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ORIGINAL RESEARCH

Pre-hospital 'dirty adrenaline': A descriptive case series of patients receiving peripheral dilute adrenaline infusions in Central Australian remote nurse-led clinics prior to aeromedical retrieval

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Abstract

Objectives: 'Dirty adrenaline' is the informal term used for a rapidly made peripheral dilute adrenaline infusion in the emergency treatment of shock, most commonly 1 mg adrenaline in 1 L 0.9% NaCl. It has long been part of the remote clinician's arsenal despite no supporting scientific literature. Remote clinics in Central Australia can be hours away from critical care support. The region's high prevalence of renal and cardiac disease means that access to early vasopressors and inotropes is a necessity for treating shock. To tackle this, remote clinicians often use 'dirty adrenaline'. We present a review of 'dirty adrenaline' use in this region.

Methods: Central Australian Retrieval Service's database was screened to identify cases in which a peripheral dilute adrenaline infusion was administered in a remote clinic prior to patient aeromedical retrieval. A retrospective chart review collected: patient demographics; clinical characteristics; infusion details; adverse events; hospital lengths of stay; and mortality outcomes.

Results: Fifty-seven cases were identified. Median patient age was 50 (range: 2–96). Septic shock was the most common clinical indication (40/57). Median infusion duration was 155 min. Median systolic BP from commencement until retrieval increased from 75.5 to 91 mmHg. Survival to hospital discharge was 86% (49/57). No significant adverse events associated with 'dirty adrenaline' were recorded.

Conclusion: 'Dirty adrenaline' is safe to administer and appears to considerably improve survival when used to treat fluid-resistant shock in remote nurse-led clinics guided by an off-site critical care physician.

Key words: *epinephrine, pre-hospital, retrieval, rural health, septic shock.*

Key findings

- 'Dirty Adrenaline' is safe to administer.
- 'Dirty Adrenaline' appears to considerably improve survival in fluid-resistant shock in remote Central Australia.

Introduction

'Dirty adrenaline' is the common informal term used for a rapidly-made peripheral dilute adrenaline infusion in the emergency treatment of life-threatening shock while awaiting more definitive vasopressor or inotropic support. It is most often administered as 1 mg adrenaline in a 1 L bag of 0.9% NaCl (1 mcg/mL), and has been part of the emergency and remote physician's arsenal for many years. Despite this, the literature supporting peripheral dilute adrenaline is limited to online blog posts,[1–4] and there is almost no commentary on its use in remote and pre-hospital environments.[5] There is, however, relatively well-established evidence that short-term peripheral vasopressor infusions and 'push-dose' peripheral vasopressors can be administered safely.[6–11] There are also at least three Australasian national or regional guidelines currently referencing peripheral 1 mcg/mL adrenaline infusions, most commonly in the setting of refractory anaphylaxis.[12–14]

The geography of Central Australia means that patients presenting to remote nurse-led clinics are often several hours away from an Aeromedical Retrieval clinician with critical care capabilities based in Alice Springs Hospital (Supporting Information Appendix 1 – The geographical distribution of clinics in relation to Alice Springs). Challenging weather, resource limitations, and the limited number of night-capable airstrips, can further extend this time period. There is also a high rate of hospitalisation

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associated with renal and/or cardiac disease among the population of remote Central Australia,[15] meaning that many patients are sensitive to fluid overload and may benefit from early vasopressors or inotropes as opposed to internationally standard crystalloid fluid volumes in the treatment of shock. Remote Area Nurses have varying levels of critical care experience, and most clinics do not have the critical care equipment required for concentrated vasopressor and inotrope infusions.

As a solution to these challenges, Retrieval clinicians in Central Australia have developed a region-wide 'dirty adrenaline' infusion protocol for the management of fluid-refractory shock in remote clinics, in order to provide patients with early vasopressor and inotropic support (Supporting Information Appendix 2 – NT Health Adrenaline Infusion PHC Remote Guideline 2018). This protocol is available to all remote healthcare staff in the region, and provides structured guidance around setting up and commencing a 1 mcg/mL peripheral adrenaline infusion under the telephone guidance of the Medical Retrieval and Consultation Centre based in Alice Springs Hospital.[16]

We present a review of all cases between January 2017 and October 2023 in which a patient received 'dirty adrenaline' in a remote nurse-led clinic prior to aeromedical retrieval by a Retrieval doctor from the Central Australian Retrieval Service (CARS) and a nurse from the Royal Flying Doctor Service SA/NT (RFDS).

Methods

All patient retrievals by the Central Australian Retrieval Service since January 2017 are logged in the service's online audit database. The database was accessed and screened to identify every case in which a patient had received a peripheral dilute adrenaline infusion in the remote nurse-led clinic prior to the arrival of a CARS doctor.

