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a neutrophil phenomenon, with little stimulatory effect from the plasma. In this group CD18 was able to inhibit completely fibronectin degradation, whereas in the group of patients whose plasma had a significant effect, the antibody could not prevent endothelial injury.

Use of antibodies against the leucocyte integrins to modulate adhesion and leucocyte-induced endothelial damage is effective in rabbit and dog models of neutrophil-mediated vascular injury.[31,32] The CD18 antibody we used was effective in reducing endothelial damage in the less severe cases. Although there is much experimental work yet to do, this study suggests that targeting neutrophil adhesion to endothelium, by means of either "humanised" monoclonal antibodies or specific peptides (eg, that block the Arg-Gly-Asp sequence) early in the course of the disease before extensive neutrophil activation and systemic degranulation, may have important therapeutic implications.

These findings directly implicate the neutrophil in endothelial damage in HUS. It is unlikely that our findings of neutrophil-mediated vascular injury are unique to HUS. In other acute inflammatory states where there is neutrophil activation (such as sepsis), part of the vascular damage is probably attributable to the neutrophil, and treatment aimed at inhibiting neutrophil adhesion to endothelium will be valuable.

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TRIAL OF NORMOBARIC AND HYPERBARIC OXYGEN FOR ACUTE CARBON MONOXIDE INTOXICATION

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Summary The value of hyperbaric oxygen in the treatment of acute carbon monoxide intoxication was assessed in 629 adults who had been poisoned at home in the 12 h before admission to hospital. In patients without initial impairment of consciousness (group A) the effect of 6 h of normobaric oxygen (NBO) (group A0, n = 170) was compared with that of 2 h of hyperbaric oxygen (HBO) at 2 atmospheres absolute (ATA) plus 4 h NBO (group A1, n = 173). At the 1 month follow-up 66% of A0 and 68% of A1 patients had recovered. In patients with initial impairment of consciousness the effect of one session of HBO (group B1, n = 145) was compared with that of two sessions (group B2, n = 141); all group B patients also received 4 h of NBO. At 1 month of follow-up 54% group B1 and 52% group B2 patients had recovered. The 7 patients left with neuropsychiatric sequelae (3 B1, 4 B2) and the 4 who died (2 B1, 2 B2) had all presented with coma. HBO was not useful in patients who did not lose consciousness during carbon monoxide intoxication, irrespective of their carboxyhaemoglobin level, nor were two sessions of HBO in patients who sustained only a brief loss of consciousness. The prognosis is poorest for those presenting with coma; the trial needs to be pursued in this

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group of patients until the power of the study is sufficient to demonstrate the value or otherwise of HBO.

Introduction

THE frequency of acute carbon monoxide intoxication at home remains high.[1-9] Oxygen is the usual treatment for this intoxication but, because of lack of controlled studies, indications for hyperbaric oxygen (HBO) remain controversial.[10,11] Some doctors give HBO routinely,[9,12-14] others prescribe it according to the initial severity of the intoxication,[15-18] but there is no wide agreement on criteria of initial severity. Some doctors recommend repeated HBO sessions for comatose patients.[16-18]

For our study we assumed that initial impairment of consciousness carries a poor prognosis[2,9,19] and so we grouped patients according to initial state of consciousness. To find out whether patients who did not sustain impairment of consciousness (group A) would benefit from HBO, we compared the effect of 6 h of normobaric oxygen (NBO) with that of 2 h of HBO plus 4 h of NBO. To find out whether patients with initial loss of consciousness (group B) would benefit from two HBO sessions, we compared the effect of one HBO session plus 4 h of NBO with that of two HBO sessions plus 4 h of NBO.

Patients and Methods

We included in our trial patients over 15 years of age admitted to hospital within 12 h (time from end of exposure) of being accidentally poisoned by carbon monoxide (CO) at home; intoxication was confirmed when the presenting carboxyhaemoglobin level was greater than or equal to 10% and 5% for smokers and non-smokers, respectively. The following were criteria for exclusion: (i) multiple intoxications such as a combination of CO poisoning with drug poisoning or with exposure to another toxic gas as may be encountered in fires; (ii) pregnancy; (iii) contraindications to HBO in a monoplace unit (haemodynamic collapse, pulmonary oedema); (iv) non-feasibility of HBO for technical reasons (breakdown, non-availability of the unit—eg, when several patients were simultaneously admitted and priority was given to group B patients); (v) difficulty in classifying patients as group A or B; (vi) specific request for or refusal of randomised treatment by patient.

