Acute intracranial hypertension after nalidixic acid administration

Nalidixic acid (Negram) is an antimicrobial agent widely used in the treatment of urinary tract infection. Some years ago Boréus and Sundström (1967) reported intracranial hypertension in a 6-month-old boy treated with nalidixic acid at the manufacturer's recommended dose. Only a few cases have been reported since, mostly in children treated either with large doses (Fisher, 1967) or for prolonged periods of from 16 days to 6 weeks (Guran, Moriette, and Blanc, 1972; Anderson, Anderson, and Nashold, 1971). 2 babies were recently admitted with the diagnosis of acute intracranial hypertension, both having been treated with nalidixic acid for less than 24 hours.

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Case 1. A 6-month-old baby weighing 7.2 kg presented with recurrent urinary tract infections. At the age of 6 weeks a first infection was successfully treated with ampicillin and cephalothin. At 6 months of age a repeat episode of urinary tract infection was treated with nalidixic acid. The prescribed dose was 80 mg/kg per day (manufacturer's recommended dose: 60 mg/kg per day). Drug administration was started in the morning. 12 hours later the baby became markedly irritable and presented with vomiting and bulging of the fontanelle. At this time a total dose of 80 mg/kg nalidixic acid had been administered in 3 divided doses. On admission to hospital he was an afebrile, drowsy, hypotonic baby with marked bulging of the fontanelle. At lumbar puncture, the pressure was >200 mm H2O. CSF was clear, colourless, with normal protein and without cells. Lumbar puncture was followed by an immediate symptomatic improvement. Nalidixic acid was discontinued and within 24 hours the infant's condition was normal. Radioisotopic lumbar cisternography and air encephalography were normal.

Case 2. A 4-month-old boy weighing 7.1 kg presented with otitis media and was treated for 10 days with penicillin. Because of persisting fever, he was admitted to a country hospital and myringotomy was performed. Urinary tract infection was diagnosed and treatment with nalidixic acid was started. Less than 24 hours later, when the child had received a total dose of 85 mg/kg nalidixic acid, given in 4 divided doses, irritability and vomiting occurred. Soon after, bulging of the anterior fontanelle was observed. He was referred to us with a diagnosis of acute meningitis. On admission he was afebrile, pale, conscious, and inactive. There was marked bulging of the anterior fontanelle, without other neurological symptoms. Lumbar puncture showed a clear, colourless fluid, with no cells and normal proteins. Pressure was 220 mm H2O. After withdrawal of a few ml CSF, the anterior fontanelle was much softer.

Nalidixic acid was discontinued and 24 hours later the infant's recovery was complete. Urine culture grew Pseudomonas. Gentamicin 1 mg/kg was given for 10 days with good results.

Comment

In 2 infants acute intracranial hypertension occurred less than 24 hours after starting therapy with nalidixic acid; symptoms disappeared rapidly after discontinuing drug administration. In neither case was the dose greatly above the manufacturer's recommended dose of 60 mg/kg per day. Attention is called to the fact that intracranial hypertension can occur acutely, and in the absence of prolonged administration of nalidixic acid, or of significant overdosage.

Summary

Two infants treated with nalidixic acid for urinary tract infection presented with acute intracranial hypertension. Symptoms appeared during the first 24 hours of treatment when total doses of 80 and 85 mg/kg, respectively, of nalidixic acid were given. It is concluded that occurrence of intracranial hypertension can be acute, and does not require large doses or prolonged administration of the drug.

References


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A simple device for applying both CNP and CPAP in newborn infants suffering from respiratory distress syndrome

The expiratory grunt in newborns with the respiratory distress syndrome (RDS) is caused by expelling air against a partially closed glottis. This
Reflex mechanism enables positive alveolar pressure to be maintained at the end of expiration (Chu et al., 1967). Since the grunting mechanism lessens the chance of alveolar collapse and thus allows more time for gas exchange, the number and extent of intrapulmonary shunts will be decreased. To keep the alveoli constantly open in cases of RDS, it is essential to maintain continuously a positive transpulmonary pressure (TPP), i.e. the pressure difference between intrapleural and airway pressure. This leads to improved oxygenation and lessens the requirement for exposure of the lung to high O₂ concentrations. Moreover, early improvement of oxygenation may by itself prevent a further downhill course of the disease, and lessen the need for mechanical ventilation. There are two ways to increase TPP in the spontaneously breathing infant. (a) By increasing positive airway pressure. This is known as continuous positive airway pressure (CPAP) (Gregory et al., 1971). (b) By applying negative pressure around the thorax. This is known as continuous negative pressure (CNP) (Vidyasagar and Chernick, 1971). Both measures are equally effective, since the chest wall in the newborn is very compliant.

