A retrospective study on carboxyhaemoglobin half-life in acute carbon monoxide poisoning in patients treated with normobaric high flow oxygen

接受正壓高流量氧氣治療之急性一氧化碳中毒病者的碳氧血紅蛋白半衰期：一個回顧性的研究

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Objective: There has been a vast difference in the reported value for carboxyhaemoglobin (COHb) half-life ($COHbt_{1/2}$) in carbon monoxide (CO) poisoning patients breathing 100% normobaric oxygen (O_2). This could be due to the fact that all previous studies were performed on heterogeneous groups of patients with different aetiology. We wished to determine the $COHbt_{1/2}$ in a homogenous group of acute CO poisoning patients who attempted suicide by burning charcoal and were treated with normobaric high flow oxygen. *Methods:* It was a retrospective descriptive cohort study for a period of 60 months (January 2001 to December 2005). *Setting:* Accident and Emergency Department of Tuen Mun Hospital, serving a population of 1.5 millions. *Population:* We recruited all cases of CO poisoning by burning charcoal for suicidal attempt and we excluded the cases if (1) there was only one COHb measurement; (2) the patient had not received high flow O_2 therapy via tightly fitting facial mask with O_2 reservoir, given before the first blood sample or throughout the period until a second blood sample was taken; (3) the first COHb was <10%; (4) the second COHb was <2%; (5) there was significant co-poisoning; (6) the patient was haemodynamically unstable; or (7) the time of blood sampling was not documented. We believed that the elimination of COHb under 100% normobaric O_2 was constant and followed a simple exponential decay. *Results:* Forty-three (27.4%) cases met all of the selection criteria and the mean $COHbt_{1/2}$ was 78±9 minutes. *Conclusion:* We believed that our patients (i.e. CO poisoning patients who committed suicide by burning charcoal) represented a homogenous group of acute CO poisoning of unique aetiology. The estimated $COHbt_{1/2}$ would be useful in deciding the length of normobaric oxygen therapy for this group of patients. (*Hong Kong j.emerg.med.* 2006; 13:205-211)

目的：在呼吸 100% 正壓氧之一氧化碳中毒病者的碳氧血紅蛋白半衰期報告中，數值有極大的差別，這可能是因為以往所有的研究都在不同成因及不同種類的病人群組中進行。我們希望可以確定在一個同類型群組因燒碳企圖自殺引致急性一氧化碳中毒而接受正壓高流量氧氣的病者之碳氧血紅蛋白半衰期。**方法：**這個回顧性描述組列研究為期 60 個月（2001 年 1 月至 2005 年 12 月）。**研究環境：**屯門醫院急症室，服務一百五十萬人口。**研究對象：**我們招募所有燒碳企圖自殺的一氧化碳中毒個案，但不包括以

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下個案：（1）碳氧血紅蛋白只量度一次，（2）在第一個血液樣本收集之前或至收集第二個血液樣本整段時期，沒有接受由安裝緊貼的面罩及儲氧袋輸送高流量氧氣治療的病者，（3）第一個碳氧血紅蛋白數值<10%，（4）第二個碳氧血紅蛋白數值<2%，（5）伴隨有其他重要的中毒，（6）血液動力不穩定的病者，（7）血液樣本收集的時間沒有記錄。我們相信在 100% 正壓氧氣下，碳氧血紅蛋白的消除是持續不斷及跟隨着單一指數曲線地衰變。**結果：**43 個案（27.4%）達到挑選的所有準則而碳氧血紅蛋白半衰期的平均值為 78 ± 9 分鐘。**總結：**我們相信我們的病者（燒碳自殺的一氧化碳中毒病者）代表一個有獨特成因的急性一氧化碳中毒同類群組。評估碳氧血紅蛋白半衰期對決定給予這些病者正壓氧療的時間長度會有幫助。

Keywords: Carbon monoxide poisoning, carboxyhaemoglobin half-life, charcoal burning, normobaric oxygen

