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CRITICAL CARE

Intensive therapy for chloroquine poisoning

A review of 29 cases

A. G. McKenzie

Objective. To obtain a data base of the features of chloroquine poisoning and to assess existing intensive therapy for it.

Design. Retrospective review of all confirmed cases of acute chloroquine poisoning admitted to intensive care between November 1990 and October 1994. All available records were scrutinised.

Setting. The intensive care units of Harare Central and Parirenyatwa hospitals, which are referral centres in Harare.

Patients. Selection of patients depended on positive confirmation of chloroquine ingestion. Cases of concomitant ingestion of other drug(s) were not excluded.

Main outcome measures. Cardiac arrest or not; death or survival to discharge from hospital.

Main results. Of a total of 29 patients, aged 16 - 51 years, 69% (20) were female and 31% (9) male. The commonest clinical features were respiratory failure, depressed level of consciousness, hypothermia, hypotension, cardiac arrest and hypokalaemia. Eleven patients had at least one cardiac arrest; 5 of these were successfully resuscitated. Management included gastric lavage, intravenous diazepam, mechanical ventilation when necessary, and occasionally inotropic infusions. Four patients suffered cardiac arrest during gastric lavage. There were 6 deaths (mortality 20.7%).

Conclusions. This study indicates the common clinical features of acute chloroquine poisoning. A survival rate of about 80% is being achieved by intensive therapy at Harare Central and Parirenyatwa Hospitals. Rapid utilisation of the treatment regimen described should reduce the mortality to less than 10%.

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Chloroquine plays an important role in both prevention and treatment of malaria in Zimbabwe. Justifiably it is readily available to the public — it can be purchased from supermarkets and general dealers. Unfortunately, pathology records for Harare Central and Parirenyatwa hospitals reveal a fairly steady incidence of deaths due to suicidal overdose since 1990.

Division of Anaesthetics, Parirenyatwa Hospital, Harare, Zimbabwe

A. G. McKenzie, M.B. CH.B., F.C.ANAES. (Present address: Department of Anaesthesia, Eastern General Hospital, Seafield Street, Edinburgh)

Acute chloroquine poisoning is life-threatening — ingestion of as little as 2 g base (14 tablets) has been reported to be fatal in an adult.[1] However, prompt supportive therapy, preferably in an intensive care unit (ICU), can achieve high survival rates.[2]

Aiming to obtain a data base of the features of chloroquine poisoning in Zimbabwean practice, and to assess the intensive therapy for it, a retrospective study was made of all cases admitted to the ICUs at Harare Central Hospital and Parirenyatwa Hospital during the 4-year period November 1990 - October 1994.

Patients and methods

Inclusion criteria were confirmation of chloroquine poisoning by patient confession, evidence from relatives/friends/police, or blood chloroquine measurement. Patients were not excluded if they had also ingested alcohol or other drugs or poisons. Data were obtained from ICU record books, laboratory records and, wherever possible, the case notes.

Results

There were 29 patients with acute chloroquine poisoning admitted to intensive care. The mean age was 25 years (range 16 - 51 years); 20 were females and 9 males. The dose of chloroquine ranged from 'unknown' to 6 g base. Complete case notes were found for 14 of the 29 cases. Early features of the poisoning, i.e. on admission to hospital, are shown in Table I.

The prevalence of the common symptoms, signs and laboratory findings is set out in Table II. No case of hypoglycaemia was found.

Standard management included gastric lavage in the casualty department and intravenous diazepam there and/or after admission to the ICU (initial dose range 5 - 60 mg). Four patients suffered cardiac arrest during gastric lavage; 2 of these died later. Twenty-three patients were mechanically ventilated. Eleven of the patients suffered at least one cardiac arrest; 5 of these were successfully resuscitated. All patients who had a cardiac arrest were given boluses of adrenaline during resuscitation, but inotropic infusions were given less frequently. Initial cardiac arrest occurred in the casualty department in 9 of the 11 cases; in the remaining 2 cases this event occurred in the ICU, 3 hours after admission in 1 patient (who had respiratory difficulty) and after 5 days in the other. Duration of stay in the ICU ranged from a few hours to 11 days. There were 6 deaths (20.7% mortality) — 3 were primarily from cardiotoxicity, 1 followed aspiration pneumonia, 1 occurred after brainstem death, and the last took place 6 days after the patient was discharged from the ICU in a persistent vegetative state.