The diagnosis of accidental poisoning was made on circumstantial evidence; screening for drug poisoning was done only in suspicious cases, and cases were not included when doubt remained. Randomisation was carried out after inclusion and exclusion criteria had been verified and patients had been assigned to group A (no initial loss of consciousness) or group B (initial loss of consciousness consisting either of a loss for a few seconds, or of coma, defined as inability to be roused by rescue staff). Treatment was randomly selected by means of sealed envelopes and randomisation was stratified according to patient group. The four therapeutic arms were: A0—6 h NBO at a fraction of inspired oxygen (FiO_2) of 100%; A1—2 h HBO and 4 h NBO; B1—same as A1; B2—4 h NBO at fraction of inspired oxygen of 100% plus two sessions of HBO 2–12 h apart. Patients were not informed of the randomisation procedure because informed consent would have been difficult to obtain in an emergency[20] setting and was not required by French regulations at the time. However, the treatment to be given was explained in detail to the patient (or family if the patient was comatose). If patients refused the allocated treatment after randomisation they were still retained in the study and analysed according to the treatment intended. The ethics committee of the Société de Réanimation de Langue Française approved the protocol.

NBO was delivered either through a facial mask or by mechanical ventilation if required, at an FiO_2 of 100%. HBO was given in a monoplace unit (Vickers model RHS). Each session lasted 2 h, which included half an hour for compression, 1 h at a pressure of 2 atmospheres absolute (ATA), and half an hour for decompression. Diazepam (10 mg) was injected intramuscularly before each session. Carboxyhaemoglobin level was measured at the end of therapy. In the case of vascular collapse or pulmonary oedema, supportive therapy was provided as needed.

Patients were seen a month after admission. They first had to complete a self-assessment questionnaire, answering yes or no to questions on: headaches, tiredness, memory impairment, difficulty in concentrating, difficulty in sleeping, impairment of vision, and difficulty in adjusting to the social or professional environment. They then underwent a physical examination. Recovery was defined as the absence of signs and symptoms of the intoxication; moderate sequelae as the persistence of at least one symptom without any neurological signs; and severe sequelae as the presence of at least one neurological sign. Patients who could not turn up for follow-up were sent the questionnaire by post, and if a reply was not obtained they were contacted by telephone; the physical

TABLE I—COMPARISON OF GROUPS AT TIME OF RANDOMISATION

—	A0 (n=170)	A1 (n=173)	B1 (n=145)	B2 (n=141)
Clinical features				
Sex ratio (M/F)	91/79	76/97	67/78	56/85
Mean (SD) age (yr)	35·6 (14·2)	35·2 (13·8)	37·8 (18·5)	37 (17·3)
Proportion positive for medical history	78/170 *(42%)*	65/173 *(37%)*	57/145 *(40%)*	51/141 *(36%)*
Proportion poisoned by gas water heater	90/170 *(53%)*	88/173 *(51%)*	64/145 *(44%)*	69/141 *(49%)*
Mean (SD) duration of intoxication (h)	6·2 (7·0)	6·9 (7·3)	7·3 (12·7)	5·3 (5·1)
Mean (SD) time to randomisation (h)	6·4 (2·8)	5·8 (2·3)†	5·3 (2·8)	5·3 (2·5)
Mean (SD) COHb level (%)	21·5 (9·7)	21·3 (8·9)	26·0 (11·8)	25·1 (12·1)
Mean (SD) time from end of exposure to COHb measurement (h)	2·4 (2·0)	2·1 (2·7)	2·3 (2·3)	2·2 (1·8)
Proportion with following features before admission:				
Headaches	152/170 *(89%)*	152/173 *(87%)*	109/144 *(75%)*	112/140 *(80%)*
Dizziness and/or muscle weakness	130/170 *(76%)*	136/173 *(79%)*	112/144 *(78%)*	110/140 *(78%)*
Gastrointestinal dysfunction	81/170 *(48%)*	88/173 *(51%)*	79/143 *(55%)*	81/140 *(58%)*
Loss of consciousness	2/170*	5/173*	102/143 *(71%)*	102/140 *(73%)*
Seizures	1/170*	0	8/143 *(5%)*	9/140 *(6%)*
Coma	0	0	43/145 *(30%)*	39/141 *(28%)*
Oxygen therapy	135/170 *(79%)*	130/173 *(75%)*	135/144 *(94%)*	131/141 *(93%)*
Proportion with following features at admission:				
Obtundation or confusion	0	0	20/145 *(14%)*	19/141 *(13%)*
Coma	0	0	11/145 *(7%)*	7/141 *(5%)*
Motor deficit	0	0	4/145	2/141
Proportion receiving treatments other than oxygen				
Mechanical ventilation	0	0	11/145 *(7%)*	11/141 *(8%)*
Vascular expansion and/or vasoactive drugs	2/170 *(1%)*	2/173 *(1%)*	15/145 *(10%)*	17/141 *(12%)*

