Systemic Corticosteroid as an Adjunct for Acute Respiratory Distress Syndrome in Non-Fatal Fresh Water Drowning: An Evidence-based Case Report

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ABSTRACT

Background: *Acute lung injury or acute respiratory distress syndrome (ARDS) is one of the most common complications of non-fatal drowning. Although respiratory societies' guidelines endorse the role of systemic corticosteroids in ARDS, the evidence for systemic corticosteroids use in ARDS due to non-fatal drowning is limited.* ***Methods:*** *A search was conducted on Pubmed, OVID, and EuropePMC, assessing the clinical question using inclusion and exclusion criteria. The selected studies were critically appraised, and the results were summarized.* ***Results:*** *A total of six retrospective studies were selected and assessed, all studies showed poor validity and a high risk of bias. Out of six studies, only four informed us of steroid administration's effect on outcomes. In two studies, mortality associated with corticosteroid administration seemed to be higher. On the contrary, one study found no mortality in the corticosteroid group, but 100% mortality was observed in the control group. In another study, steroid therapy seemed to not affect hospital length of stay or mechanical ventilation rates.* ***Conclusion:*** *Corticosteroid administration for non–fatal drowning and its impact on clinical outcomes remain equivocal. Routine administration of corticosteroids is not indicated and should be done on a case-by-case basis.*

Keywords: *Non-fatal drowning, corticosteroid, acute respiratory distress syndrome, evidence-based case report.*

INTRODUCTION

Drowning is a process of respiratory impairment due to submersion or immersion in liquid.[1] When the respiratory impairment is stopped before death, the drowning event is known as non–fatal drowning.[1] A myriad of complications is associated with drowning, with acute lung injury or acute respiratory distress syndrome (ARDS) as one of the most common complications.[2,3] When more than 1 – 3 mL/kg of liquid is aspirated into the lungs, the surfactant's ability to prevent alveoli collapse is impaired, leading to respiratory compromise and hypoxemia.[3] Although the respiratory societies' guidelines endorse the role of systemic corticosteroids for ARDS, the evidence for

systemic corticosteroids use in the case of ARDS due to non-fatal drowning is limited.[4] Herein, we report a case of an 82-year-old woman who presented to the emergency department due to freshwater non–fatal drowning, who subsequently evolved into ARDS. Our case wants to highlight and review the current literature on the role of systematic corticosteroids in non-fatal drowning–induced ARDS.

CASE ILLUSTRATION

An 82-year-old Asian woman was brought to the E.D. by her family due to breathlessness after being found drowning in a freshwater pool more than 30 minutes two hours before admission. Her previous medical history was significant for Alzheimer's disease and arterial hypertension. On initial presentation, her vitals were significant for tachypnea and low peripheral oxygen saturation (SpO2). Her laboratory findings showed severe hyponatremia, severe hypoxemia, increased CRP values, and increased AST and ALT concentrations. Her chest x-ray showed bilateral infiltrates on the middle and lower lung zones. Initial findings were consistent with acute respiratory distress syndrome, type 1 respiratory failure, severe hyponatremia, pneumonia, and transaminitis.

After she was stabilized, she was sent to the intensive care unit for further monitoring. She received total parenteral nutrition from the central venous catheter, 500 mL of 3% sodium chloride given for 24 hours, 750 mg of levofloxacin once daily IV, and 40 mg of esomeprazole once daily IV. Her oral medications consisted of 2.5 mg bisoprolol once daily and 40 mg telmisartan once daily, 20 mg atorvastatin once daily, and symptomatic treatments. For her oxygenation, she received 6 – 15 liters of oxygen per minute via a non-rebreathing mask with a peripheral oxygen saturation target of 94 – 95%. The hepatologist was consulted for the investigation of elevated liver enzymes and a neurologist was consulted for Alzheimer treatment.

On the second day of care, 1 gram of meropenem thrice daily was added as her procalcitonin serum was elevated. We also performed a diagnostic bronchoscopy on her to evaluate and evacuate any foreign bodies due to drowning. The bronchoscopy showed no foreign bodies and her bronchoalveolar lavage was consistent with pulmonary infection. The BAL specimen was sent for bacterial and fungal culture, tuberculosis PCR, and fluid cytology.

