

Dangers of Anaesthesia in Children with Rickets

By

MAGDA KOCSIS

First Department of Paediatrics (Director: Prof. P. GEGESI KISS),
University Medical School, Budapest

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The most dreaded complication of inhalation anaesthesia is cardiac arrest, the syncope. Numerous reviews have dealt with its causes; the factors mentioned are as follows.

(i) Hypoxia, anoxia, asphyxia, aspiration [1, 2, 4, 5, 8, 9, 10, 11, 15, 16, 19, 22, 23, 25, 28, 30].

(ii) Local stimuli, vagal reflex [4, 7, 10, 11, 15, 19, 22, 28].

(iii) Toxic effect of the anaesthetic agent [2, 5, 8, 10, 11, 15, 22, 26, 30].

(iv) Individual hypersensitivity to the anaesthetic agent [10, 15, 20].

(v) Anaemia, haemorrhage [2, 4, 22, 26].

(vi) Dehydration, fever [2, 7, 9, 30].

(vii) Previous heart disease [4, 9, 11, 26].

(viii) Primary disorder of myocardial metabolism [17].

(ix) Sudden discontinuing of cortisone treatment [9].

(x) Unknown factors [4, 10, 14].

In addition to the above causes, some authors emphasize the influence of the dead space, further the predisposing effect of the disturbances of electrolyte and water metabolism, of chronic respiratory acidosis, the nutritional state of the patient and

that of vitamin deficiency [7]. KISS emphasized the role of calcium and phosphor metabolism in the occurrence of syncope during childhood [15a].

Most of the reviews are discussing the cases in childhood separately, the mortality rate in children being higher than in adults. According to CASTEN, it is twice as high [7]; on the basis of DELÈGUE's data [8], 82 per cent of the deaths due to anaesthesia occur under 3 years of age; from among TERMET-GRÉGOIRE's 7 lethal cases, 6 were children [29]; 20 per cent of BEECHER's material fell to children under 10 years of age [3]. Among the 26 lethal cases observed by KOK [16] in children under 10 years of age, 25 occurred in the introductory phase.

OWN OBSERVATIONS

Among 2600 children subjected to inhalation ether anaesthesia, in 6 cases the sudden appearance of a grave state was noted at the beginning of anaesthesia. One of the patients died; in three cases the disturbance could be controlled and in two its full manifestation inhibited. In three further

cases it seemed probable that the complication had been prevented.

Anaesthesia after due introduction was carried out with ether, with the open drip technique. About two minutes after the administration of ether had begun, following inhalation of 20 to 25 drops, a conspicuous pallor of the face occurred and the pulse was slowing and weakening without any signs of excitation or of the usual apnoea due to too concentrated anaesthetics. One or two minutes later, respiratory volume and rate were progressively depressed; there was bradycardia (40 to 60/min) with weak heart sounds; then respiration ceased, the skin was cyanosed, the pupils dilated, rigidity to light set in.

Except in the one lethal case, the state could be controlled in a few minutes, by immediately discontinuing ether administration, and applying artificial respiration, oxygen inhalation and analeptic drugs. After spontaneous respiration had started the pupils narrowed, the pulse became normal, and anaesthesia could be resumed without any further disturbance.

Case 1. a) A male newborn 11 days of age was operated upon in June, 1958, for a pygopagus-like deformity in the sacral region; two independent limbs were removed. Anaesthesia and postoperative course were uneventful.

b) At the age of 16 months, in November, 1958, another operation had to be carried out because of an inguinal hernia on the left side. The intervention was performed under ether anaesthesia without any complication. The child at this time already displayed signs of rickets on the skull and chest. He had two months

previously been given an injection of vitamin D₂ and had had calcium treatment. Thoracic X-ray showed dextrocardia. The heart sounds were normal and so was the ECG record.

c) At the age of 2 years, in June, 1960, the patient was to undergo a third operation, this time for pes equinovarus. After he had inhaled about 2 ml of ether, sudden pallor, bradycardia, respiratory arrest, cyanosis ensued. Attempts at resuscitation were unsuccessful. Autopsy revealed dextrocardia, an enlarged heart with myocardial scars and relative mitral insufficiency. The bones showed signs of rickets. The parietal bone was thinned, transparent, the costal cartilages were swollen. The thymus was normal.

Case 2. A male child 20 months of age, with signs of rickets on skull and chest. Dentition had begun late. He had had several courses of antirachitic treatment. In September, 1958, he was admitted for operation of inguinal hernia on the right side. Premedication was carried out with phenobarbital on the previous evening and cocktail lytique intramuscularly prior to operation. At the beginning of ether anaesthesia, sudden pallor, bradycardia, respiratory depression, cyanosis and dilatation of the pupils occurred. The state was controlled with analeptic drugs and artificial respiration. Subsequent anaesthesia was uneventful. The intervention was carried out without further disturbance.