*Patients mistakenly classified in group A, †$p < 0.05$.

TABLE II—TREATMENT OBSERVANCE AND COMPLICATIONS

—	A0 (n = 170)	A1 (n = 173)	B1 (n = 145)	B2 (n = 141)
Mean effective duration of NBO (h)	6·0	4·3	4·2	4·0
Number of patients who did not receive HBO*	169	3	2	4
Number of patients who received 1 HBO session	1+	170	142	9*
Number of patients who received 2 HBO sessions	0	0	1†	128
Mean (SD) COHb level (%) after treatment	1·5 (1·3) (n = 158)	1·1 (0·8)¶ (n = 162)	1·0 (0·6) (n = 139)	0·8 (0) (n = 135)
Proportion intolerant of NBO	2/170 (1%)	4/173 (2%)‡	2/145 (7%)	5/141 (3%)‡
Intolerance of HBO 1 % (n)	1/1	6/170 (3%)	15/142 (10%)	10/137 (7%)§
Intolerance of HBO 2 % (n)	0	0	0	7/128 (5%)
Proportion with confirmed barotrauma	0	1/170	3/143	1/137

*HBO was not carried out in case of patient's refusal, occurrence of contraindications after randomisation, or technical failure. †1 A0 patient was given an HBO session and 1 B1 patient received an additional 1 by mistake. ‡NBO was interrupted in 3 patients (1 A2, 2 B2). §HBO was interrupted in 2 patients (1 B1, 1 B2). ¶$p < 0.05$.

examination was done by their own doctor. The major end-point was the percentage of patients who had recovered 1 month after the intoxication. Our hypothesis was that, to demonstrate a significant difference, the estimated recovery rate in group A would have to be 50% for group A0 and 70% for A1, and that in group B would have to be 40% for B1 and 60% for B2. With values of $\alpha = 0.05$ and $\beta = 0.05$ and for a one-tailed test, an appropriate sample would require 256 group A patients and 266 group B patients (total 522). The percentage of patients expected to be lost to follow-up was 10%, so we included 600 patients in the trial.

Carboxyhaemoglobin concentration was measured by a spectrophotometer ('Co oxymeter-2000', Corning Medical). The statistical tests used were the χ^2 and Student's t test.

Results

From Nov 1, 1983, to Sept 1, 1987, 974 patients were admitted for acute carbon monoxide intoxication and 345 of them were excluded for one or more of the following reasons: probable exposure to another toxic gas (183), COHb level lower than that stipulated by the protocol (63), pregnancy (44), time to randomisation longer than 12 h (23), possibility of associated drug intoxication (12), contraindications to HBO (16), non-availability of HBO unit (11), specific request for HBO (11), refusal of HBO (9), technical breakdown of the unit (5), and difficulty in assigning patient group (3). 629 patients were included—group A0, 170; group A1, 173; group B1, 145; group B2, 141 (table I). The only notable difference between the groups was the time to inclusion which was significantly shorter for group A1 than for group A0. The commonest presenting features were headaches, dizziness, muscle weakness, and non-specific gastrointestinal symptoms (diarrhoea, vomiting). 8 patients with initial loss of consciousness were erroneously classed as group A (3A0, 5A1). Coma was diagnosed in 82 group B patients (43 B1, 39 B2), but only 18 were still comatose (11 B1, 7 B2) at inclusion. Mechanical ventilation was required in 22 group B patients. 33 patients needed vascular expansion and/or vasoactive drugs to correct haemdynamic collapse. Treatments received by patients and their complications are shown in table II.