A retrospective chart review was then performed on the clinic, retrieval, and hospital notes for each of these cases in order to collect the following data: patient demographics (age, biological sex and ethnicity); comorbidities increasing fluid overload risk; clinical indication for the peripheral dilute adrenaline infusion; systolic BP at the time of commencement, and on the arrival of the Retrieval doctor to the remote nurse-led clinic; location and size of the intravenous cannula used; duration of time that the patient received the infusion; amount of crystalloid fluid received as part of the infusion, and the total amount of pre-hospital crystalloid fluid that the patient received; any adverse events that were potentially or suspected to be associated with the infusion; further vasopressors/inotropes that the patient was treated with following the infusion; patient hospital and ICU lengths of stay; and patient mortality outcomes.

These results were then analysed by the research team before being presented in a local clinical governance meeting in order to obtain further discussion and conclusion points.

No statistical analysis was carried out because of the small patient numbers and descriptive nature of this case series.

Results

Fifty-seven cases were identified in which a patient received a peripheral dilute adrenaline infusion in a nurse-led clinic prior to the arrival of a Retrieval doctor from Alice Springs Hospital. Eight of these cases represent four patients, who each received an infusion on two separate occasions. The cohort demographics and clinical diagnoses for these cases are summarised in Table 1. Septic shock was the most common reason for a patient to receive peripheral dilute adrenaline. Female patients were disproportionately represented in the cohort at a ratio of 3:1.

Details of peripheral adrenaline infusion strengths, cannula sizes and cannula locations are summarised in Table 2. There was no documentation of the clinical rationale behind any divergence from the 1 mcg/mL protocol, and this subgroup of patients was a

TABLE 1. *Demographics, comorbidities and diagnoses*

Cohort demographics (53 patients)
40× Female (75%), 13× Male (25%)
46× Indigenous (87%), 7× Non-indigenous (13%)
Median age: 50 years (range: 2–96 years)
Comorbidities increasing fluid overload risk: 31 of 57 cases (65%)
16× Chronic kidney disease (28%)
6× Chronic kidney disease and Heart failure (11%)
4× Heart failure (7%)
2× Chronic kidney disease and Heart failure and Rheumatic heart disease (4%)
2× Chronic kidney disease and Rheumatic heart disease (4%)
1× Rheumatic heart disease and Heart failure (2%)
Clinical diagnosis (57 cases)
40× Septic shock (70%)
6× Cardiogenic shock (11%)
3× Refractory anaphylaxis (5%)
2× Status asthmaticus (4%)
2× Haemorrhagic shock (4%)
2× Post-ROSC hypotension (4%)
1× Mixed drug overdose (2%)
1× Intracranial haemorrhage (2%)

TABLE 2. *Infusion and cannula details*

Infusion strengths
49 cases: 1 mcg/mL (86%)
43 remained at 1 mcg/mL
4 escalated to 2 mcg/mL
1 escalated to 3 mcg/mL
1 escalated to 6 mcg/mL
3 cases: 60 mcg/mL (5%)
2 cases: 2 mcg/mL (4%)
3 cases: Not documented (5%)
Cannula sizes:
19 cases: 18G (33%)
11 cases: 20G (19%)
8 cases: 22G (14%)
2 cases: 16G (4%)
1 case: Intraosseous cannula (2%)
16 cases: Not documented (28%)
Cannula locations:
24 cases: Antecubital Fossa (42%)
14 cases: Forearm (25%)
1 case: Upper arm (2%)
18 cases: Not documented (32%)

heterogeneous one with no identifiable patterns of illness.

Table 3 summarises the durations of the peripheral adrenaline infusions, the volumes of crystalloid fluid received, the changes in systolic BP, further vasopressor and inotrope infusions received, length of ICU and hospital stays, mortality outcomes and adverse events.

Figure 1 demonstrates the change in systolic BP between adrenaline infusion commencement and patient retrieval for all cases with the available data.

Of the six patient deaths, three have been retrospectively reviewed and deemed to have been non-survivable illness episodes: two patients with prolonged cardiorespiratory arrest (greater than 40 min) prior to ROSC, and one patient with a catastrophic sub-arachnoid haemorrhage. The other three deaths were attributed to septic shock (two cases) and cardiogenic shock (one case). The one patient who chose to self-discharge from the care of the retrieval team prior to transfer to hospital (with the mental capacity to do so), is still alive as of 2 January 2024.