Case 3. A female child 12 months of age, with signs of rickets on skull and chest. She had had antirachitic treatment. In February, 1959, operation for inguinal hernia on the right side was started after premedication with phenobarbital and cocktail lytique. After inhalation of about 10 ml of ether the patient suddenly became pale, the pulse was slow, she did not breathe and was cyanosed. The state was controlled by repeated intravenous injections of analeptic drugs. Anaesthesia was continued with no further disturbance.

Case 4. A male infant who in April, 1958, at the age of 5 months, had under-

gone an operation for harelip under ether anaesthesia. The patient had a rachitic chest and had received prior to operation a booster dose of vitamin D₂ and calcium treatment. Premedication for the operation was carried out with chlorpromazine.

b) At the age of 30 months, in May, 1960, the patient was admitted for cleft palate operation. Swelling of the costal cartilages, caput quadratum were found. Between the two admissions the patient had again had vitamin D₂ treatment. As premedication before the operation phenobarbital and cocktail lytique were administered. At the very beginning of ether anaesthesia sudden pallor, bradycardia, and then apnoea and cyanosis set in. Analeptics were administered repeatedly, but in spite of artificial respiration and oxygen administration the state was controlled with difficulty so that the intervention was postponed. One hour later the patient was awake and well.

c) Five days later the cleft palate operation was carried out under careful oxygen-ether anaesthesia. The intervention was uneventful, respiration and circulation were normal throughout.

Case 5. A female child 8 months of age, with signs of rickets on skull and chest. She had received several courses of antirachitic treatment. In August, 1959, after premedication with phenobarbital and cocktail lytique an operation was begun to remove the left hydronephrotic kidney. Ether was administered from the beginning very slowly and supported by large doses of oxygen. After two minutes the face suddenly became pale, the pulse rate fell from 120 to 80, respiration was slow. After the inhalation of 10 g of ether the pulse rate returned to 110/min, respiration became deeper and more frequent. The subsequent course of anaesthesia was undisturbed.

Case 6. A male child 7 months of age; dentition had not yet begun, he could not sit. The thorax was rachitic; Harrison's groove, swelling of the costal cartilages were present. In December, 1958, because

of a polycystic kidney on the left side, nephrectomy was indicated. Oxygen-ether anaesthesia was started. After a few inhalations the patient suddenly became pale, the pulse rate decreased, respiration became superficial, the pupils somewhat dilatated. Inhalation of pure oxygen resulted in 1 to 2 minutes in deep and regular respiration, the pupils narrowed, the heart rate became normal. No further disturbance occurred.

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In the above clinical observations, two interesting circumstances called for special attention. First, that the disturbance due to ether inhalation began with bradycardia; second, that in all the patients signs of rickets were present. On the basis of these observations, the following investigations were carried out.

a) In 100 non-rachitic young children the changes of the pulse rate were observed during the first 10 minutes of ether anaesthesia. Following the first inhalations, in 82 per cent of the patients the pulse rate decreased with 20 to 60 beats to reach in 2 to 4 minutes again the initial frequency. During the subsequent excitation phase the usual tachycardia ensued. In 5 per cent of the cases the depression of the pulse rate occurred on the effect of the very first drops of ether; in 13 per cent, the pulse rate remained unchanged. Pallor or respiration disturbances were observed in none of the cases.

b) According to our animal experiments, rats develop bradycardia at the beginning of ether anaesthesia in 80 per cent; the usual heart rate of above 200/min falls in the first 10 seconds to

120—160/min, to resume the original rate in 30 to 40 seconds. In animals fed a rachitogenic diet, this bradycardial reaction is prolonged, the restitution of the original heart rate takes 60 to 80 seconds (Fig. 1).

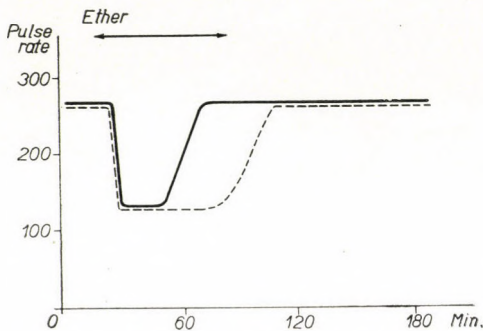


FIG. 1. Response of heart rate to ether inhalation in normal rats and in rats fed on a rachitogenic diet

— Normal animals
 - - - Animals with rickets.

DISCUSSION

The above described disturbance noted at the beginning of ether anaesthesia and characterised by bradycardia, secondary respiratory disturbance, cyanosis, dilatation of the pupils, etc., was noted only in patients ranging in age from 7 to 30 months and displaying signs of rickets: The occurrence of the complication was not seasonal as it presented itself in spring, summer, autumn and winter alike. It could not be prevented by ganglion blocking agents, phenothiazine drugs or reflex inhibition, but was never observed if previously calcium had been administered further if the ether was given slowly and with an excess of

oxygen. This method seemed to be able to prevent the full manifestation of the disturbance.

X-ray examination carried out before anaesthesia showed in none of the cases a thymus shadow, neither was an enlarged thymus found at autopsy of one lethal case.