Most patients received the treatment allocated. 9 patients (3 A1, 2 B1, 4 B2) refused HBO, 2 group A0 received one HBO session by mistake, and 9 patients received only one HBO session for the following reasons—refusal to undergo the second session (5); non-availability (3) and non-functioning (1) of HBO unit. Oxygen therapy was badly tolerated by 13 patients receiving NBO (anxiety), and by 31 receiving the first HBO session, and 7 the second session (anxiety, agitation, ear pains). In 2 patients (1 B1, 1 B2) the HBO session was interrupted because of accidental extubation in 1 and respiratory pauses in the other. 5

TABLE III—EVALUATION AT ONE MONTH

—	A0 (n = 170)	A1 (n = 173)	B1 (n = 145)	B2 (n = 141)
Lost to follow-up	22/170 (12·9%)	14/173 (8·0%)	18/145 (12·4%)	16/141 (11·3%)
Recovered	98/148 (66·2%)	108/159 (67 9%)*	68/127 (53·5%)	65/125 (52·0%)*
Moderate sequelae	50/148 (33·8%)	51/159 (32·1%)	54/127 (42·5%)	54/125 (43·2%)
Severe sequelae	0	0	3/127	4/125
Deaths	0	0	2/127	2/125
Resumption of former activity †	135/139 (97%)	147/152 (96·7%)	112/123 (91%)	108/119 (90·7%)
Asthenia	42/148 (28·3%)	38/159 (28·3%)	50/127 (39·3%)	47/125 (37·6%)
Headaches	26/148 (17·5%)	33/159 (20·7%)	27/127 (21·2%)	27/125 (21·6%)
Memory impairment	13/148 (8·7%)	15/159 (9·4%)	13/127 (10·2%)	22/125 (17·6%)
Disturbed sleep	13/148 (8·7%)	12/159 (7·5%)	20/127 (15·7%)	20/125 ((16·0%)
Difficulty in concentrating	9/148 (6·0%)	8/159 (5·0%)	11/127 (8·6%)	16/125 (12·8%)
Behavioural impairment	10/148 (6·7%)	2/159 (1·2%)	13/127 (10·2%)	11/125 (8·8%)
Visual disturbances	10/148 (6·7%)	3/159 (1·9%)	10/127 (7·8%)	5/125 (4·0%)

*$p = 0.75$. †Low denominators due to missing data on this item.

TABLE IV—EVALUATION AT ONE MONTH OF GROUP B PATIENTS ACCORDING TO INITIAL COMA

—	Without coma		With coma	
	B1 (n = 102)	B2 (n = 102)	B1 (n = 43)	B2 (n = 39)
Lost to follow-up	13/102 (12·7%)	14/102 (13·7%)	5/43 (11 6%)	2/39 (5%)
Recovery (n)	53/89 (59·5%)	47/88 (53·4%)	15/38 (39 4%)	18/37 (48·6%)
Moderate sequelae	36/89 (40·4%)	41/88 (46 5%)	18/38 (47·3%)	13/37 (35 1%)
Severe sequelae	0	0	3/38 (7·8%)	4/37 (10 8%)
Deaths % (n)	0	0	2/38 (5·2%)	2/37 (5·4%)

TABLE V—RECOVERY RATE ACCORDING TO INITIAL COHb LEVEL

Treatment regimen	Recovery rate
COHb < 25%	
A0 (n = 100)	65/100 *(65%)*
A1 (n = 107)*	71/107 *(66%)*
B1 (n = 62)†	31/62 *(50%)*
B2 (n = 63)	33/63 *(52%)*
COHb ⩾ 25%	
A0 (n = 48)	33/48 *(69%)*
A1 (n = 50)	35/50 *(70%)*
B1 (n = 62)	35/62 *(56%)*
B2 (n = 62)	32/62 *(52%)*

*Missing data for 2 patients.
†Missing data for 3 patients.

patients sustained barotrauma confirmed by otological examination. After treatment, COHb concentration was lower in group A1 than in A0 patients (table III).

70 patients were lost to follow-up (table III), the main reasons being non-response to postal questionnaire and not having a telephone (17); wrong or incomplete address (17); change of address (12). The proportion of patients who had recovered at 1 month was 66% in group A0, 68% in A1 ($p = 0{\cdot}75$, two-sided test), 54% in B1, and 52% in B2 ($p = 0{\cdot}75$ two-sided test). The differences remained non-significant even when all patients lost to follow-up were assumed to have recovered or when all were assumed to have been left with sequelae. Asthenia and persisting headaches were the most commonly mentioned complaints (table III). Over 90% of patients had resumed their occupations 1 month after the intoxication (table III). Serious sequelae or death occurred only in group B patients with coma (table IV). 4 patients died (2 B1, 2 B2)—2 soon after the intoxication and 2 from their delayed neurological syndrome. Neurological abnormalities were seen in 7 other patients (3 B1, 4 B2): early cortical blindness which eventually improved in 1, sciatic nerve impairment due to compression during coma in 1, and delayed neuropsychiatric disorders in 5.

