Treatment of hypertensive emergency with nifedipine. *Japanese Journal of Pediatrics* (in Japanese) (in press).

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Sublingual nifedipine in acute severe hypertension

Sir,

We read with interest the recent article by Evans and associates in which sublingual nifedipine was shown to be safe and effective for the treatment of acute severe hypertension in children¹; this is consistent with previous studies. However, van Harten *et al*² and McAllister³ reported negligible sublingual absorption of nifedipine in adults, suggesting that significant nifedipine plasma concentrations are not achieved until the contents of the capsule reach the stomach and are then absorbed. They observed a higher peak nifedipine plasma concentration and a shorter time to reach peak concentrations when a patient bites the capsule to liberate its liquid contents, and then swallows, compared with when they squeeze the contents under the tongue.

Siegler and Brewer reported a mean of 57 minutes (range 15 to 90 minutes) for the time to achieve maximum decrease in blood pressure when nifedipine was administered orally to children while sublingual administration resulted in a mean time to maximum effect of 24 minutes (range 10 to 45 minutes).⁴ In this study, nifedipine was administered by the oral route in young patients for whom reliable sublingual administration could not be assured. Thus a possible explanation for the longer time to maximum effect observed in this study with the oral route may be due to pharmacokinetic differences between infants and children. It would be interesting to know the change in blood pressure observed at 15 minutes in the study by Evans and colleagues. This information could then be compared with the onset of action in adults who swallowed the contents of the capsules after biting them and to the onset in infants and children who swallowed the contents of the capsules.

In addition some patients do not tolerate the strong mint taste of the liquid contents of a nifedipine capsule; this can result in nausea and vomiting of the medication. Therefore, in these patients oral administration may be an appropriate alternative as time to peak nifedipine plasma concentrations after oral administration of the capsule in adults appears to occur within 30 minutes.³

The data presented by Evans and associates further supports the effectiveness of nifedipine for the purpose of rapidly lowering blood pressure; however, the sublingual route may not be the optimal route of administration in children who can swallow a capsule.

References

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Drs Evans, Shaw, and Brocklebank comment:

In our study in those subjects where we recorded values for fall in blood pressure at 15, 30, and 60 minutes after the administration of sublingual nifedipine the maximum fall in blood pressure was seen at 30 minutes.

The mean fall in mean arterial pressure at 15 minutes was 22 mm Hg and at 30 minutes was 32 mm Hg (this excludes values on two non-responders). These results are consistent with the rapid onset of action reported by Siegler and Brewer. However, we fear they do not further our knowledge as to the route of absorption. It may well be that the oral route is preferable (particularly in infants) not because of better absorption but because it produces a slower fall in blood pressure.

Heparin and suspected Sanfillipo syndrome

Sir,

Initial screening of urine from a child with undiagnosed severe learning difficulties suggested a diagnosis of Sanfillipo syndrome. One dimensional electrophoretic separation of mucopolysaccharides¹ from this child's urine showed a large band migrating in the heparan sulphate region (figure). The child had no other features of Sanfillipo syndrome and further urine samples from the same child were normal. Examination of other children, however, from the same school resulted in the fortuitous identification of Sanfillipo A in a previously undiagnosed child.

It seemed unlikely that the original specimen had been collected from the wrong child. It was suggested that the urine sample could have been inadvertently collected into a cytogenetics sample tube. Blood samples for cytogenetic analysis are collected into heparinised 25 ml universal tubes that are otherwise identical to the tubes used by chemical pathology laboratories for urine samples. Repeated analysis of normal urine samples collected into cytogenetics tubes confirmed that the abnormal band originally identified as heparan sulphate was, in fact, heparin.

Figure One dimensional electrophoretic separation of mucopolysaccharides stained with alcian blue. Lane 1: standards: CS, chondroitin sulphate; DS, dermatan sulphate; HS, heparan sulphate. Lane 2: urine collected into cytogenetics bottle; lane 3: urine from a child with Sanfillipo syndrome; and lane 4: urine from a normal child.

The diagnosis of Sanfillipo syndrome should always be confirmed by white cell enzyme analysis. Heparin contamination is a previously unreported cause of abnormal urine mucopolysaccharide electrophoresis.

Reference

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Duration of protection against tuberculosis conferred by BCG vaccination in infancy

Sir,

Recent studies confirm that BCG vaccination in the newborn and in infants confers valuable protection against tuberculosis.¹ However, little is known about the duration of protection provided by BCG vaccination. It is often implied that tuberculin skin sensitivity induced by BCG

Table Decreasing effect of BCG with time after vaccination

Age band (years)	No of cases	Protective efficacy of vaccination (%)	95% Confidence interval (%)
0-3	36	77	53 to 89
4-6	36	60	7 to 83
7-9	21	49	-41 to 82
10-12	15	27	-193 to 92

vaccination equates with immunity provided by BCG, and that sequential tuberculin skin testing therefore gives information about the duration of protection provided by BCG.² Nevertheless, there is contrary evidence which suggests that the level of immunity provided by BCG is unrelated to the degree of tuberculin skin sensitivity.³

In order to study the duration of protection provided by BCG we reanalysed the data from a recently published study looking at the effectiveness of BCG given to infant Asian children.⁴ In brief, this showed that 57% (62/108) of Asian children who developed tuberculosis had received vaccination, compared with 78% (336/432) of a group of age and sex matched controls who did not develop tuberculosis. The overall protective efficacy of BCG vaccination was 64% (95% confidence interval: 43% to 77%).

The further analysis we undertook consisted of subdividing the cases and controls into four age bands determined by the age at which the cases developed tuberculosis. The proportion of patients and controls within each age band who had received BCG was then ascertained, and the percent efficacy of BCG vaccination calculated as described previously.⁴ The table shows the results.

The numbers of cases and controls within each age band were relatively small compared with the overall analysis therefore the 95% confidence interval for each estimate of protective efficacy is wide, and the results must be interpreted with caution. However, the figures for protective efficacy suggest that BCG vaccination in infancy may confer useful protection against tuberculosis for at least nine years after vaccination. More importantly, the maximum protection is provided during the first three years after vaccination—the time when children are at greatest risk from disseminated tuberculosis.

We suggest that the above data reinforce the view expressed in our original publication that BCG vaccination in infant Asians is a valuable protective measure against tuberculosis.

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