關鍵詞：一氧化碳中毒、碳氧血紅蛋白半衰期、燒碳、正壓氧氣

Introduction

Carbon monoxide (CO) poisoning was uncommon in Hong Kong before 1998. In November 1998, a 35-year-old Hong Kong woman committed suicide by burning charcoal in her apartment with windows closed.[1] The incident was sensationally reported by all local news media. Burning charcoal was believed by many people in Hong Kong as a romantic and comfortable way to commit suicide. Since then, all local hospitals in Hong Kong began to receive CO poisoning patients as a result of burning charcoal to commit suicide. Tuen Mun Hospital (TMH) is a local regional hospital in the west New Territories region with a catchment area serving a community population of around 1.5 millions. The Accident and Emergency Department (AED) has a daily attendance around 600 and we received 40-50 cases of burning charcoal suicidal cases per year (i.e. around 1 in 5,000 patient-year). There are great differences among reported carboxyhaemoglobin half-lives ($COHbt_{1/2}$) in CO poisoning patients breathing 100% oxygen (O_2) under normobaric pressure.[2] Burney et al quoted 137 minutes,[3] Myers et al quoted 131±133 minutes,[4] and Pierce and Bensky quoted 126±246 minutes.[5] Based on our own clinical observation, the carboxyhaemoglobin (COHb) dropped rapidly and we had an impression that $COHbt_{1/2}$ would be much shorter than those previously reported. The goal of our investigation was to determine the $COHbt_{1/2}$ in acute CO poisoning patients treated with normobaric high flow oxygen.

Material and methods

Case selection

This was a retrospective study by analysing the medical records of relevant patients. We included all the cases of (1) CO poisoning by burning charcoal for suicidal attempt and (2) presented to the AED of TMH (3) between January 2001 and December 2005 (60 months). Cases were excluded from study if (1) there was only one COHb measurement; (2) the patient had not received high flow O_2 therapy (15 L/min) via facial mask with O_2 reservoir given before the first blood sample or throughout the period until a second blood sample was taken; (3) the first COHb was lower than 10%; (4) the second COHb was lower than 2%; (5) there was significant co-poisoning e.g. cyanide; (6) there was clinically significant hypotension with reduced cardiac output; or (7) the time of sampling of blood COHb could not be determined either directly or indirectly. Eligible patients were all transferred to the hospital by ambulance with supplemental oxygen started at the scene. After arrival at the AED, all patients were given high flow O_2 (15 L/min) via a tightly fitting non-rebreathing O_2 mask with oxygen reservoir. An arterial blood sample would be taken immediately after initial stabilisation. The same oxygen therapy would be continued after admission and throughout the period until a second sample of blood had been taken.

Method of measurement

All blood samples taken were kept in ice in a bubble-

free sealed syringe and sent to the laboratory expeditiously as a routine. We therefore believed that the laboratory arrival time could be used as an alternative to estimate the sampling time. The COHb measurement was performed with a CO-oximeter (Chiron 865 blood gas analyser, Chiron diagnostics, NV, USA) machine. In our hospital, we have two machines of the same model. All the blood samples received by the laboratory were processed immediately and most were performed within 10 minutes. Blood samples not taken nor stored satisfactorily (e.g. not in ice pack / not in sealed syringe) would be discarded.

Statistical method

We believed that blood COHb concentration would decrease in a single exponential manner, at least in the initial few hours.[2] The $COHbt_{1/2}$ was calculated using the equation:

$Ct = C_0 \times e^{(kt)}$

Where Ct is the concentration at any time t,
C_0 is the initial concentration at time zero,
k is the decay constant

$t_{1/2} = \Delta t \times \log 2 / \log(Ct_1/Ct_2)$

Where Δt = interval between t_2 and t_1

The values were expressed in mean and 95% confidence interval (CI).

When there were more than two samples of COHb taken; individual values of $COHbt_{1/2}$ were calculated. The mean of all calculated values was taken as the reading for that particular case.