At the end of normal expiration, airway pressure falls to zero (i.e. the atmospheric level). The intrapleural pressure, resulting from the fact that the thoracic wall on account of its own elastic properties will not entirely follow the elastic recoil of the lungs, remains negative. Application of continuous positive pressure to the airway during the respiratory cycle will result in an increase in lung volume, while intrapleural pressure tends to become less negative or even positive, and thus TPP will increase. The other approach is to apply negative pressure around a compliant thorax which assists the expansive forces of the thoracic wall. In this case the intrapleural pressure becomes more negative and thus TPP increases. From the practical point of view, CNP has some advantages over CPAP. (a) Access to the newborn's head for cleaning and care (i.e. suction of oral and nasal secreta, scalp vein infusion, gastric feeding) is restricted in CPAP. (b) In CNP there is no need for intubation (Daily and Cave-Smith, 1971).

![Diagram of CNP method](http://adc.bmj.com/)

**Fig. 1.**—The unit used as a CNP method. a, Perspex cylinder; b, 'O' rings; c, plastic sleeves; d, Velcro bands; e, connecting tube to a vacuum pump; f, connecting tube to a water manometer.
A simple device for applying increased TPP in both ways (CNP and CPAP) has been developed at the Free University Hospital, Amsterdam. The unit consists of a Perspex cylinder, 18 cm in length and 20 cm in diameter, with both ends open. Thin plastic sleeves* are mounted on each open end and are fixed in place by 'O' rings. The infant is placed in the cylinder through the sleeves with its trunk as the only part inside the cylinder. The sleeves are tied around the infant's neck and pelvis with bands (Velcro fastener). CNP can be applied by connecting the unit to a suction or vacuum pump. The pressure is read by a water manometer, which at the same time functions as a safety valve. Additional oxygen can be administered through a box over the head. Nursing care can be given to the infant without difficulty and without interrupting the negative pressure around the infant's thorax. Umbilical catheters and the leads of monitoring equipment can be led through the sleeve at the pelvic region (Fig. 1). The whole unit is placed in an intensive care incubator.

If one wants to use the cylinder for CPAP, an airtight lid can be fitted to the opening at one end. On the other

Discussion

As compared with the iris diaphragm (Gregory et al., 1971; Vidyasagar and Chernick, 1971; Fanaroff et al., 1973; Bancalari, Gerhardt, and Monkus, 1973), the thin plastic sleeve has the following advantages. Since it is pliable it is not necessary to keep the infant with its neck and pelvis in the centre of the cylinder to avoid excessive pressure on the skin. An iris diaphragm fits well only on a cylindrical object like an infant's neck, but not on an oval one like a pelvis. Moreover, the CNP pressure applied tends to mould the soft thin sleeve to the contour of the neck, shoulders, and pelvis, whereas end a thin plastic sleeve is mounted and fixed to the cylinder by an 'O' ring. The infant's head is placed in the cylinder through the sleeve. The sleeve is tied around the infant's neck with a band. Continuous positive pressure can be applied by connecting the unit to a warm humidified gas inflow at the lid. The pressure, which is regulated by a screw clamp, is read by a water manometer. The manometer at the same time acts as a safety valve. Access to the infant's head is possible through the lid (Fig. 2).

Fig. 2.—The unit used as a CPAP method. a, Perspex cylinder; b, 'O' ring; c, plastic sleeve; d, Velcro band; e, screw clamp; f, connecting tube to a water manometer; g, lid; h, gas inflow; i, oxygen-sampling port.

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an iris diaphragm fails to do so. Thus, a better seal around the infant's neck and pelvis can be achieved by this method. If used for CPAP, less leakage occurs around the neck so that gas inflow can be reduced to 6–7 l./minute.

Summary

A new, simple device for applying both CNP and CPAP is described. The method offers a better seal around the infant's neck and pelvis than the classical iris diaphragm.

References


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A simple device for applying both CNP and CPAP in newborn infants suffering from respiratory distress syndrome.
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Arch Dis Child 1974 49: 743-746
doi: 10.1136/adc.49.9.743-a

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