When final outcome was stratified according to the presenting COHb concentration, the difference between treatment groups in proportions recovering still did not reach statistical significance (table V). To examine whether patient group rather than COHb level was of prognostic value, the recovery rate in group A was compared with that in B—68% of group A1 recovered, compared with 54% of group B1 patients ($p = 0{\cdot}02$, table III), but COHb level was not predictive of the final outcome in either group, since the mean was 23·0% (SD 9·93) in patients who recovered *vs* 23·4% (SD 11·2) in those who did not ($p = 0{\cdot}76$).

Discussion

The half life of COHb shortens as fraction of inspired oxygen increases. It is about 5 h at room air, 90 min with pure oxygen at a pressure of 1 ATA, 20 min with pure oxygen at 2 ATA.[10,18,21] COHb concentration decreases more rapidly with HBO than with NBO.[22,23] However, there is no evidence that this biological effect is of any clinical benefit. Apart from death by anoxia, the main complications of acute carbon monoxide intoxication include initial impairment of consciousness of various degree and/or delayed occurrence of various neuropsychiatric disturbances which may result in profound and sometimes irreversible mental deterioration.[2,12,18,19,24,25] Anatomical,[26,27] and, more recently, computed tomographic[28,29] findings are consistent with brain lesions predominantly in the white matter, the pallidus, the hippocampus, and especially the globus pallidus. The purpose of HBO would be to reduce the prevalence of these anomalies, but this has not been demonstrated in man. Large trials claiming a beneficial effect of HBO were uncontrolled,[2,9,12,15,16] retrospective,[2,12,15] or based on historical controls.[12] Recommendations of repeated HBO sessions for patients with persistent impairment of consciousness are not supported by controlled studies.[16,17] The lack of a proper evaluation of the clinical benefit of HBO has been pointed out before[10,11,30] and was the main incentive in designing the present study.[31]

The second reason for our study stemmed from problems of the feasibility of HBO therapy. The rise in prevalence of acute carbon monoxide intoxication[1,4,6,7,9] increases demand on hyperbaric centres.[8] Our department has one monoplace HBO unit. In the Greater-Paris area (population 13 million) there are only two other monoplace units, one mobile multiplace unit, and one multiplace chamber. These units do not have facilities for intensive care, which may explain why over 200 patients are admitted annually to our department. Because, generally, more than 1 person is poisoned at the same time (507/627—81% in our series), and because intoxications occur seasonally, we often have to manage several patients simultaneously. Consequently, any recommendation that HBO be given routinely[12] would mean that doctors would have to refer patients to hyperbaric centres, and the distance from home could be inconvenient for patients. The availability of HBO facilities is probably a concern in all countries since in many reports[3,19,25] not all patients were able to receive HBO. The usefulness of HBO would have to be confirmed to justify an increase in facilities for hyperbaric therapy.

Although late administration of oxygen therapy has been said to be still beneficial,[17] we sought to test treatment given as soon as possible after exposure since early HBO therapy is said to be more effective than late.[12] Our study was limited to poisonings occurring at home because they represent the commonest setting.[2,3,7,16,25] In this setting the source of carbon monoxide was, in 49% of cases (311/629, table I), an improperly maintained gas water heater. These devices may produce predominantly carbon monoxide by incomplete combustion of carbon. Less common causes of CO intoxication raise additional issues: fires may affect the bronchial tree and be complicated by exposure to gases emitted by combustion of plastic,[32-34] and gas leaks and exhaust fumes may include various saturated hydrocarbons (butane, methane, propane) that have specific brain and myocardium toxicity.[2,12] Thus, the main exclusion criterion in our study was the suspected involvement of gas other than CO. Intoxication in pregnant women also could not be addressed here.[35] We grouped our patients by neurological status, irrespective of COHb concentration, the prognostic value of which has previously been questioned.[2,9,12,26] COHb concentration depends on the interval since end of exposure and oxygen therapy given before admission. Some authors have stressed that initial loss of consciousness indicates a poor final prognosis.[2,9,16,19] Hence we chose not to include patients whose loss of consciousness may have been caused by an intoxication other than carbon monoxide and those whom we could not classify (3 patients). The diagnosis of an initial coma need not be questioned since it was certified by a doctor. However, since the diagnosis of loss of consciousness was dependent on the judgment of the patient or family, some patients may have been misclassified as group B. Since group A patients presumably represent the less severe intoxications, we compared the effect of NBO with that of NBO and HBO in this group of patients. Group B patients