All adverse clinical events occurred in separate cases. One case had documentation of 'cold fingers' in the limb receiving the infusion, but no lasting neurovascular complications following this. There was one case of tachycardia of 135 bpm, resolved by the clinic staff reducing the rate of the infusion. There was one case in which the adrenaline infusion was stopped because of hypertension, with no further concerns following this. The single documented case of intravenous cannula leakage had no concerning features of extravasation injury, and the case of extravasation from an intraosseous device was managed conservatively with no long-lasting complications. The case of pain at the infusion cannula site was resolved by changing to another cannula. There was one case of poor patient compliance, with the patient complaining that the infusion pump was too noisy, resulting in the adrenaline infusion being stopped. Two cases had fluid overload documented in the patient's hospital notes, although neither specifically mentioned an association with the adrenaline infusion.

This review has also identified many interesting non-septic shock cases, in which it is felt that there was likely clinical benefit from the 'dirty adrenaline' that these patients received. These include:

- A 44 years old female, with traumatic intra-abdominal haemorrhagic shock, who received 'dirty adrenaline' in order to maintain mean arterial pressure >60 mmHg prior to retrieval from the remote clinic. She made a full recovery following surgical intervention and multiple blood transfusions in hospital.
- A 29 years old male with status asthmaticus, presenting to the remote clinic obtunded with profound type 2 respiratory failure, who had recovered back to their baseline after 3 h of 'dirty adrenaline' and manual assisted bag-mask ventilation.
- A 48 years old female with a mixed drug overdose, and resultant reduced conscious level and hypotension. Following a 'dirty adrenaline' infusion, the patient was awake with an improved BP by the time of the retrieval doctor's arrival to the remote clinic, and went on to make a full recovery.
- An 18 years old female with refractory anaphylaxis, who made a full recovery following a 'dirty adrenaline' infusion started when peri-arrest.
- A 58 years old female with a haemodynamically unstable bradyarrhythmia, for whom atropine was not helping. After a short period of time receiving 'dirty adrenaline', the patient's bradyarrhythmia and associated hypotension resolved, and they made a full recovery.

Discussion

This case series provides both quantitative and qualitative evidence of clinical benefit from 'dirty adrenaline'. Although only modest physiological

TABLE 3. *Clinical progress, patient outcomes and adverse events*

Adrenaline infusion progress (median and range)
Duration: 155 min (20–554 min)
Crystalloid fluid as part of infusion: 320 mL (30–3200 mL)
Total pre-hospital crystalloid fluid: 2200 mL (280–5500 mL)
Median systolic blood pressures (median and range)
At start of adrenaline infusion: 75.5 mmHg (50–162 mmHg)
At time of retrieval doctor arrival: 91 mmHg (54–160 mmHg)
Further vasopressor/inotrope infusions received
17× Noradrenaline alone (30%)
8× Metaraminol alone (14%)
8× Metaraminol and noradrenaline (14%)
4× Concentrated adrenaline alone (7%)
2× Concentrated adrenaline and metaraminol (4%)
2× Concentrated adrenaline and noradrenaline and vasopressin (4%)
1× Concentrated adrenaline and metaraminol and noradrenaline (2%)
1× Concentrated adrenaline and metaraminol and noradrenaline and vasopressin (2%)
1× Concentrated adrenaline and noradrenaline (2%)
1× Metaraminol and noradrenaline and vasopressin (2%)
1× Noradrenaline and vasopressin (2%)
1× Dobutamine (2%)
10× No further vasopressor/inotrope (18%)
Length of stay (median and range)
In ICU: 2.5 days (0–27 days)
In hospital: 5.5 days (0–56 days)
Mortality outcomes (57 cases)
49× Survival to hospital discharge (86%)
6× Died in hospital (11%)
1× Took own leave before arrival at hospital (2%)
1× Unknown (2%)
Directly associated adverse events from peripheral adrenaline infusion
1× potential distal neurovascular compromise (cold fingers) – > no lasting complications
1× tachycardia – > infusion rate reduced
1× hypertension – > infusion stopped
1× cannula leakage × > no extravasation injury
1× intrasseous cannula extravasation – > no lasting complications
Potentially associated adverse events from peripheral adrenaline infusion
2× fluid overload
1× pain at cannula site
1× patient non-compliance

parameter improvement was seen in the median systolic BP between infusion commencement and patient retrieval (75.5–91 mmHg), there were several cases containing anecdotal evidence of more than modest clinical benefit. Many of these recovered from peri-arrest situations shortly after the commencement of a

