A CASE OF RECOVERY FROM COMA PRODUCED BY THE INGESTION OF 250 ML OF HALOTHANE

BY

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SUMMARY

A case is reported of narcotic coma in a female lasting 36 hours as a result of deliberate ingestion of 250 ml of halothane. Aspiration of gastric contents led to cardiac arrest which was successfully treated. Artificial ventilation was needed. Halothane hepatitis did not develop despite prolonged episodes of respiratory and circulatory failure and medication with drugs known to interfere with liver function. The patient had fully recovered when discharged from the clinic eleven days after admission. No alteration of hepatic function was found at periodical examinations over a period of four months.

A search of the available literature failed to reveal a report of a case of coma following halothane ingestion. We recently had the opportunity of managing such a case and an account is presented here.

CASE REPORT

A female patient, aged 48, was brought to the Emergency Hospital, Bucharest, on May 27, 1966, in a state of coma, 4½ hours after having ingested 250 ml of halothane for suicidal purposes.

Superficial examination showed a normal constitution with normal colour of the skin and mucous; the smell of halothane was unbearable. The pupils were equal with moderate mydriasis (5–6 mm diameter); corneal and photomotor reflexes were present. There was a disorientative response to very painful stimuli; no meningeal signs were elicited. Respiration was shallow and rales could be heard on both sides of the chest.

The blood pressure was 110/60 mm Hg and the pulse rate was 60 beats/min, regular and of good volume. The heart sounds were normal.

On examination of the abdomen the epigastrium and bladder were found to be distended. The liver and spleen were within normal limits and the kidneys could not be palpated. The extremities were dry, warm, of normal colour and there was no oedema.

The patient was admitted to the intensive therapy unit. When she was lifted off the stretcher on to the resuscitation bed she vomited. The vomitus (500 ml approx.) contained food remains and smelled strongly of halothane. Part of the vomitus was inhaled and the patient remained intensely cyanosed and increasing pulses disappeared at the moment of intubation. The chin region was required. The carotid and femoral pulsations were absent. The respiration was shallow and rales could be heard on both sides of the chest. The heart sounds were normal.

The blood pressure was 110/60 mm Hg and the pulse rate was 60 beats/min, regular and of good volume. The heart sounds were normal.

One hour after extubation the systolic blood pressure had fallen to 70 mm Hg; the pulse continued at 64 beats/min. Respiration was shallow and the level of consciousness diminished. The endotracheal tube was therefore withdrawn.

A case is reported of narcotic coma in a female lasting 36 hours as a result of deliberate ingestion of 250 ml of halothane. Aspiration of gastric contents led to cardiac arrest which was successfully treated. Artificial ventilation was needed. Halothane hepatitis did not develop despite prolonged episodes of respiratory and circulatory failure and medication with drugs known to interfere with liver function. The patient had fully recovered when discharged from the clinic eleven days after admission. No alteration of hepatic function was found at periodical examinations over a period of four months.
Electroencephalogram—transversal leads. Galileo apparatus. Time constant: 0.3 sec.; filter: 25 Hz. The patient in coma, resuscitation after cardiac arrest. The voltage of the tracing is almost flat on the fronto-frontal lead (coinciding clinically with mydriasis). Predominant frequency of the waves oscillating between 8-14 c.p.s., alternating with strips of Α band. The voltage ranged from 5 to 25 μV. Accentuated tendency to hypersynchronism. No pathologic discharges were recorded.

TABLE I

Acid-base balance measured on the capillary blood using Astrup technique.