justified a more aggressive approach, so in this group we compared two HBO sessions with one. To minimise the number of patients lost to follow-up we chose a simple clinical end-point (recovery) for assessment at a sufficient interval from time of intoxication, since delayed neuropsychiatric manifestations are said to occur 7–20 days after the intoxication.[2,12,18,24,25,36] Recovery was defined as absence of symptoms and signs of intoxication. It is, however, possible that the method used was not sensitive enough to detect subtle changes. The prevalence of the symptoms of CO poisoning (asthenia, headaches, abnormal behaviour, impaired memory or vision, occupational difficulty[9]) has not been estimated, and since these complaints are non-specific, they may be reported by patients even though they may not be related to the intoxication; this could lower the recovery rate. The randomisation procedure and the high power of our study were expected to keep the percentage of these "functional" patients similar in each therapeutic arm. There was also the possibility that, although patients were unaware of the randomisation procedure, HBO in group A1 or its repetition in B2 might have a placebo effect and increase recovery rate in these two groups. A double-blind trial with sham HBO therapy might have been the ideal solution but both feasibility and security problems would have made it impossible to conduct such a study on a large scale.

Our study showed that HBO had no advantage over NBO in the treatment of patients without loss of consciousness. No serious sequelae occurred in these patients, 97% of whom resumed their usual occupational and social activities irrespective of the treatment received. Although the number of patients lost to follow-up was quite high, it was evenly distributed between the two groups, which was why the difference in recovery rate remained non-significant when all those lost to follow-up were assumed to have recovered, or when all of them were assumed to have been left with neurological sequelae. Group A1 patients should have fared best since their mean inclusion time was 0·4 h shorter than that for group A0 and also because the HBO could have had a placebo effect, yet the two groups did not differ in morbidity rates or in intolerance of therapy. 1 patient experienced barotrauma confirmed by an otological examination. The only expected and tangible effect of HBO was to lower COHb level more rapidly than did NBO. In view of the high power of the trial (97%) we suggest that HBO not be used for patients with no loss of consciousness.

For patients with initial loss of consciousness two HBO sessions had no advantage over one session. Morbidity rates were 1 to 3% with NBO, 10% during HBO for those receiving one session of HBO, and, for those receiving two sessions of HBO, 7% with the first session and 5% with the second. Morbidity consisted of transient intolerance to treatment except for 4 cases of barotrauma (3 B1, 1 B2), accidental extubation in 1, and respiratory pauses in another. As expected, COHb levels were similar whether one or two sessions of HBO were given. The overall outcome in this group correlated with the presence or absence of initial coma. In patients with only a transient loss of consciousness, the recovery rate was 60% for those who received one session, and 54% for those who received two sessions of HBO. Patients lost to follow-up were evenly distributed and no serious sequelae were observed. Since the power of the study was high (94%) it is reasonable not to recommend two HBO sessions in these patients. In patients who presented with initial coma, two sessions of HBO had a slightly better effect than one session on recovery rate (49% *vs* 39%, $p = 0.42$), the effect being due mainly to fewer moderate sequelae with two sessions. The number of serious sequelae or deaths was not influenced by two HBO sessions. This is consistent with the conclusions of Sawada et al,[29] who showed that the correlation between initial computed tomographic findings and the occurrence of severe neurological sequelae persisted irrespective of the number of HBO sessions, which ranged from three to twenty-three, at three ATA. However, because of the small sample size, further studies are required in the comatose patients before any conclusions may be drawn.

