PREHOSPITAL CARE

Review of prehospital sodium bicarbonate use for cyclic antidepressant overdose

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Objective: To describe the clinical presentation of patients with cyclic antidepressant (CA) and use of sodium bicarbonate (NaHCO_3) in the treatment of this overdose in the prehospital setting.

Methods: A three year retrospective observational review of records was performed using the San Diego County Quality Assurance Network database for prehospital providers. All adult patients who were treated with NaHCO_3 by paramedics for a CA overdose were included. Demographic data, presenting cardiovascular and neurological symptoms, paramedic treatments, and any changes in status were reviewed.

Results: Twenty one patients were treated by paramedics with NaHCO_3 for CA overdose. Seventeen patients (80%) presented with mental status changes, including 11 presenting with a GCS < 8. Seven of the 21 (33%) presented with a cardiac arrhythmia expected to possibly respond to NaHCO_3 treatment. Seven of the 21 (33%) were hypotensive, and five (24%) patients had reported seizure activity. Only 2 of the 21 patients (10%) treated with NaHCO_3 had recorded improvements after administration of the drug, while the other 19 remained stable without any deterioration. Sixteen of 21 patients (76%) were given NaHCO_3 for indications on standing order, while five patients were treated outside the standing order indications by base physician order with none of the five patients having any change in status after treatment.

Conclusions: After prehospital NaHCO_3 use in patients with CA overdose, there were no complications reported, two patients improved in status and the others remained unchanged. Base hospital physician orders of NaHCO_3 for indications beyond the standing orders were not associated with changes in patient status.

Death due to overdose of cyclic antidepressants (CA) represents the second leading cause of mortality attributable to an ingested pharmaceutical poison in the United States.¹ Poisonings attributable to all antidepressants represent only 3.0% of reported toxic exposures, with CA overdose accounting for the majority of these exposures. In contrast, death attributable to antidepressant overdose accounts for about 20% of the total deaths due to poisonings.¹ In one retrospective review of coroner's records, over 70% of successful CA suicides are pronounced dead without ever reaching a health care facility.²

Recommendations for the use of NaHCO_3 in CA overdose are controversial. United Kingdom treatment guidelines recommend using NaHCO_3 in patients with widened QRS complex or any arrhythmia. The current recommendations in San Diego County for prehospital use of NaHCO_3 in the treatment of tricyclic overdose include widened QRS > 100 ms, heart block, hypotension, or multiple PVCs in the setting of CA overdose. In contrast, accepted indications for NaHCO_3 treatment in other sources of the emergency medicine literature include either a widened QRS > 100 ms or 120 ms or ventricular tachycardia with a history of CA overdose.^{3–5} We sought to evaluate the prehospital presentation of adult patients with CA overdose, examine the indications used for the administration of NaHCO_3 treatment, and examine the effects of treatment in the prehospital setting.

METHODS

A retrospective observational review of records was performed using the San Diego County Quality Assurance Network database for prehospital providers. The database is an extensive collection of prospectively obtained prehospital information entered by prehospital providers. The information in the database is comprised of specific fields that contain information

such as patient age, vital signs, Glasgow coma score (GCS), chief complaint, brief history, electrocardiogram readings, response times, and list of treatments given.

San Diego County consists of a population of about 2.6 million people residing in urban, suburban, and rural areas. About 150 000 calls are received annually by nine 911 dispatch agencies. Eighteen advanced life support ground transport agencies and one aeromedical rotor wing (helicopter) agency operate in San Diego County, employing about 800 paramedics to provide emergency medical services to these areas. There are about 37 basic life support units that initially respond to 911 calls, and each has advanced life support backup available. San Diego has 23 basic emergency departments with one level 1 trauma centre and five level 2 trauma centres. Medical direction for prehospital care personnel is provided by written protocols with available online medical direction from a mobile intensive care nurse or a base hospital physician (BHP) when necessary.

We searched the computer database of prehospital providers for paramedic responses in which NaHCO_3 was given for CA overdose in adults age 18 years or older between 1 January 1996 and 1 January 1999. No exclusion was made on the basis of sex or ethnicity. Patient demographics, clinical presentation, treatments, and any recorded responses to therapy were collected and analysed. In addition vital signs were obtained in each case and were analysed for abnormalities. Hypotension was defined as a systolic blood pressure less than 100 mm Hg.

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Abbreviations: CA, cyclic antidepressant; GCS, Glasgow coma score; BHP, base hospital physician

Table 1 Glasgow coma score (GCS), hypotension, and seizures in patients with CA overdose

GCS	All patients (n=21)	Hypotensive patients (n=7)	Patients with reported seizures (n=5)
13–15	6/17 (35)	3/7 (42)	2
12–8	3/17 (18)	1/7 (14)	0
≤8	8/17 (47)	2/7 (28)	3
GCS not recorded	4/21 (19)	1/7 (14)	0
Total seizures for category	5/21 (24)	1/7 (14)	5/21 (24)

The table compares GCS, hypotension, and seizure activity. No correlation between categories is noted. Percentages are shown in parentheses.

Committee approved this study. Statistics were performed with Microsoft Excel spreadsheets.

