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Original Article

# Palliative Care on Patients With Paraquat Poisoning: Analysis of 90 Cases From 2005–2016

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SUMMARY

*Background:* Paraquat poisoning has high mortality rate. Hospice services have been provided by National Health Insurance program in Taiwan since 2000, and were expanded to noncancer illnesses in September 2009. The palliative care strategy and the impact of this expanded palliative care policy on patients with paraquat poisoning remain unclear.

*Methods:* The study included 90 in-patients with paraquat poisoning, hospitalized between January 2005 and April 2016. We analyzed these patients by two factors, survivors vs. non-survivors and patients admitted between 2005 and 2010 vs. between 2011 and 2016, to compare the differences in life-sustaining treatment orders, symptom management, and use of non-beneficial life-sustaining treatments.

*Results:* The mortality rate was 75.6% and patients progressed rapidly to death (mean time: 74.69 h). 91.2% of non-survivors had a do-not-resuscitate order. Within the 24 h before death, non-survivors in the 2011–2016 group had significantly less treatment with vasopressors ($p < 0.001$) and mechanical ventilation ($p = 0.004$), and cardiopulmonary resuscitation ($p = 0.008$) than those in the 2005–2010 group. There was no difference in use of antibiotics, immunosuppressive agents, hemoperfusion, and opioids or benzodiazepines.

*Conclusion:* Patients with paraquat poisoning are suitable candidates to have palliative care, owing to the extremely high mortality rate and rapid disease progression. The expanded palliative care policy had a positive impact on terminal paraquat poisoning patients; it decreased non-beneficial life-sustaining treatments in the end-stage of disease. Nevertheless, there is still much room for improvement in our management of paraquat poisoning by reducing non-beneficial life-sustaining treatments and reinforcing palliative treatments.



## 1. Introduction

Paraquat is one of the major herbicides used in the agricultural countryside of Taiwan, and it can be ingested accidentally or during a suicide attempt.[1] In fact, paraquat poisoning accounts for two-thirds of the herbicide suicides in Taiwan.[2] The high toxicity of paraquat results in extremely high mortality.[3] In current practice, the therapeutic regimen mainly consists of immunosuppressive agents, cyclophosphamide (CP), and methylprednisolone (MP). The use of CP and MP pulse therapy comes from the experience of treating patients with severe lung injury secondary to systemic lupus erythematosus,[4,5] since lung injury is also the primary cause of mortality in paraquat poisoning.[6] Activated charcoal hemoperfusion is also used to decrease the concentration of paraquat in plasma.[7,8] Traditionally in Taiwan, any aggressive treatment to maintain the patient's vital signs were used, and the quality of life of the patients were often neglected. In spite of the aggressive disease management, the mortality of paraquat poisoning is still

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high. From the data analyzed by Wu et al. between 1997 and 2009, the mortality rate was 78.6% for the 1811 patients hospitalized for paraquat poisoning in Taiwan.[9]

The central principle of palliative care, as defined by the World Health Organization, is to prevent and relieve suffering by "early" identification, assessment, and treatment of pain and other types of physical, psychological, emotional, and spiritual distress.[10] Thus, terminal patients with paraquat poisoning can also be candidates for palliative care. Hospice services have been provided by the National Health Insurance program in Taiwan since 2000, and were expanded to noncancer illnesses in September 2009. The expanded hospice services to noncancer illness include the diagnosis of organic psychotic conditions, brain deterioration, heart failure, chronic obstructive pulmonary disease, other diseases of the lung (such as severe fibrotic lung disease), liver cirrhosis, and acute or chronic renal failure in the funding program. The expanded policy is a landmark shift and has positively impacted noncancer hospice care in Taiwan.[11] The impact of this expanded palliative care policy on patients with paraquat poisoning remains unclear. Therefore, we conducted a study on the medical treatment of paraquat poisoning, comparing patients before and after this expanded palliative care policy.

## 2. Materials and methods

### 2.1. Subjects

This retrospective observational study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Mackay Memorial Hospital, with IRB number 15MMHIS072. The patient records and information were anonymized and de-identified prior to analysis. Patients with paraquat poisoning admitted in Taitung Mackay Memorial Hospital between January 2005 and April 2016 were included in this study, and Taitung Mackay Memorial Hospital is a regional teaching hospital in eastern Taiwan providing 500 beds and 24 h accident and emergency service. Patients who had age <20 years old or unavailability of follow-up data were excluded from the study. 90 consecutive patients with paraquat ingestion were admitted to the Taitung Mackay Memorial Hospital. Of the 90 patients, 22 survived and 68 died. Medical history, clinical signs, and laboratory examinations were used to diagnose paraquat poisoning. Without a spectrophotometer to measure plasma paraquat concentration, a qualitative urine-sodium dithionite reaction was used. Demographic data, do-not-resuscitate (DNR) orders, prescribed medications, length of stay, and intra-hospital course were obtained from the hospital medical registry.