On her third day, as her oxygenation improved, we changed NRM with a simple mask. On the fourth day, she experienced supraventricular tachycardia, and her condition deteriorated. Cardiology was consulted and consequently she received a bolus of diltiazem 25 mg intravenous followed by 5 mcg/kg/minute maintenance. Following diltiazem administration, her heart rate decreased to 80 – 100 BPM and her oxygen saturation was stable at 96 – 100% on 10 LPM of NRM. On the fifth day in the morning, she became dyspneic and tachypneic, and her SpO2 dropped to 90% with 15 LPM of NRM. Pulmonary auscultation revealed wheezing on all lung fields. Laboratory findings showed increased CRP and procalcitonin Therefore, she was nebulized with salbutamol and an IV methylprednisolone (MP) 62.5 mg twice daily and she was put on a high flow nasal cannulation with FiO2, and oxygen flow titrated accordingly Her SpO2 improved to 99%. On sixth day of hospitalization, her D-dimer was increased and she was diagnosed with non-overt DIC. Consequently, we gave her unfractionated heparin (UFH) 2500 unit/ 24 hours.

On the tenth day of hospitalization, IV MP was tapered to 62.5 mg once daily. As she was stabilized, on the eleventh day of hospitalization she was stepped down from the ICU to medicine ward. The IV MP was switched to 16 mg MP twice daily for the next two days and UFH administration was being planned for the next several days.

On 12th she experienced hematochezia, UFH administration was immediately stopped, and a gastroenterologist was consulted for gastrointestinal bleeding treatment. Her GI bleeding resolved completely with the double dose esomeprazole. A multidisciplinary management was pursued with a geriatrician and a physical medicine and rehabilitation physician were consulted to expedite her recovery. As patient complained of continuous abdominal pain, she was consulted to the gastroenterologist surgeon, which no significant findings were found.

Over the next five days, her condition improved drastically, and her vitals were stable. Finally, after seventeen days of hospitalization, she was discharged from the hospital with stable vitals. The patient's hospitalization course is depicted in the **Figure 1.**

One month after hospitalization, the patient returned for follow-up visits to a respirologist, gastroenterologist, cardiologist, and neurologist. The patient came with complaints of hardened stool painful bowel movements and was still experiencing hematochezia, otherwise normal vitals and physical examination. Follow-up laboratory results showed resolution of transaminitis, improved CRP and D-Dimer values, without apparent signs of thrombosis and/or embolism.

CLINICAL QUESTION

In this complicated case, we want to investigate the role of steroid as an adjunct for ARDS for non-fatal drowning as the evidence regarding it is equivocal. The following PICO was investigated.

Patients (P): Drowning victims.
Intervention: Corticosteroid administration.
Control: No corticosteroid administration.
Outcome: Mortality, length of stay, mechanical ventilation, and pneumonia incident Clinical improvement and mortality.

METHODS

We performed a systematic search on 17 November 2022 in Pubmed, OVID, and EuropePMC, with the following keywords and their synonyms: Drowning AND Steroid, from the inception up to 17 November 2022. The keywords used for search strategies are presented in **Table 1**.

Eligibility criteria and Article Selection

The evidence-based case report included articles with human participants with non-fatal drowning that received steroid administration. The outcome of interests were mortality, length of stay, mechanical ventilation, and pneumonia incident.

We included the following type articles: case-series, observational studies, randomized controlled trials, and systematic review with or without meta-analysis that were available in English language. We excluded case report and a letter to the Editor. We also examined each included articles' references and we included them if they met the inclusion criteria.

