MALIGNANT HYPERPYREXIA CAUSED BY TRIMEPRAZINE

Case Report

D. G. MOYES

SUMMARY

A fatal malignant hyperpyrexial reaction in a three-year-old child followed oral administration of an accepted dose of trimeprazine for preanaesthetic medication.

A Caucasian male child aged 3 years, weighing 15 kg, was admitted for elective removal of a bifid terminal phalanx of the right thumb. He had been a healthy child and had had no previous anaesthesia. He was apyrexial on admission (36.6°C) and again on the following day when surgery was to be performed. Routine examination by two anaesthetists revealed no clinical abnormality. A dose of 12 ml (72 mg) of trimeprazine (Vallergan Forte Syrup; May & Baker) was ordered for the child, calculated on the basis of 2 mg/lb. body weight. A dose of atropine 0.3 mg was scheduled to be given 30 min later. The dose of trimeprazine was administered orally by an experienced paediatric ward sister. After some 15 min, she noticed that the child had become distressed and the axillary temperature was noted to be 39.5°C. This proceeded to rise, until after 45 min the temperature was 41.1°C. The thermometer was checked against two other mercury-in-glass thermometers and the readings were found to coincide. The child was by then unconscious, dyspnoeic, cyanosed, hot, flushed, and had marked muscular rigidity. Surface cooling restored the temperature to 36.4°C and there was marked improvement in the clinical state, although the level of consciousness remained, at best, drowsy. The scheduled dose of atropine 0.3 mg was unfortunately given at this stage. Sodium bicarbonate 10 m.equiv was given empirically and 180 ml of 0.9% saline which was infused rapidly. The rectal and skin temperatures were measured by means of an electric thermometer (Light Laboratories). Blood pressure, pulse rate, respiratory rate were measured frequently and the level of consciousness noted. The temperature subsequently began to rise sharply, reading 40°C at 10.30 p.m., 8 hours after the dose of trimeprazine had been given. The pyrexia was accompanied by increased muscle tone, particularly noticeable in the limbs, and by a mild degree of shivering. Cold sponging was supplemented by ice packs. Analysis of capillary blood at this stage showed: pH 7.43; Pco2 32.5 mm Hg; standard bicarbonate 23 m.equiv/l.; base excess —1 m.equiv/l.

It was decided that artificial ventilation should be started. Alcuronium was injected and ventilation carried out using a Bird ventilator, set to “air mix” via 4.5-mm Jackson-Rees nasotracheal tube. Ventilation was adjusted so that the arterial carbon dioxide tension remained slightly above the normal value. At this stage the presence of methaemoglobinemia was considered but excluded by examination of the spectrophotometric absorption curve.
At 6.00 the following morning, 16 hours after administration of trimeprazine tartrate, the base deficit was 7 m.equiv/l. and sodium bicarbonate 22 m.equiv was given. The temperature had been successfully controlled by the combination of muscle paralysis, the use of a cold sponge, and an air fan.

At 22 hours the capillary blood sample showed 

Pco₂ 45 mm Hg; pH 7.3; standard bicarbonate 20.5 m.equiv/l. and base deficit 4 m.equiv/l. The pulse rate had fallen to 120 beats/min, and in view of the risk of the return of the pyrexial trend it was decided to continue pulmonary ventilation for 48 hours. A nasogastric tube was passed at this stage in view of the likelihood of ileus. Further investigations gave the following results: haemoglobin 13.5 g/100 ml; sodium 144 m.equiv/l.; potassium 4 m.equiv/l. and chloride 102 m.equiv/l. Ventilation at this stage was complicated by the development of collapse of the left lung. Bronchoscopy was performed and a considerable quantity of secretion was aspirated. The latter was managed by aspiration of air with a needle and syringe. Further management was complicated by the recurrence of technical problems in the management of artificial ventilation, collapse of the left lung recurred and pneumothorax developed. It is thought that the high inspiratory pressures required in consequence of reduced compliance caused the pneumothorax. On two further occasions the child developed a rapidly rising temperature in response to allowing the degree of muscle relaxation to be reduced.

After 36 hours a blood sample drawn following administration of sodium bicarbonate 12 m.equiv showed: pH 7.38; Pco₂ 38 mm Hg; standard bicarbonate 22 m.equiv/l.; base excess −2.5 m.equiv/l.; haemoglobin 11.4 g/100 ml and packed cell volume 38%. At 72 hours after, the Pco₂ was 65 mm Hg; pH 7.26; standard bicarbonate 23 m.equiv/l.; base excess −1 m.equiv/l. In response to attempts to make ventilation more effective, the compliance of the lungs progressively diminished and cyanosis increased. This was unrelieved by the use of an inspired oxygen concentration of 100% and the child died at 80 hours after the dose of trimeprazine tartrate.

Postmortem examination was not contributory and did not reveal pre-existing disease.

DISCUSSION

The child was the only child of fit parents, aged about 30 years. Both parents had previously been given anaesthetics without incident and near relatives had normal anaesthetic histories. Permission to perform biochemical investigations on the family was not obtained.

The ward temperature was 19°C. The specimens of trimeprazine were analysed and found to be well preserved. The batch had been used extensively in other hospitals without report of any ill effects. Other contents of the ward drug cupboard were examined and found to be satisfactory and of accepted paediatric concentrations.

Administration of trimeprazine to dogs at dose levels of 1, 3 and 5 mg/kg is reported to be unassociated with any abnormal reactions (Britt, 1969).

Trimeprazine is widely used and is generally regarded as a relatively satisfactory drug for preanaesthetic medication in children. Pallor has been described as a complication, but serious side effects have not been reported.

The dose of atropine (0.3 mg) was equivalent to a dose of 1.5 mg in a 70-kg adult. The signs of pyrexia had begun before the atropine was given at 1 hour. It was considered nevertheless that this complication was attributable to trimeprazine rather than atropine.

ACKNOWLEDGEMENTS

I am grateful to Dr D. Wall for her permission to report this case and for her encouragement. I am grateful to Professor J. S. Robinson, Dr G. Hall-Davies, Mr Keith Roberts, and the staff of the Intensive Care Unit, Birmingham Children's Hospital, for their help with this case.

I am also indebted to Dr C. Day, Pharmacist, May & Baker Ltd, for his willing help in investigating the batch of trimeprazine.

REFERENCE


HYPERTHERMIE MALIGNE ENGENDREE PAR LA TRIMEPRAZINE

ZUSAMMENFASSUNG

Nach oraler Verabreichung einer zulässigen Dosis von Trimeprazine zur Prämédikation vor der Narkose kam es bei einem drei Jahre alten Kind zu einer fatalen malignen Hyperpyrexie-Reaktion.

HIPERPIREXIA MALIGNA CAUSADA POR TRIMEPRAZINA

RESUMEN

A la administración oral de una dosis aceptable de trimeprazina, para premedicación anestésica, siguió una hiperpirexia maligna y fatal en un niño de tres años.