### 2.2. Before and after the expanded policy regarding noncancer illness

The patients are categorized by their admission date. We chose 2010/2011 as the division point because we theorized that the expanded policy regarding terminal noncancer conditions may take time to influence physicians' clinical practice. We also show the treatment administered to patients within the 24 h before the death. This included the continuous use of antibiotics, immunosuppressive agents, hemoperfusion, and the administration of opioids or benzodiazepines.

### 2.3. Definition of do-not-resuscitate and do-not-intubate orders

DNR orders instruct medical staff not to administer cardiopulmonary resuscitation when a patient progresses to cardiac arrest. The procedures of resuscitation include cardiac massage, airway management with endotracheal intubation, epinephrine/vasopressin injection, or even defibrillation if the electrocardiogram shows ventricular arrhythmia. Beyond resuscitation attempts, the patients with DNR orders can still receive varieties of aggressive disease management in clinical practice, such as immunosuppressive therapy and hemoperfusion. In general, a do-not-intubate (DNI) order is in effect immediately after patients sign the DNR consent form. However, some patients receive DNR orders after they have already been intubated. In these situations, the DNR orders are consented by their surrogate decision-makers (e.g., family members and legal guardians) because of the impaired communication ability with an endotracheal tube.[12]

### 2.4. Statistical analysis

Results are expressed as the mean ± standard deviation or as percentages. Student's *t*-test was used to compare differences between groups for continuous variables, and the chi-square test was employed for categorical data. A p-value <0.05 was considered significant. All statistical analyses were performed using the SPSS software, version 22 (IBM SPSS Statistics, Armonk, NY).

## 3. Results

### 3.1. Survivors vs. non-survivors

The mean age of the 90 patients with paraquat poisoning was 55.16 ± 17.44 years, and 56 patients (62.2%) were men. As seen in Table 1, the overall mortality rate for the entire population was 75.6% (68 of 90 patients). Non-survivors were significantly older (57.72 ± 17.42 years vs. 47.23 ± 15.27 years, p = 0.01), received more DNR orders (91.2% or 62 of 68 patients vs. 18.2% or 4 of 22 patients, p < 0.001), received more endotracheal intubation for respiratory failure (47.1% or 32 of 68 patients vs. 0% or 0 of 22 patients, p < 0.001) (Table 1). In fact, all non-survivors experienced respiratory failure before death, significantly higher than the survivors (0 experienced respiratory failure). The percentage of patients experiencing unstable hemodynamic condition was also significantly higher in non-survivors; therefore, more of them used a vasopressor (36.8% or 25 of 68 patients vs. 0% or 0 of 22 patients, p < 0.001). The proportion of patients receiving pulse therapy of immunosuppressive agents, CP and MP, and hemoperfusion was insignificantly different between non-survivors and survivors.

**Table 1**
Comparisons between survivors group and non-survivors group.

| Data field | Survivors (n = 22) | Non-survivors (n = 68) | P value |
|---|---|---|---|
| Male (%) | 9 (40.9) | 47 (69.1) | 0.02 |
| Age (years) | 47.23 ± 15.27 | 57.72 ± 17.42 | 0.01 |
| DNR orders (%) | 4 (18.2) | 62 (91.2) | <0.001 |
| CPR (%) | 0 (0) | 6 (8.8) | <0.001 |
| Endotracheal Intubation (%) | 0 (0) | 32 (47.1) | <0.001 |
| Respiratory failure (%) | 0 (0) | 68 (100) | <0.001 |
| CP + MP pulse therapy (%) | 18 (81.8) | 61 (89.7) | 0.14 |
| HP (%) | 22 (100) | 61 (89.7) | 0.29 |
| Use of vasopressor (%) | 0 (0) | 25 (36.8) | <0.001 |
| LOS in hospital (hours) | 350.86 ± 186.58 | 74.69 ± 120.07 | <0.001 |

DNR = do-not-resuscitate; CPR = cardiopulmonary resuscitation; CP = cyclophosphamide; MP = methylprednisolone; HP = hemoperfusion; LOS = length of stay.

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