Critical Appraisal

Critical appraisal was performed using the critical appraisal tools available on the internet from the Center for Evidence Based Medicine (CEBM) at the University of Oxford. JH and AS conducted independent critical appraisals of the study and any discrepancies were resolved through discussion and adjudicated by EDT. (**Table 2**)

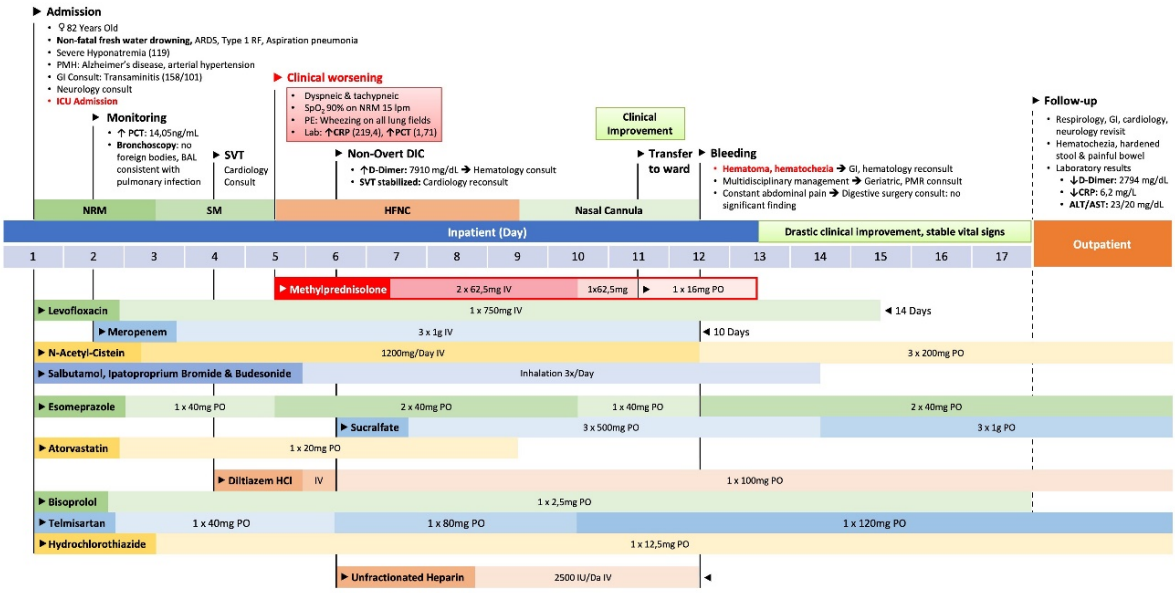

Figure 1. Patient's Hospitalization Course.

Table 1. Keywords used for search strategies.