The Mann Whitney test was used to compare the $COHbt_{1/2}$ between patients of age 40 or above with patients aged below 40, and also the COHb level in patients presenting within 30 minutes and those longer than 30 minutes.

Results

There were 157 cases of CO poisoning identified between the period from January 2001 to December 2005. The number of cases of CO poisoning by burning charcoal was high in 2001 and 2002 (47 and 45 cases respectively) and the number of cases showed a gradual decrease in the subsequent years (Table 1). There were 91 males and 66 females and the male to female ratio was 1.4 to 1. The mean age was 36 years (range 14-75). We excluded 114 cases from the study by using the exclusion criteria (Table 2). Forty-three cases fulfilled the selection criteria and they were included for the analysis of $COHbt_{1/2}$. Among these 43 cases, there were 25 male and 18 female. The male to female ratio was again 1.4 to 1. The mean age was 38 years (range 17-60). There was no significant difference in mean age and male to female ratio between the cases we included in the study and the cases excluded from the study. Among the 43 cases recruited in our study, there were 8 cases (18.6%) with documented collection time while the other 35 cases (81.4%) had only documented laboratory arrival time.

The mean $COHbt_{1/2}$ for all the 43 patients was 78±9 minutes (range of $COHbt_{1/2}$ 21-154 min). Three patients had more than two COHb measurements

Table 1. Number of cases of carbon monoxide poisoning and number of cases fulfilling the selection criteria between 2001 and 2005

	Cases included	Cases excluded	Total
2001	10	37	47
2002	13	32	45
2003	6	18	24
2004	10	20	30
2005	4	7	11
Total	43 (27.4%)	114 (72.6%)	157

Table 2. Reasons and number of cases excluded

	Not giving 100% O_2	Low 1st COHb %	Low 2nd COHb %	Only one reading	Haemodynamically unstable	Treated with HBO	Record not available	Intubation
Number (%)	4 (2.5%)	27 (17.2%)	33 (21.0%)	20 (12.7%)	4 (2.5%)	9 (5.7%)	4 (2.5%)	13 (8.3%)

COHb=carboxyhaemoglobin; HBO=hyperbaric oxygen; O_2=oxygen

during the whole admission. The mean $COHbt_{1/2}$ calculated from the second and third COHb was 75 minutes, which was similar to the 78 minutes of the first $COHbt_{1/2}$ (Table 3). There was no statistically significant difference (P=0.98, 2-tailed) between the groups of patient aged 40 or above (n=17) and those below 40 (n=26).

The time between stopping CO exposure (the time the patient was found by others or the time reported by the patient) and the AED arrival time were reviewed. Only 26 out of the 43 cases had clear documentation of the time of stopping CO exposure. The mean time lag was 59 minutes (range 14-141 minutes). Seven patients were brought to the AED within 30 minutes and 19 patients were more than 30 minutes. We compared the COHb of those patients who arrived the AED within 30 minutes and those who arrived after more than 30 minutes and found that there was no statistically significant difference (P=0.07, 2-tailed).

All of the patients admitted for CO poisoning received comprehensive psychiatric assessment. The psychiatric diagnosis and psychiatric consequences after the carbon monoxide poisoning were reviewed (Table 4). Seventy patients (44.6%) were diagnosed as having adjustment disorder, acute stress reaction or transient depressive episode and they were followed up in the psychiatric outpatient clinic for a short period without long term psychiatric consequence. Seven patients (4.5%) were found to have no psychiatric problem after assessment by the psychiatrist and they did not require further psychiatric follow up. Thirty-three patients (21.0%) were newly diagnosed as having depression and 25 (75.8%) of them were admitted to the psychiatric ward after medical treatment for CO poisoning. Seventeen (10.8%) patients were found to have pre-existing psychiatric illness like depression or psychosis and 10 (58.8%) of them were admitted to psychiatric ward. Seven patients (4.5%) were noted to have neuropsychiatric impairment and required long term