<table>
<thead>
<tr>
<th>Time after admission</th>
<th>pH</th>
<th>pH&lt;sub&gt;B&lt;/sub&gt; (mm Hg)</th>
<th>Standard bicarbonate (m.equiv/l.)</th>
<th>Base excess (m.equiv/l.)</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>On admission</td>
<td>7.34</td>
<td>18.50</td>
<td>15.25</td>
<td>-13.0</td>
<td>Resuscitation after cardiac arrest, mechanical ventilation</td>
</tr>
<tr>
<td>4 hours</td>
<td>7.28</td>
<td>37.00</td>
<td>17.30</td>
<td>-9.60</td>
<td>After relapse into coma; administration of 250 ml 5% NaHCO₃ soln., mechanical ventilation</td>
</tr>
<tr>
<td>12 hours</td>
<td>7.11</td>
<td>75.00</td>
<td>15.60</td>
<td>-12.0</td>
<td>Blood pressure 70/30 mm Hg</td>
</tr>
<tr>
<td>36 hours</td>
<td>7.39</td>
<td>40.50</td>
<td>24.00</td>
<td>0</td>
<td>Stable haemodynamics, spontaneous ventilation (10 l./min); tracheostomy</td>
</tr>
<tr>
<td>60 hours</td>
<td>7.56</td>
<td>20.50</td>
<td>25.50</td>
<td>+4.20</td>
<td>Tracheostomy cannula removed</td>
</tr>
<tr>
<td>84 hours</td>
<td>7.44</td>
<td>37.00</td>
<td>24.60</td>
<td>-1.00</td>
<td>Tracheostomy cannula removed</td>
</tr>
<tr>
<td>8 days</td>
<td>7.57</td>
<td>24.00</td>
<td>25.00</td>
<td>+1.30</td>
<td>Patient with tracheal cannula</td>
</tr>
<tr>
<td>9 days</td>
<td>7.49</td>
<td>41.00</td>
<td>30.00</td>
<td>+7.25</td>
<td></td>
</tr>
<tr>
<td>6 weeks</td>
<td>7.45</td>
<td>34.00</td>
<td>24.50</td>
<td>+0.50</td>
<td></td>
</tr>
</tbody>
</table>
Tracheostomy was performed and large quantities of purulent-sanguineous secretion were aspirated from the tracheo-bronchial tree. Artificial ventilation was maintained. Within the next 24 hours the following drugs were given intramuscularly: penicillin 20 mega units; streptomycin 1 g; oxytetracycline 1 g; 20 per cent glucose (2000 ml); 5 per cent sodium bicarbonate (250 ml); hydrocortisone hemisuccinate 1 g; vitamins (B₁, B₂, B₆, B₁₂, C, K); arginin 6 g; digitalis glycosides (isolamide 0.6 mg); noradrenaline (0.5 mg); gallamine (240 mg). 500 ml of blood was also transfused.

Despite this treatment blood pressure values were unstable until the evening, by which time the patient was able to obey simple orders. Spontaneous respiration was still inadequate. Blood pressure was 110/60 mm Hg and the pulse rate 132-140 beats/min.

By the second morning the patient had regained consciousness, was capable of obeying simple orders and was resisting mechanical ventilation. The blood pressure was stable at 110/60 mm Hg. Mechanical ventilation was discontinued and the patient breathed spontaneously at 40 b.p.m., the minute volume being 7.8 l./min. The smell of halothane persisted. Atropine 0.3 mg and neostigmine 1 mg were administered intravenously. The minute volume of ventilation increased to 10 l./min, the respiratory rate remaining unchanged. Diuresis reached 1800 ml/24 hours. The patient was slightly febrile (38.2°C). The fluid balance was slightly positive (3900 ml output as against 4000 ml input). The medication was similar to that of the preceding day. Hydrocortisone hemisuccinate was reduced to 500 mg/24 hours.

On the third day after admission the general state of the patient was markedly improved. She was conscious and reproachful, and angry with the doctors for having saved her life. She confirmed that she had ingested 250 ml halothane. Clinically respiration was unobstructed; however, atelectasis was demonstrated radiographically in the right upper lobe. Blood pressure was 110/55 mm Hg and pulse rate 120 beats/min, regular and of good volume. The urine output was 1000 ml/24 hours. The temperature was 38°C. An incipient bedsore was present in the sacral region. Treatment was continued as on the preceding day.

On the fourth day the general state continued to improve. The temperature returned to normal. The tracheostomy tube was removed and oral hydration started.

The next day there were clinical and radiological signs of pneumomediastinum, with interstitial and massive subcutaneous emphysema involving the thorax, neck and face up to the eyebrows. The tracheostomy cannula was reintroduced.

Five days later the tracheostomy cannula was removed because the emphysema was much reduced and on the sixth day the patient was transferred to the Institute of Neuropsychiatry where she was treated with meclofenoxate.*

Two weeks later the patient was discharged; she was feeling well, optimistic, and regretted what she had done and was happy to have been saved.

At follow-up examinations four weeks and fourteen weeks later she exhibited the same optimism and had gained weight. The tracheostomy wound was healed.