	Search Terminology	Results
PUBMED <November 15, 2022>		
#1	("Non-Fatal"[All Fields] AND ("drowning"[MeSH Terms] OR "drowning"[All Fields] OR "drown"[All Fields] OR "drowned"[All Fields] OR "drownings"[All Fields] OR "drowns"[All Fields])) OR ("near drowning"[MeSH Terms] OR ("near"[All Fields] AND "drowning"[All Fields]) OR "near drowning"[All Fields]) OR ("near drowning"[MeSH Terms] OR ("near"[All Fields] AND "drowning"[All Fields]) OR "near drowning"[All Fields]) OR ("Wet"[All Fields] AND ("drowning"[MeSH Terms] OR "drowning"[All Fields] OR "drown"[All Fields] OR "drowned"[All Fields] OR "drownings"[All Fields] OR "drowns"[All Fields])) OR (("neoplasm metastasis"[MeSH Terms] OR ("neoplasm"[All Fields] AND "metastasis"[All Fields]) OR "neoplasm metastasis"[All Fields] OR "secondaries"[All Fields] OR "secondary"[MeSH Subheading] OR "secondary"[All Fields]) AND ("drowning"[MeSH Terms] OR "drowning"[All Fields] OR "drown"[All Fields] OR "drowned"[All Fields] OR "drownings"[All Fields] OR "drowns"[All Fields])) OR (("immersion"[MeSH Terms] OR "immersion"[All Fields] OR "submersion"[All Fields] OR "submersions"[All Fields] OR "submersed"[All Fields] OR "submersible"[All Fields] OR "submersibles"[All Fields]) AND ("injurie"[All Fields] OR "injuried"[All Fields] OR "injuries"[MeSH Subheading] OR "injuries"[All Fields] OR "wounds and injuries"[MeSH Terms] OR ("wounds"[All Fields] AND "injuries"[All Fields]) OR "wounds and injuries"[All Fields] OR "injurious"[All Fields] OR "injury s"[All Fields] OR "injuryed"[All Fields] OR "injurys"[All Fields] OR "injury"[All Fields]))	3757
#2	"adrenal cortex hormones"[MeSH Terms] OR ("adrenal"[All Fields] AND "cortex"[All Fields] AND "hormones"[All Fields]) OR "adrenal cortex hormones"[All Fields] OR "corticosteroid"[All Fields] OR "corticosteroids"[All Fields] OR "corticosteroidal"[All Fields] OR "corticosteroide"[All Fields] OR "corticosteroides"[All Fields] OR ("steroidal"[All Fields] OR "steroidals"[All Fields] OR "steroidic"[All Fields] OR "steroids"[MeSH Terms] OR "steroids"[All Fields] OR "steroid"[All Fields]) OR ("prednisolon"[All Fields] OR "prednisolone"[MeSH Terms] OR "prednisolone"[All Fields]) OR ("prednison"[All Fields] OR "prednisone"[MeSH Terms] OR "prednisone"[All Fields]) OR ("methylprednisolone"[MeSH Terms] OR "methylprednisolone"[All Fields] OR "methylprednisolon"[All Fields]) OR ("hydrocortisone"[MeSH Terms] OR "hydrocortisone"[All Fields] OR "hydrocortisones"[All Fields]) OR ("dexamethason"[All Fields] OR "dexamethasone"[MeSH Terms] OR "dexamethasone"[All Fields] OR "dexamethasone s"[All Fields] OR "dexamethasones"[All Fields])	1291.542
#3	1 AND 2	96
	Europe PMC <November 15, 2022>	
#1	("Non-Fatal Drowning" OR "Near Drowning" OR "Near-Drowning" OR "Wet Drowning" OR "Secondary Drowning" OR "Submersion Injuries")	2.897
#2	("Corticosteroid" OR "Steroids" OR "Prednisolone" OR "Prednisone" OR "Methylprednisolone" OR "Hydrocortisone" OR "Dexamethasone")	854.734
#3	#1 AND #2	367
	Journals@Ovid Full Text <November 15, 2022>; Your Journals@Ovid	
1	(Non-Fatal Drowning or Near Drowning or Near-Drowning or Wet Drowning or Secondary Drowning or Submersion Injuries).mp. [mp=ti, ab, tx, ct]	2227
2	(Corticosteroid or Steroids or Prednisolone or Prednisone or Methylprednisolone or Hydrocortisone or Dexamethasone).mp. [mp=ti, ab, tx, ct]	559105
3	1 and 2	280

Data Extraction

A predesigned data extraction form was utilized to include the following data: Author's name, study origin, population, intervention group, comparison group, and outcomes. Data extraction was performed independently by EDT and JH.

RESULTS

Our search yield 743 articles. After the removal of duplicates, 622 articles remained. Then, after the title and abstract screening, only 17 articles were available for full – text review. Finally, only six articles were eligible for critical appraisal.[5–10] (**Figure 2**)

Critical Appraisal

We performed a critical appraisal using Oxford CEBM tools to appraise validity, importance, and applicability of the included studies.[11] As there were several study types, we chose the appropriate tool for each the study

Table 2. Validity of selected studies (Retrospective Cohorts).

	Modell JH	Sladen A	Caroll MAJ	Simcock AD	Van Berkel	Saidel-Odes LR
Was the defined representative sample of patients assembled at a common point in the course of their disease?	Yes	Yes	Yes	Yes	Yes	Yes
Was patient follow-up sufficiently long and complete?	Unclear	Yes	Unclear	Unclear	Yes	Unclear
Were outcome criteria either objective or applied in a 'blind' fashion?	Unclear	No	No	No	Yes	No
If subgroups with different prognoses were identified, did adjustment for important prognostic factors take place?	Unclear	Yes	No	No	No	No

types. (**Table 2)** Overall, the validity of all included studies was poor and prone to bias.