Measurement of blood chloroquine levels was not routinely done. However, this investigation was diagnostic in 1 case — a young man who had collapsed in a park and was brought to hospital unidentified.

Discussion

Oral chloroquine is rapidly and almost completely absorbed from the gut, resulting in high blood levels. Chloroquine is a

Table I. Features of chloroquine poisoning on admission in 29 patients

Patient No.	Age/sex	No. of chloroquine tablets* ingested	Temp. (°C)	Systolic arterial pressure (mmHg)	Cardiac events	Serum K^+ (mmol/l)	Outcome
1	23/F	25	N	100	Nil	3.3	Survival
2	20/M	24	< 35	80	Nil	2.8	Survival
3	26/M	?	35.0	UR	Arrest	3.8	Death
4	27/M	24	?	UR	Arrest	4.6	Survival
5	19/F	16	35.5	90	Nil	3.7	Survival
6	37/F	20	35.8	110	Nil	2.2	Survival
7	20/F	20	<35	UR	Ventric. ectopics, arrest	2.3	Death
8	17/F	20	< 35	80	Nil	?	Survival
9	29/F	?	35.0	100	Nil	?	Survival
10	16/F	?	N	100	Nil	?	Survival
11	18/F	?	?	90	Nil	?	Survival
12	24/F	?	N	90	Nil	?	Survival
13	16/F	?	< 35	60	Arrest	?	Death
14	30/M	?	N	UR	Nil	?	Survival
15	27/F	?	< 35	120	Arrest	3.6	Death
16	35/F	20	< 35	99	Nil	4.5	Survival
17	23/F	16	35.0	UR	Arrest	2.7	Survival
18	51/F	20	35.0	UR	Arrest	3.1	Death
19	26/M	40	35.0	UR	Arrest	1.6	Death
20	19/M	?	?	UR	Arrest	?	Survival
21	30/F	?	?	96	Nil	?	Survival
22	26/M	40	35.2	127	Nil	5.1	Survival
23	33/F	25	35.8	110	Nil	3.0	Survival
24	19/F	?	?	UR	Arrest	?	Survival
25	29/M	?	35.0	90	Nil	?	Survival
26	22/F	?	N	102	Nil	?	Survival
27	20/F	?	35.0	90	Nil	?	Survival
28	32/F	?	N	90	Nil	?	Survival
29	16/M	24	34.2	UR	Arrest	2.8	Survival

* Each tablet = 150 mg chloroquine base.
N = in normal range; UR= unrecordable.

Table II. Clinical features of chloroquine poisoning in 29 patients

	No. of patients
Respiratory difficulty*	24
Depressed level of consciousness	20
Hypothermia†	17 (result found in 24 cases)
Hypotension‡	13
Cardiac arrest	11
Hypokalaemia§	10 (result found in 15 cases)

* Respiratory rate > 35/min or mechanical ventilation required.
† Core temperature < 35.5°C.
‡ Systolic arterial pressure < 80 mmHg.
§ Serum potassium < 3.5 mmol/l.

vasodilator and a powerful myocardial depressant,[3] so that cardiorespiratory collapse often follows in less than 2 hours.[4] The terminal elimination half-life is 1 - 2 months, but toxic effects are usually much shorter than this (rare beyond 24 hours) because chloroquine is extensively distributed into body tissues. The apparent volume of distribution is approximately 204 l/kg.

The first step in treatment of acute chloroquine poisoning should be prompt intravenous access for possible inotropic support. Rapid intubation (to protect the airway) is usually recommended, since there is a high risk of aspiration of gastric contents; this will also facilitate mechanical ventilation. Next gastric lavage should be performed (to remove as much ingested drug as possible) and activated charcoal left in the stomach. A prospective trial[2] in Paris, France, published in 1988 reported the benefit of immediate infusion of adrenaline (starting at 0.25 µg/kg/min) and diazepam (2 mg/kg over 30 minutes followed by 1 - 2 mg/kg/d). Ten out of 11 patients, each of whom had ingested more than 5 g of chloroquine, survived following this treatment, compared with only 1 survivor in a comparable (retrospective) control group. Adrenaline is clearly helpful because of its positive inotropic and vasoconstrictor actions. It is well recognised that diazepam has a protective effect in chloroquine poisoning;[5] however, much lower doses may suffice. Peritoneal dialysis and haemodialysis are not helpful, because chloroquine binds extensively in the tissue.