RESULTS

During the three year study period, we found 21 patients were treated with NaHCO₃ for a CA overdose. Ten patients were male with an average age of 40 (SD 14) years (range 24–71), and 11 were female with an average age of 43 (SD 16) years (range 19–54). Fifteen of the 21 patients had records indicating whether or not coingestants were reported taken with the overdose of CA. Ten of these 15 had reported the use of coingestants (66%) while five (33%) reported no such use.

The GCS, incidence of reported seizures, and incidence of hypotension were tabulated and summarised in table 1. Seventeen of the 21 patients had a GCS recorded. Eight of these 17 (47%) were found in a comatose state as defined by a GCS of eight or less. Seven of the 21 patients (33%) were hypotensive, and five of the 21 patients had reported seizure activity. Of note, only one of the five patients with seizure activity had a widened QRS complex, defined as >0.1 s.

Eighteen of the 21 patients had some form of arrhythmia, and three patients were in normal sinus rhythm. Eleven patients had sinus tachycardia, five patients had a widened QRS complex >0.1 s (including one with ventricular tachycardia), and the final two patients had sinus bradycardia and first degree heart block. Thus, by traditional standards, only seven patients presented with an arrhythmia that might have been expected to respond to NaHCO₃.

Indications for starting NaHCO₃ treatment are displayed in table 2. Sixteen of the 21 patients (76%) had one or more of the previously mentioned San Diego County indications for treatment. Five of the 21 (24%) NaHCO₃ treatments were not indicated by the San Diego County protocol, but were given under the direction of a BHP.

Twenty of the 21 patients had both the patient's weight and the amount of NaHCO₃ administered reported in the records. The average dose of 8.4% NaHCO₃ (1 mEq/cc) was 1.0 mEq/kg

Table 3 Average dose of NaHCO₃

Average dose of NaHCO ₃ (mEq/kg)	Total n=20 patients with both recorded weight and sodium bicarbonate amount given
>2 mEq/kg	1 (5)
1–2 mEq/kg	8 (40)
0.75–1 mEq/kg	7 (35)
<0.75 mEq/kg	4 (20)

Twenty of the 21 patients had both weight and amount of NaHCO₃ recorded. Eight of these 20 patients (40%) were given the recommended 1–2 mEq/kg dose of NaHCO₃. Percentages are shown in parentheses.

with a range of 0.55 to 2.20 mEq/kg. Eleven of the 20 patients received less than 1 mEq/kg, and 4 of this 11 received less than 0.75 mEq/kg. Average doses given in the prehospital setting are summarised in table 3.

Two of the 21 patients had recorded improvement. The first patient, who was found in ventricular tachycardia, was initially treated with two attempts of electrical cardioversion, and one dose of lignocaine (lidocaine) without a response. The patient converted to sinus rhythm after the administration of a 0.6 mEq/kg dose of NaHCO₃. The second patient had a recorded narrowing of a wide QRS complex and an increase in level of consciousness after the administration of 1.1 mEq/kg of NaHCO₃. There were no reported complications associated with the use of NaHCO₃, including no evidence of extravasation.

DISCUSSION

The primary antidepressant activity of CA is believed to be related to the inhibition of reuptake of noradrenaline (norepinephrine) and serotonin by the presynaptic neurons of the central nervous system. However, the most important danger of CAs comes from their antimuscarinic, α receptor blocking, and sodium channel blocking effects on the myocardium.⁶ Despite the serious neurotoxic effects of seizures, respiratory depression, and coma, it is the cardiovascular effects of arrhythmias and hypotension that are the principal cause of death in tricyclic CA overdose.⁶ The use of NaHCO₃ for CA poisoned patients with conduction delays may help reverse the cardiac side effects by antagonising the sodium channel block and by reversing the metabolic acidosis and therefore, NaHCO₃ is considered an important drug for use as early treatment in the prehospital setting. Given the severe toxicity being treated with the bicarbonate, other potential complications and side effects, including extravasation and local tissue injury as well as transient hypokalaemia are less of a concern.

The severity of CA overdose can vary widely on presentation and patients can deteriorate rapidly. In one study, 50% of patients who subsequently died in the hospital after CA poisoning had minimal signs of overdose when presenting to

Table 2 Paramedic indication for administering NaHCO₃

Indication	Total n=21
QRS >100 ms	5 (24)
Heart block	1 (5)
Hypotension (systolic BP ≤100)	9 (42)
Multiple PVCs or sustained Vtac	4 (19)
Both wide QRS and hypotension	2 (10)
Both PVCs and hypotension	1 (5)
Base hospital physician order without any of the above criteria	5 (24)

Sixteen of the 21 patients (76%) were given NaHCO₃ by one or more indication from a standing order. Five of the 21 were given NaHCO₃ by order of the base hospital physician. Percentages are shown in parentheses.

the emergency department.² In the same study, 44% of deaths from CA overdose occurred while en route to the hospital. Because of the variation in presentation and rapid deterioration of patients, obtaining a history of CA overdose is critical for early initiation of the appropriate treatment.