Data Extraction

As mentioned above, the following data: Author's name, study origin, population, intervention group, comparison group, and outcomes were extracted and are presented in **Table 3**.

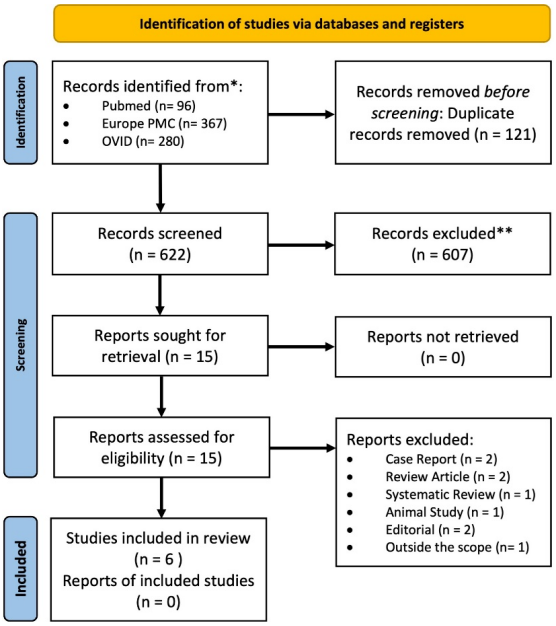

Figure 2. PRISMA Flowchart for Systematic Review.

*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools. (From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71)

DISCUSSION

We identified six studies in our search for the answer to our clinical question. Overall, the studies' quality were very low. The studies ranged from 1967 – 2003. Before 2003, there was no uniform reporting guideline (Utstein style) for data on drowning. Thus, preventing adequate comparisons between studies.[12]

Moreover, before 2005, the definitions used for drowning were heterogeneous.[13] Therefore, we can see interchangeable terminologies for non-fatal drowning in the identified studies in the systematic review, i.e., near drowning, submersion, and immersion syndrome. Today, only two terminologies are recognized, i.e., fatal drowning and non – fatal drowning.[1] Other terminologies should be avoided.

The rationale for corticosteroid administration for drowning patients was because it was considered a subtype of aspiration pneumonia and it was observed that in the prototypical aspiration pneumonia (Mendelson syndrome), corticosteroid administration can improve patient's survival rate. Corticosteroids exert anti-inflammatory effects both nonspecifically and locally, thereby directly targeting and reducing acute inflammatory processes, ultimately resolving pulmonary edema.[6]

In our EBCR, out of six studies, only four informed us of steroid administration's effect on outcomes, i.e., mortality, mechanical ventilation, and ICU and hospital length of stay.

Overall the results regarding steroid administration on clinical outcomes were

Table 3. The characteristics of included studies in this evidence-based case report.

First Author and Study Origin	Year of Study	Study Design	Population	Age (Years)	Male (%)	Intervention	Comparison	Outcome
Modell JH, USA	1967	Retrospective review of charts	91 patients with n ear drowning	N/A	N/A	Steroid therapy (n= 52)	No Steroid (n= 36)	Mortality 8/52 (15%) vs 2/36 (5.6%)
Sladen A, USA	1971	Prospective case series	10 patients with near drowning and pulmonary edema	N/A	N/A	Methylprednisolone sodium succinate 5 mg/ kg/ 24 hours in 6 divided doses (n= 7)	No steroid (n= 3)	Mortality 0/7 (0%) vs 3/3 (100%)
Caroll MAJ, USA	1971	Retrospective case records review	64 patients with near–drowning	18 months - 59 years (Min-Max)	N/A	Steroid therapy (n= 9)	No steroid (n= 55)	No difference in clinical and radiological recovery. No data
Simcock AD, Netherland	1986	Retrospective case review	130 patients with near drowning/ immersion syndrome	N/A	N/A	Methylprednisolone 30 mg/kg BW, IV, as soon as the patient is admitted and repeated 8 hours later (n= 68)	No steroid (n= 53)	Mortality 12/68 (17.6%) vs 0/53 (0%)
van Berkel, Netherland	1996	Retrospective study	125 patients with near drowning	30.7 ± N/A (Mean ± SD)	69.6	Steroid therapy (n= 44) The mean loading dose: is 10.6 mg prednisolone/ kg BW, and the mean maintenance dose: is 2.5 mg prednisolone/kg BW/day	No steroid (n= 58)	No effect of mechanical ventilation, ICU length of stay, and hospital length of stay
Saidel-Odes LR, Israel	2003	Retrospective observational analysis	69 patients with near drowning	66 ± 13.5 (Mean ± SD)	49.3	Steroid therapy (n= 21)	No steroid (n= 48)	All patients survived

