | 36.5±19 | 40.5±21.3 | 0.735 |
| spO ₂ | 84.5±11.8 | 87.9±8.9 | 0.518 |
| pH | 7.32±0.11 | 7.28±0.17 | 0.975 |
| Lactate | 2.77±1.53 | 3.1±2.7 | 0.829 |
| Troponin | 0.59±1.17 | 0.62±0.05 | 0.193 |
| GCS | 8.25±4.25 | 8.36±5.06 | 0.779 |
| Prokalsitonin | 4.78±7.8 | 0.42±1.23 | 0.003 |
| C-reactive protein | 134.7±108.7 | 40.53±38.4 | 0.05 |

Mann-Whitney U test; pO₂: arterial partial pressure of oxygen; pCO₂: arterial partial pressure of carbon dioxide; spO₂: arterial oxygen saturation; GCS: Glasgow Coma Scale

Table 7. Comparison of patients dying and living

| | Dying (n=7) | Living (n=16) | p value |
|---------------|-------------|---------------|---------|
| Age (year) | 54.29±27.29 | 40.75±18.60 | 0.300 |
| Sex | F:3, M:4 | F:5, M:11 | 0.657 |
| GCS | 7.81±4.21 | 9.42±5.41 | 0.497 |
| MV time (day) | 3.28±4.42 | 4.56±5.78 | 0.524 |
| Lactate | 2.84±2.02 | 2.96±2.23 | 0.920 |
| pH | 7.32±0.12 | 7.28±0.15 | 0.592 |
| Saturation | 83.41±9.81 | 87.32±10.73 | 0.349 |

GCS: Glasgow Coma Scale; MV: mechanical ventilation; Mann-Whitney U and chi-square test

Table 8. Organophosphate poisoning cases, relation between mortality by level of cholinesterase

| Cholinesterase | Dying (n=3) | 473±432 |
|----------------|--------------|---------|
| | Living (n=9) | 865±787 |

Mann-Whitney U test ($p=0.354$)

a result of dothiepin + paracetamol intoxication, 1 died because of amphetamine + alcohol, and 1 died because of lithium + chlorpromazine + alcohol intoxications that caused brain edema. Singh et al. (19) have reported that 3 cases died due to aluminum phosphide intoxication; all 3 patients died during mechanical ventilator support because of refractory hypotension unresponsive to vasopressor drugs, metabolic acidosis, and respiratory failure. In our study of the 7 patients who died, died because of respiratory failure developed as a result of

organophosphate intoxication, 1 died because of ventricular tachycardia and ventricular fibrillation episodes as a result of bupropion intoxication, 1 died because of cardiac dysfunction as a result of high dose of digoxin, 1 died due to propranolol + amitriptylin, and 1 died due to kinapril hidrochlortiazide + salicylate intoxication that caused bradycardia and refractory hypotension.

The World Health Organization estimates that annually, 3,000,000 patients apply to hospitals due to pesticide intake, 2,000,000 of these are suicidal attempts and 220,000 of these cases died (20). In the study by Bilgin et al. (21), the mortality rate because of organophosphate was detected as 21.6%. However, in the study by Dong and Simon (22) conducted in 2001, this rate was reported as 8.3%; they have noted that this rate rapidly increases each year. In our study, 3 (3.1%) cases died. Our mortality rates because of organophosphate intoxications were detected lower than those previously reported.

Intensive care unit mortality rates have different results. For instance, in the study by Schwake et al. (23), they have followed all the intoxication cases in the intensive care unit and reported the mortality rate as 0.7%. These and similar results are enormous. Further, in our study, the general mortality rate is 0.33%. Our mortality rate was lower than the similar studies. In this respect, closely following up all intoxication cases in toxicology unit can be effective or similar to the study conducted by Schwake et al. (23), following all patients in the intensive care unit may be effective. This may be because of the different inclusion criteria for the intensive care unit. Rates of admission to intensive care unit are highly effective on the intensive care unit mortality rate. For instance, in a study, while 29.2% of the patients who took tricyclic antidepressant drugs were admitted to the intensive care unit (9), in another study, 88% of the organophosphate intoxications were admitted to the intensive care unit (24).

Şencan et al. (17) have divided the cases in two groups as died and survived; they demonstrated that in the dead group, the mean age was high, admission GCS was low, and duration of attachment to MV was longer ($p < 0.05$, $p < 0.001$, and $p < 0.001$, respectively). In our study, no significant difference was detected between the dead and survived groups.

In the study conducted by Lam et al. (18) with 265 intoxication cases followed up in intensive care unit, 67.9% of the patients required mechanical ventilation. The most common reason for mechanical ventilation was unconsciousness. The mean mechanical ventilation requirement was detected less than 1 day. In patients who required mechanical ventilation more than 1 day, aspiration pneumonia, rhabdomyolysis, and acute renal failure has been detected.

Singh et al. (19) conducted a study with 138 intoxication cases that were followed up in the intensive care unit and have reported that 13 cases required mechanical ventilation. Henderson et al. (13) in their study with 732 patients have reported the need of mechanical ventilation as 79.5%. Further, Göksu et al. (25) in their study with 179 patients have reported that 16 (8.9%) patients required mechanical ventilation, and the mean duration of mechanical ventilation of these cases was 3.81 ± 1.12 days.

In our study, as we considered all 2118 intoxication cases that were hospitalized during the 2-year-period, 23 (1.1%) of them required mechanical ventilation and only 7 (0.33%) cases died. The most common reasons of the mechanical ventilation were unconsciousness and respiratory failure. Only 2 cases were connected to mechanical ventilator because of cardiopulmonary arrest. The mean duration of the connection to mechanical ventilator was 4.17 days, at least 1 day and maximum 23 days.

Demir et al. (26) have found significant difference between the substance that caused intoxication and duration of mechanical ventilation ($p < 0.01$). For the cases that have carbon monoxide (CO) intoxication, the duration of mechanical ventilation was 8.50 ± 19.84 days and was detected as significantly higher than that of other substances ($p < 0.05$). In our study, the mean duration of mechanical ventilation of organophosphate intoxication cases was 6.92 days, and the other non-organophosphate group was 1.18 days. There is significant difference between the two groups ($p < 0.01$). Moreover, the initial admission prolactin levels of the organophosphate group is significantly different from the other group ($p = 0.003$). These two values suggest that organophosphate intoxications lead to more inflammatory response and cause more damage to the systems.

Study limitations

The small number of patients and a wide range of patients is a disadvantage for the statistical reliability of our results. For more accurate judgments about the intoxication cases requiring mechanical ventilation, multicenter large case series are required. Further, different approaches about the hospitalization indications of intoxication cases to intensive care units hinder the standardization of the studies about this issue. In particular, mortality rates are quite variable. Lower mortality rates in our clinic may be because all the intoxication cases followed up in the toxicology intensive care unit.

Conclusion

Intoxication cases requiring mechanical ventilation can differ from classical intoxication epidemiology for age and sex. No marked difference was observed between the dead and survived intoxication cases requiring mechanical ventilation for age, sex, admission consciousness status, blood gas pH, saturation, lactate level, and the duration of mechanical ventilation. Organophosphate intoxications are one of the intoxication types requiring mechanical ventilation and have the highest mortality. To reduce the mortality rates of intoxication cases, fully equipped private toxicology units should be more developed.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Necmettin Erbakan University Faculty of Medicine.

Informed Consent: Written informed consent wasn't obtained from patients who participated in this study because our study is a retrospective study and the data obtained by screening of the patient files.

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