The Zimbabwean mortality rate (20.7%) is higher than that in the Paris prospective trial (9.1%), but much lower than that for the controls studied retrospectively (90.9%). Strictly speaking, however, a direct comparison should not be made, because many of the Zimbabwean patients ingested less than 5 g of chloroquine; also there is little doubt that some of them fared better because early vomiting reduced absorption of chloroquine.

Table III. Treatment guidelines for chloroquine poisoning

A. Mild poisoning	B. Severe poisoning
Toxic dose ingested (> 1.3 g base in an adult or ⩾ 20 mg/kg)	Criteria — any 1 of the following a) dose ingested > 2.5 g base in an adult or > 35 mg/kg b) dyspnoea c) systolic BP < 80 mmHg d) QRS duration > 120 ms e) tremor, convulsions, coma.
Where identity of drug ingested is in doubt* look out for early symptoms: drowsiness, visual disturbances, weakness, dizziness, tinnitus.	
1. Intravenous access.	1. Intravenous access.
2. Empty stomach by gastric lavage and leave activated charcoal in stomach.	2. Tracheal intubation to secure and maintain patent airway; administer oxygen and assisted or controlled ventilation.
3. Monitor pulse, BP, ECG and serum K^+ in a high-dependency unit for 4 h minimum and keep in hospital for 24 h minimum.	3. Empty stomach by gastric lavage and leave activated charcoal with a cathartic in stomach.
4. Give IV diazepam 0.3 - 0.5 mg/kg over 30 min.	4. Commence IV diazepam 0.5 - 2 mg/kg initially followed by infusion at 0.05 - 0.1 mg/kg/h.
5. If condition deteriorates, follow B.	5. IV fluids at sufficient rate to maintain urine output. Central venous pressure (CVP) catheter recommended.
	6. Inotropic support in the form of dopamine or adrenaline — starting at low dose and increasing incrementally as required to achieve an adequate systolic arterial pressure (⩾ 100 mmHg).
	7. Full monitoring in an ICU: pulse, BP, ECG, serum K^+, glucose, arterial blood gases, urine output and possibly CVP.
	8. For arrhythmias — follow Advanced Cardiac Life Support guidelines.
	9. For seizures — further IV diazepam in 5 mg increments.
	10. Consider forced acid diuresis, e.g. with ammonium chloride.

* Useful to send 10 ml blood in heparinised tube for blood chloroquine level.

Some areas of the Zimbabwean management could be improved. For example, 4 patients had a cardiac arrest during gastric lavage and 1 aspirated stomach contents (all in the casualty department). Another patient had a cardiac arrest in the ICU after being allowed to breathe spontaneously by facemask, despite respiratory distress. All these events (which resulted in 4 deaths) could perhaps have been averted by *initial* measures to correct cardiovascular disturbances, protect the airway and support ventilation.

A remarkable feature of this study is the fact that 5 patients were successfully resuscitated after cardiac arrest. This contrasts with zero success following cardiac arrest in the Paris study.[2]

Although not often mentioned in the literature, hypokalaemia was a frequent finding in this study. This is noteworthy, because the threshold for chloroquine-induced arrhythmias may be lowered by concomitant hypokalaemia, especially if adrenaline infusion is used. This suggests that hypokalaemia should be corrected promptly. It is also reported that a small fall in plasma potassium (K^+) follows intravenous injection of diazepam.

A treatment algorithm based on the latest information[6] is presented in Table III.

It is hoped that attention to this study will improve management and survival of acute chloroquine poisoning. It must be stated that many such patients die before admission to the ICU, or even before arrival at hospital. The introduction of mobile intensive care teams could improve this. Better still would be avoidance of attempted suicide by improvement of social services.

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