Our results indicate the appropriateness of classifying patients according to the presence or absence of loss of consciousness, rather than by COHb concentration. Among 629 patients, 4 (0·6%) died and 7 had severe neurological sequelae. These 11 patients had initial coma. Other recent reports give a neurological morbidity of 1–4%,[3,9,16,25] a striking decrease from earlier reports of 12–26% for deaths and 6–15% for neurological morbidity.[12] These reductions were attributed to the wider use of HBO,[16] but in a recent report in which HBO was not given, the neurological morbidity was 1·1% (1/90).[3]

We hope that our findings will help in the management of patients with acute CO intoxication occurring at home and in rationalising admissions to hyperbaric centres. Patients who do not sustain loss of consciousness may be treated solely with NBO irrespective of their initial COHb concentration. Patients who sustain only a brief loss of consciousness may be treated with one session of HBO irrespective of their COHb level. These patients seem to be at risk only of subjective disturbances; thus what they gain from HBO may be debatable and is not settled by our results. Patients with coma are those at high risk. Although we did not find that two sessions of HBO were more beneficial than one, further evaluation is required. However, it is highly doubtful whether two HBO sessions would significantly reduce the mortality and the prevalence of delayed severe neuropsychiatric sequelae in these patients. We are not able to say whether more than two sessions of HBO would be indicated for these patients.

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Preliminary Communication

PRENATAL DIAGNOSIS OF A RED-CELL ENZYMOPATHY: TRIOSE PHOSPHATE ISOMERASE DEFICIENCY

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Summary A child with triose phosphate isomerase deficiency was born to non-consanguineous parents, and died at 13 months of age. The parents were both found to be heterozygous for this enzyme deficiency. At a subsequent pregnancy, analysis of fetal red blood cells obtained by cordocentesis at 19 weeks' gestation enabled prenatal diagnosis of the heterozygous state. This technique may allow diagnosis of other red-cell enzymopathies during the second trimester.

INTRODUCTION

THE benefits of prenatal diagnosis of haemoglobinopathies and inherited bleeding disorders are widely recognised. However, severe red-cell enzymopathies may also cause a high morbidity and lead to early death. For example, triose phosphate isomerase deficiency not only causes haemolysis, but also early central nervous system degeneration and cardiac failure, with death usually before the age of 15 years. We report a child with triose phosphate isomerase deficiency who died at 13 months; in a subsequent pregnancy, prenatal diagnosis at 19 weeks' gestation could be made by comparison with the characteristics of the mutant enzyme and red-cell metabolic changes detected in the first child, the heterozygous parents, and adult and fetal controls.

SUBJECTS AND METHODS

Enzyme Analysis

Red-cell enzymes were measured as recommended by the International Committee for Standardisation in Haematology.[1] Red-cell glycolytic intermediates were measured on deproteinised extracts of fresh whole blood according to Lestas et al's[2] modification of the fluorimetric methods of Segel et al.[3] Triose phosphate isomerase thermostability was defined as the activity of freshly prepared haemolysate kept at pH 8·0 and 50°C for 15 min, expressed as a percentage of the original enzyme activity. All measurements of red-cell enzymes and intermediates were done within 24 h of collection. Fetal blood samples were obtained by cordocentesis.[4] Haemoglobin (Hb) and red-cell indices were measured on a Coulter 'STKR' counter and reticulocytes were counted on films stained supravitally with new methylene blue. Adult control blood samples were obtained from laboratory personnel. Fetal control samples were obtained from fetuses that underwent cordocentesis between 18 and 24 weeks' gestation for other indications (eg, haemophilia).

Case History

The first child weighed 2·5 kg at birth and was born at 35 weeks' gestation of fit, non-consanguineous parents. Jaundice was noted at 24 h: haemoglobin was then 12·0 g/dl and bilirubin 245 μmol/l, with no evidence of rhesus or ABO incompatibility. Phototherapy was started and continued for 9 days, after which transfusion was started for anaemia (7·6 g/dl on day 10). Repeated transfusions were required in the first two months of life, after which no further transfusion was necessary. Haemoglobin was subsequently maintained at 8–10 g/dl, with continued evidence of haemolysis (10–15% reticulocytes). The infant otherwise developed normally. At 4 months, investigations showed abnormal autohaemolysis (12·5%) which only partly corrected with glucose (8·6%). Screening tests for red cell pyruvate kinase and glucose-6-phosphate dehydrogenase activities were normal, as were haemoglobin electrophoresis and heat stability tests. Normal development, with continued haemolysis, was observed up to the age of 9–10 months, when the parents first reported difficulty in feeding and failure to thrive. General flaccidity and failure to hold the head up were soon noted. At 1 year the child was referred for further investigation: the diagnosis of homozygous triose phosphate isomerase deficiency was established, and both parents were found to be heterozygous carriers of this enzyme deficiency (see below). The child continued to deteriorate and died of cardiorespiratory

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