The fact that the disturbance was observed exclusively in children suffering from rickets and that its occurrence seemed to be prevented by calcium, appeared to indicate the predispositional role of hypocalcaemia. Unfortunately, preoperative determinations of the serum calcium level were not carried out and no reliable data concerning previous antirachitic treatments could be collected. On the other hand, it is well-known that infants with rickets and latent tetany show a tendency to vagotonia and in that state insignificant interventions may cause cardiac arrest. Kiss in 1937 had already called attention to the cause of this phenomenon and also to the favourable effect of calcium treatment in the prevention of syncope [15a], stating that with a decrease in the serum calcium level conduction time becomes prolonged and heart contractions are weak. The excitability of the vegetative nervous system is increased and the heart predisposed to bradycardia reacts intensely to the intensified peripheral stimuli of vagotonic character.

It may be surmised that premedication with atropine would have prevented or at least mitigated the course of the episodes observed by us and preoperative administration of atro-

pine seems to be especially indicated in patients with rickets.

Strong chemical stimuli (ammonium, acids, ether) are known to cause bradycardia *via* the sensory endings of the trigeminus nerve and the lungs, as on the local effect of ether the pulmonary vessels dilate and tension decreases in the pulmonary veins [12, 13]. In the normal organism this phenomenon does not lead to circulatory disturbances; in our animals fed a rachitogenic diet, however, the normalisation of heart function was prolonged.

BERWICK investigated the effect of ether on the isolated frog muscle and found a liberation of calcium ions from the cell membrane, causing thus a calcium deficiency of the muscle and nerve cells [6]. In addition, the anaesthetics inhibit the flow of calcium into the cells and thus primarily inhibit cell reactions.

According to LABORIT [17], ether causes metabolic disturbances in the myocardial cells, inhibiting depolarization and aerobic glycolysis. This ion exchange disturbance on the cell membrane level cannot be prevented or inhibited by neuroplegic drugs.

The circulatory disturbance was favourably influenced by oxygen administration. This circumstance calls attention to the role played by hypoxia in the development of the condition but hypoxia cannot be regarded as its sole cause. At the induction of inhalation anaesthesia infants need large doses of oxygen [11, 27], but neglecting this practically never causes disturbances in non-rachitic pa-

tients. The usual hypoxic inhibition of the vasomotor centres [13, 20, 22, 24], however, seems to be enhanced by rickets or a possibly hypocalcaemic state.

According to the above observations, neither rickets *per se* nor ether inhalation *per se* cause circulatory disturbances leading to severe hypoxia. The possibility should, however, be taken into consideration if these two factors meet. As to the mechanism of the phenomenon, it may be assumed that in cases predisposed to hypocalcaemia, especially after a vitamin D₂ booster dose, the vagotonic disposition associated with rickets enhances the bradycardising effect of ether. The weakened heart contractions thus become increasingly depressed and further depression results from the ion exchange disturbance through the cell membrane due to the ether effect. The probable mechanism of the phenomenon is shown schematically in Fig. 2.

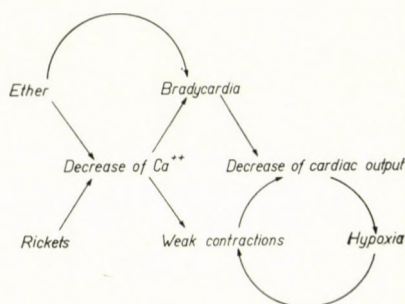


FIG. 2

The vicious circle thus arising seems to be preventable partly by supporting the heart with calcium and oxygen, and partly by decreasing the dosage

of ether, and probably by administration of atropine. After the first phase of the reaction is over, during deep anaesthesia the counterregulatory mechanisms already decrease the excitability of sensory nerves and reflex paths, prevent the manifestation of circulatory disturbances, as in a non-rachitic organism.

The clinical signs of rickets, especially when they are slight, are not easy to recognize. The possibility must be taken into account that complications due to anaesthesia and part of the cases of sudden cardiac arrest seemingly unmotivated in infancy

and early childhood, might set in according to a similar mechanism. The above-described episodes of bradycardia and apnoea might be considered a premonitory sign of cardiac arrest. Taking this possibility into account when infants with rickets have to be subjected to general anaesthesia, will perhaps help to avoid some unexplained deaths.

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SUMMARY

Among 2600 cases of ether anaesthesia in children, in 6 instances severe circulatory disturbance characterized by sudden pallor, depression of heart and respiration rate, cyanosis and dilatation of the pupils, occurred causing in one case death. The complication arose in every case at the beginning of ether anaesthesia in children ranging in age from 7 to 30 months, and showing signs of rickets. In the

development of the episode the rachitic disturbance of calcium metabolism is supposed to play a role. The syndrome should be regarded as a premonitory sign of cardiac arrest. Its development can be prevented by administration of calcium, the slow dosage of ether with an excess of oxygen, and probably by premedication with atropine.

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Dr. M. KOC SIS

Bókay János u. 53

Budapest VIII., Hungary