Table 3. Summary of the half-life and percentage of carboxyhaemoglobin

	Mean $COHbt_{1/2}$	Mean 1st $COHbt_{1/2}$	Mean 2nd $COHbt_{1/2}$	Mean 1st COHb%	Mean 2nd COHb%	Mean 3rd COHb%
Male	76.33	76.23	74.57	30.26	12.28	7.70
Female	79.95	79.95	NA	27.80	8.22	NA
Overall	77.85	77.79	74.57	29.20	10.58	7.70

COHb=carboxyhaemoglobin; $COHbt_{1/2}$=carboxyhaemoglobin half-lives

Table 4. Psychiatric outcome of carbon monoxide poisoning patients

	Newly diagnosed	Pre-existing psychiatric illness	Percentage
Adjustment disorder/acute stress reaction/ transient depressive episode	70		44.6%
Depression/psychosis (no admission to psychiatry ward)	8	7	9.6%
Depression/psychosis (need admission to psychiatry ward)	25	10	22.3%
Neuropsychiatric impairment	7		4.5%
DAMA/missing/not documented	17		10.8%
Death	6		3.8%
Normal	7		4.5%
Total (N=157)	140	17	100.0%

rehabilitation. Twelve patients (7.6%) refused psychiatric assessment and discharged themselves against medical advice and in 5 (3.2%) patients the psychiatric consequence could not be retrieved from the medical record.

Discussion

Eighty minutes is frequently quoted as the $COHbt_{1/2}$ in human breathing 100% at atmospheric pressure,[2,6,7] and our finding demonstrated a similar mean $COHbt_{1/2}$ (78±9 min). Our result matched with Weaver's on the point that there was no relationship between $COHbt_{1/2}$ and age.[2] We did not perform any analysis on the relationship of $COHbt_{1/2}$ with smoking status, history of loss of consciousness or effect of intubation because many data were not documented in this retrospective study.

The strength of our study was that all patients had the same and unique aetiology i.e. burning charcoal to commit suicide in a closed environment. Thus the possible biological uptake and elimination of CO in all these patients could be regarded as the same among each other. All the previous clinical studies included patients with CO poisoning from a variety of aetiologies and treatment modalities.[2-5] We believed that our study represented a unique group of acute CO poisoning. Besides, we applied strict inclusion criteria with an aim to minimise recall error, which is commonly found in a retrospective study. For example, in our study, all final COHb levels were higher than normal, so a spuriously prolonged $COHbt_{1/2}$ due to inappropriate lengthening of the time intervals between COHb measurements was avoided in our data, but this was common in other clinical studies.

In our study, there were three patients who had more than two measurements, the best fit of their COHb data using all COHb values to calculate the COHb was an exponential decay. Therefore we believe that blood COHb concentration decreases in a single exponential manner after CO poisoning irrespective of the time lapsed.[2] However, a recent study by Shimazu et al suggested that CO elimination might not follow a single exponential decay but a biphasic decrease compatible to a 2-component model, i.e. an initial rapid decrease with a short half-life followed by a slower phase with a longer half-life.[8] However the study was only an experimental study carried out on a sheep model.

An error in $COHbt_{1/2}$ calculation may occur if the COHb level in arterial blood and venous blood samples are different, or the sample pairs used to calculate the $COHbt_{1/2}$ were not both arterial or both venous. We assumed that the COHb levels were equivalent in both arterial and venous blood.[9] Benignus et al demonstrated that there was a difference between COHb levels in simultaneously analysed arterial and venous blood samples for up to 10 minutes following the cessation of CO exposure.[10] The magnitude of difference in arterial and venous COHb sample pairs was 4-12%. However, by 5 to 15 minutes after CO exposure, the COHb levels between paired arterial and venous specimens would be identical.[10] The patients in our study had COHb levels that were measured >15 min after removal from the CO poisoning environment. Therefore, we assumed that the COHb levels in both arterial and venous blood were equivalent.