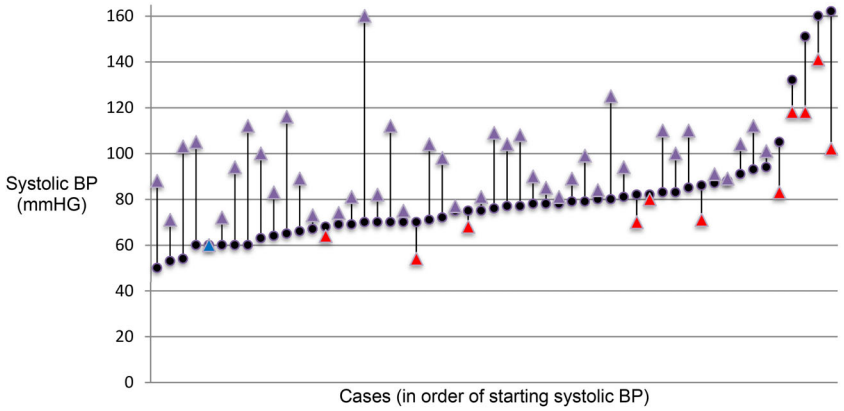

Figure 1. *Systolic BP change between infusion commencement and patient retrieval. (●) Systolic BP at infusion commencement; (▲) Systolic BP at time of retrieval.*

peripheral dilute adrenaline infusion, and went on to make a full recovery. The relatively low mortality rate of 11% in a cohort of critically unwell patients (six deaths from 57 cases) also demonstrates potential clinical benefit. This is further seen in the 5% mortality rate for the subgroup diagnosed with septic shock (two deaths from 40 septic shock cases), which compares very favourably to the 23.9% mortality rate for septic shock across Australia,[17] particularly in the context of their remote locations, high comorbidity rate and long pre-hospital times.

There were no significant adverse events or safety concerns directly linked with the use of 'dirty adrenaline' in this review. The single case of potential distal neurovascular compromise (documented as 'cold fingers') had no lasting complications, and similarly neither did the cases of cannula leakage or intra-osseous extravasation. The cases that developed tachycardia and hypertension, respectively, were also not deemed to be clinically significant, as these are both expected effects of intravenous adrenaline, and tachycardia is a common clinical feature of shock. This suggests that the protocol has an acceptable safety profile for a critically unwell population in a remote and resource-poor setting.

The most clinically significant potentially related adverse outcome is for the two patients who developed fluid overload. These patients both had chronic kidney disease, and received at least 250 mL of crystalloid fluid as part of a 1 mcg/mL peripheral adrenaline infusion. The total crystalloid fluid volumes that they received pre-hospital (750 and 1280 mL, respectively) would likely have been higher if they had not received 'dirty adrenaline'. Despite the limited evidence of benefit in higher strength peripheral adrenaline infusions in this review and elsewhere, patients at high risk of harm from fluid overload may benefit from the lower volumes required. The use of higher-strength infusions, particularly for patients at high risk of developing fluid overload, is an aspect of this topic to explore in future studies.

There was no increase in the incidence of adverse events when smaller gauge peripheral cannulae were used, or when a more distal site was chosen.

Limitations

As a retrospective chart review, the present study does not have a control group to compare patient outcomes against, nor does it take any other aspects of the patient journey into account. It would be highly challenging, both logistically and ethically to perform a prospective controlled study, and a low incidence of patients requiring the protocol means that a single centre prospective case series is not currently practicable either.

There are several areas of incomplete data (particularly in relation to documentation of cannula size and location), and it is recognised that important clinical or safety-related events may therefore not have been identified during the retrospective chart review. Recording and collecting high-quality and relevant documentation is a well-recognised challenge in Remote and Retrieval Medicine, particularly when working in an interagency environment as is the case in Central Australia.

The unique geography and demographics of this cohort mean that caution should be taken in extrapolating these results to patients in another region.

Conclusions

The use of 'dirty adrenaline' in the setting of remote nurse-led clinics in Central Australia, under telephone guidance from the Medical Retrieval and Consultation Centre in Alice Springs Hospital, has become an established and recognised clinical pathway in this region. It has been used for both paediatric and adult patients for a variety of clinical indications, and with a variety of infusion strengths and cannula sizes/locations. This retrospective case series provides no evidence of significant safety concerns for the use of peripheral dilute adrenaline in the remote environment, and provides low-grade evidence of a survival benefit in remote patients with septic shock.

A specific future focus of research within Central Australia should be on the use of these infusions in septic shock, given that this accounted for the vast majority of the diagnoses in this case series. As well as this, given the anecdotal clinical benefit that 'dirty adrenaline' has contributed to some non-shock cases in this cohort (2× status asthmaticus and 3× refractory anaphylaxis), the expansion of the indications for its use in the remote setting to include these clinical situations should be considered.

These findings may be translatable to other health systems providing telehealth and retrieval support to remote and resource-poor communities. Consideration should be given to a national retrieval data set, and broader research collaboration between services.

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Ethics statement

The present study was conducted in accordance with the NHMRC National Statement on Ethical Conduct in Human Research (2007) and was approved by the Human Research Ethics Committee of Northern Territory Health and Menzies School of Health Research (Ref. HREC-2023-4734) with the need for written patient consent waived.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting information

Additional supporting information may be found in the online version of this article at the publisher's web site:

Data S1. Supporting Information.

Data S2. Supporting Information.