Bearing in mind the gravity of the case and the problems to which it gave rise numerous investi-

* Lucidryl; Lloyd Anphar.
<table>
<thead>
<tr>
<th>After admission</th>
<th>Serum protein</th>
<th>Prothrombin</th>
<th>Serum enzymes</th>
<th>Flocculation tests</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total serum bilirubin (mg %)</td>
<td>Total protein (g %)</td>
<td>Albumin (%)</td>
<td>α-1-globulins (%)</td>
</tr>
<tr>
<td>1st day</td>
<td>1.02</td>
<td>7.20</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4th day</td>
<td>1.06</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>8th day</td>
<td>—</td>
<td>8.06</td>
<td>56</td>
<td>5</td>
</tr>
<tr>
<td>10th day</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>7 weeks</td>
<td>1.04</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>17 weeks</td>
<td>1.08</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

* Negative.
Alteration of the respiratory function was minimal and specific of halothane narcosis. Atelectasis of the right upper pulmonary lobe was the consequence of vomiting and aspiration of gastric contents.

Although it is asserted that halothane depresses neuromuscular transmission (Hanquet, 1962), administration of a comparatively large amount of gallamine was necessary in order to obtain adequate ventilation.

Halothane anaesthesia does not appear to induce metabolic acidosis. The acid-base imbalance and alteration of the blood gases encountered in our case were due to the circulatory and respiratory disturbances that were associated with the coma (table I).

The cardiac arrest in this case was not due to acute halothane intoxication but to asphyxia following aspiration of gastric contents. Although the ingested halothane dose was large, the amount absorbed cannot be estimated. Severe cardiac rhythm disturbances were not observed. Probably the blood concentration never rose to a level at which such effects might arise.

Functional liver alterations were minimal.

As stated recently by Flemming and Bearcroft (1966), "The recent controversy concerning the role of halothane in the production of hepatic necrosis is difficult to resolve by the study of human patients. Rarely, if ever, can other possible hepatotoxic factors related to disease or treatment be completely excluded and a controlled experiment in man designed to test the hepatotoxicity of the drug is impossible." Our case, however, is tantamount to an experiment in man. Liver injury was not demonstrated in this patient. It is certain that all the 250 ml of halothane was not absorbed from the alimentary tract, but bearing in mind the portal route of penetration it may be assumed that a considerable amount accumulated in the liver, at least in the initial period. Similarly, it is known from animal experiments that following the administration of halothane by inhalation its concentration is higher in the liver than in the arterial blood (Duncan and Raventós, 1959). Other factors that might have caused liver damage include the episode of respiratory and circulatory failure after cardiac arrest followed by resuscitation, the treatment
with blood, antibiotics, tetracycline and phenothiazine, after recovering from coma.

Vomiting frequently occurred and deserves mention as some authors (Novoa, 1960; Haumann, Lee and Foster, 1963) attribute a specific anti-emetic action to halothane. Vomiting was probably caused by gastric irritation and concomitant pyloric spasm. It is also possible that halothane absorbed in the blood might exercise a direct or indirect action upon the nervous centres and chemoreceptor zones, considered to form part of the reflex arc of vomiting, especially as it has been recently demonstrated that halothane does not possess a specific anti-emetic action (Dixit et al., 1966).

Renal functional alterations were minimal and do not require particular comment.

There is no satisfactory explanation for the initial leucocytosis and the severe anaemia in the final period of hospitalization, so that it is not possible to establish a correlation with the acute halothane intoxication.

**ADDENDUM**

Since writing this case report the authors have learned of a further case of ingestion of halothane for suicidal purposes. A 28-year-old male, in a state of psychic depression, ingested 250 ml of halothane. The coma lasted 72 hours. There was severe gastro-enterocolitis. The patient made a full recovery. No alterations of hepatic function were found.

Both patients who had ingested 250 ml of halothane are alive and to the time of writing do not manifest any clinical or biochemical signs of halothane hepatitis.

**REFERENCES**


**ERHOLUNG NACH KOMA WEGEN EINNAHME VON 250 ML HALOTHAN**


**UN CAS DE GUERISON D'UN COMA, CAUSE PAR INGESTION DE 250 ML D'HALOTHANE**

On rapporte un cas de coma narcotique chez une femme, d'une durée de 36 heures, consécutif à l'ingestion délibérée de 250 ml d'halothane. L'aspiration du contenu de l'estomac provoqua un arrêt cardiaque, traité avec succès. La ventilation artificielle fut nécessaire. Une hépatite par halothane ne se développa pas, en dépit de périodes prolongées d'insuffisance respiratoire et circulatoire, et de l'administration de médicaments, dont l'effet sur la fonction hépatique est bien connu. La patiente s'était rétablie complètement lorsqu'elle fut renvoyée de l'hôpital, onze jours après son admission. Aucune altération de la fonction hépatique n'a été observée lors des examens périodiques consécutifs durant une période de quatre mois.

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