The initial COHb level was regarded as poorly correlated with clinical toxicity.[11] Other parameters like initial pH, base excess, or history of loss of consciousness were regarded as better correlated with the severity of clinical toxicity.[12] Many workers pointed out that the initial COHb in hospital could not represent the on-site peak COHb concentration because of continuous washing out effect of room air or supplement oxygen once the patient was removed from the scene. However, there has been no proper study done to evaluate the prognostic significance of peak concentration of COHb (or the COHb concentration at the scene). Theoretically, we could use the half-life time of $COHbt_{1/2}$ to 'back calculate' the peak COHb at the scene if the exact time interval between end of exposure and initial blood sampling could be documented.

Two patients with similar initial COHb of 30% assessed in hospital may have very different COHb at

the scene. If patient A has an interval of 60 min (mean interval of our study) between end of CO exposure and initial blood taking and patient B has an interval of 30 min, their corresponding peak COHb at the scene would be 51% and 39% respectively (basing on the half-life interval of 78 minutes as quoted in our study). Therefore peak COHb concentration at the scene should be a much better parameter to correlate with clinical CO toxicity than initial COHb. This idea of 'back calculate' of peak COHb concentration at the scene was suggested by Clark et al who devised a normogram for five victims to estimate the peak COHb at the scene.[13] However the designed normogram was based on their assumption of non-exponential decay of COHb with life of 4 and 3 hours for room air breathing and supplemental oxygen breathing subjects respectively.

The calculation of the $COHbt_{1/2}$ in the CO poisoning patients breathing 100% normobaric pressure oxygen helps us to design the duration of oxygen therapy for CO poisoning patients. High concentration supplemental oxygen therapy has been recommended until the COHb level is <5%.[10] It is a common practice in many centres to give a session of 4 hours normobaric oxygen therapy as the initial treatment. If we use 78 min as the $COHbt_{1/2}$, a 240 min (4 hours) therapy could bring COHb to 0.118 times of the initial COHb at the end of therapy. This 88.2% reduction should be enough to normalise the COHb of most patients with measured COHb up to 40%. This serves as a rough guide to our clinical decision on the length of oxygen therapy.

Limitations

As this was a retrospective study, there might be errors in the recorded values. Errors might occur on the calculation of $COHbt_{1/2}$ because only 8 out of the 43 cases had the sampling time recorded, while the others had the laboratory arrival time only. We used the laboratory arrival time of those 35 cases to calculate the $COHbt_{1/2}$ instead of the sampling time. The FiO_2 might not be constant throughout the whole study period or between different patients although they were all breathing high flow (15 L/min) through a tightly-fitting non-rebreathing oxygen mask with oxygen reservoir. This could be a result of poorly fitting mask that might not seal the face completely, poor compliance to the oxygen therapy due to the discomfort of the mask, and also non-rebreathing is not a guarantee of giving a FiO_2 of 100%. The $COHbt_{1/2}$ would be prolonged if the FiO_2 was lower than 100%. Moreover, the small sample size (N=43), due to the strict selection criteria, led to a wide range of $COHbt_{1/2}$ (21-154 min). Benignus et al demonstrated that there was a difference between arterial and venous COHb.[10] We did not compare the arterial and venous difference because all of the COHb measurements in our study were arterial. This helped to avoid error on calculating the $COHbt_{1/2}$ if the two COHb were different. Other factors that might affect the $COHbt_{1/2}$ measurement like alveolar ventilation (respiratory rate), blood lactate level, and smoking status were not evaluated in our study as most of these data were not documented in the record.

Conclusion

The $COHbt_{1/2}$ of CO poisoning patients by burning charcoal treated with 100% normobaric oxygen was estimated to be 78±9 minutes. Most of the patients who attempted suicide because of impulsive action but it might be the first presentation of psychiatric illness or it might indicate urgent psychiatric intervention like hospitalisation for patients with pre-existing psychiatric illness. Therefore, a comprehensive psychosocial assessment by the psychiatrist and medical social worker is mandatory for all CO poisoning patients.

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