A priority in the treatment of CA overdose is managing the cardiotoxic effects of hypotension, arrhythmias, and QRS prolongation. All patients with suspected CA overdose should be given intravenous isotonic crystalloids and cardiac monitoring.³ The effectiveness of NaHCO₃ in treating both the cardiotoxic and neurotoxic effects of CA overdose has been suggested in previous animal and retrospective human studies.⁷⁻¹¹ In one study, the administration of NaHCO₃ to 91 patients with CA toxicity was strongly associated with the correction of hypotension, QRS prolongation, and the improvement of mental status. This study demonstrated improvement in hypotension after administration of NaHCO₃ in 95% of cases, 60% within the first 30 minutes, and 29% within 30 to 60 minutes. In the same study, 80% of prolonged QRS complexes were corrected, and major improvements in mental status were observed in 34% of patients who presented with altered mental status.¹¹

In our study, only two patients had recorded benefits noted after the administration of NaHCO₃. The low percentage of clinical improvements after NaHCO₃ may be attributable to a deficiency of recording patient changes, a lack of clinical effects of NaHCO₃, or the short time period that was analysed in the prehospital setting. Also, patients who were administered NaHCO₃ may not have been sick enough to show any benefit of the drug. Additionally, the doses of NaHCO₃ used are considered small doses in the face of significant CA overdose. Thus, the treatment may have been started in the prehospital setting without a noted change but with the continuum of care into the emergency department may have been more effective than if it had not been started in the out of hospital setting. Another possibility is that the patients had ingested other drugs that were causing the clinical manifestations instead of the CA overdose, and thus would not expect to respond to NaHCO₃ therapy. Although history is often unreliable, there were no other drugs with cardiac side effects reported as coingestions in the study population. Despite the low percentage of clinical improvements, one patient was converted from a life threatening arrhythmia to sinus tachycardia after NaHCO₃, and another patient had narrowing of a widened QRS to <0.1 s and an improvement in mental status.

Interestingly, the two patients who had improved status after receiving NaHCO₃ were among the patients who received treatment under the prehospital standing orders. None of the patients treated outside the guidelines by BHP order showed improvement. However, none of these patients had any further deterioration. Thus, with the study design and small numbers of patients, the true clinical effect of the medication cannot be fully ascertained.

In a previous study of 36 patients with tricyclic antidepressant overdose, Liebelt *et al* concluded that QRS measurements are significantly greater and remain abnormal longer in patients who develop seizures or ventricular arrhythmias.¹² Looking closer at the data, of the 15 patients who experienced seizure activity, only eight had QRS measurements greater than 0.1 s; however, the mean QRS interval length was 0.150 s, which was statistically higher than the mean QRS complex of those without seizure or arrhythmias. In contrast, five patients in our study had recorded seizure activity, but only one had a widened QRS complex. Of the four remaining patients who experienced a seizure, three had sinus tachycardia, and one had a normal sinus rhythm. Additionally, a total of five patients had widened QRS complexes but only one was recorded to have seizure activity.

This study has the limitations of a retrospective review. One of the limitations is the use of a computer database. The infor-

mation recovered from the records is only as complete as what was entered by the paramedics and the mobile intensive care nurses. Therefore, percentages of patients who improved with NaHCO₃ may be underestimated. Because of the configuration of the computer system, patients with CA overdose who were not treated with NaHCO₃ are not able to be retrieved. Therefore, a direct comparison of patients with CA overdose both treated and not treated with NaHCO₃ cannot be made. Clearly, the small number of patients treated is a limiting factor, which allows for trends and speculation but not clear statistical evaluation.

Future research should look into which physiological parameters best indicate the need for early treatment with NaHCO₃. Current emergency medicine, toxicology, and prehospital literature cannot come to a consensus as to who should be treated with NaHCO₃. The San Diego indications for NaHCO₃ are more liberal when compared with the emergency medicine literature, and future work needs to define whether PVCs or heart block should be treated in the absence of a widened QRS. Possibly, the only patients who may have any outcome difference with prehospital bicarbonate treatment may be those presenting with ventricular tachycardia or supraventricular tachycardias. To get meaningful numbers of patients and complete sets of data, prospective work with multiple regions will probably need to be coordinated.

In conclusion, we surveyed the use of NaHCO₃ in the prehospital care of CA poisoning in San Diego County over a 36 month period. Twenty one patients received NaHCO₃ during this time, 76% by standing order. Improvements were recorded in 2 of 21 patients. No patients during this period experienced worsening after NaHCO₃ was administered. NaHCO₃ seemed safe and possibly effective when administered in the prehospital setting in our patient population. Further study is needed to more accurately define the role of NaHCO₃ in the prehospital treatment of CA poisoning.

Contributors

Thomas Calkins initiated the research, participated in data collection, discussed core ideas, and helped draft the manuscript. Gary Vilke, the principal investigator, initiated the research, participated in protocol design, and assisted in writing the paper. Richard Clark participated in protocol design, data analysis and interpretation, and contributed to the writing of the paper. Barbara Stepanski initiated the study, participated in protocol design, data collection, and contributed to the writing of the paper. Theodore Chan initiated research, participated in protocol design, data analysis, writing and editing of the paper, and statistical analysis.

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