mixed. In two studies, mortality associated with corticosteroid administration seemed to be higher [8/52 (15%) vs. 236 (5.6%); 12/68 (17.6%) vs. 0/53 (0%)].[5,8] However, the corticosteroid groups disproportionately consisted of patients with more severe clinical presentations.

In study by Sladen et al., no mortality was observed in the corticosteroid group while 100% mortality was observed in the control group [0/7 (0%) vs 3/3 (100%)].[6] Compared to the previous two studies, this study compared patients with the same degree of disease severity, i.e., patients with near–drowning presenting with pulmonary edema. Nonetheless, there was no blinding for the corticosteroid administrators, and the number of subjects enrolled was small (n= 10; 7 in the corticosteroid group vs. 3 in the control group). In another study, steroid therapy did not affect hospital length of stay or mechanical ventilation rates.[9] However, it was not associated with incident pneumonia, a complication that was feared because it attenuates infection response.[14]

Regarding corticosteroid doses, only three studies used a standardized dose. The dosing protocols for these studies were also variable. In Sladen et al. study, they administered intravenous (IV) methylprednisolone sodium succinate with a 5 mg/kg/24-hour dose in 6 divided doses.6 In Simcock et al. study, they administered IV methylprednisolone with a dose of 30 mg/ kg as soon as the patient was admitted and repeated after 8 hours later.[8] Finally, the study by van Berkel et al. showed a loading dose of prednisolone of 10.6 mg/kg and continued with a maintenance dose of 2.5 mg/kg.[9]

Compared to the studies mentioned above, our case used a much lower steroid dose (125 mg, 62.5 mg, and 32 mg of methylprednisolone per day). We also initiated steroids much later and continued for more than 72 hours (started on day 5 of hospitalization due to clinical deterioration and stopped on 11th day of hospitalization) compared to what was recommended by Sladen et al. (early and continued for 72 hours).

However, the steroid dose that we gave was comparable to the dose used in a randomized clinical trial (20 mg dexamethasone or equivalent to 106 mg) and a meta-analysis (2 mg/kg

methylprednisolone) for acute respiratory distress syndrome, which significantly decreased the mortality rate, time to unassisted breathing, and ICU length of stay.[15,16]

Since the landmark paper by Calderwood et al. that examined the role of corticosteroid (IV methylprednisolone 30 mg/kg) on dogs that had aspirated distilled water (22 or 44 mL/kg), and did not find differences in survival rates, pulmonary shunts, and arterial blood gases compared to the control group, the practice of corticosteroid administration for non – fatal drowning victims have become rarer.[17] Nonetheless, we argue that human studies should be performed before making such an assertive statement.

The major limitation of our EBCR is limited by the quality of the evidence. The included studies were very poor in quality and no definite conclusion can be drawn.

CONCLUSION

We concluded that the evidence of corticosteroid administration for non–fatal drowning patients and its impact on patients' clinical outcomes remain equivocal. Furthermore, there were no standardized dosing protocols and appropriate timing for corticosteroid administration. Well-designed randomized controlled trials are needed to evaluate the evidence. Until robust evidence on this matter is available, routine administration of corticosteroids for non–fatal drowning victims is not indicated and should be done on a case-by-case basis. Nonetheless, if ARDS developed, systemic corticosteroid should be considered. In our case, dramatic improvement was seen after the administration of corticosteroids, and might be due to beneficial effect.

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