Gastro-oesophageal reflux in near-miss sudden infant death syndrome or suspected recurrent aspiration

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SUMMARY We have compared barium swallow with a radionuclide gastro-oesophageal scintigraphy (milk scan) method of detecting gastro-oesophageal reflux in 26 infants. In 17 cases, presenting as near miss sudden infant death syndrome, reflux was detected in 2 by barium swallow and in 8 by scintigraphy. In the remaining 9 infants with suspected pulmonary aspiration, reflux was demonstrated by barium swallow in 2 and by scintigraphy in four. Aspiration after gastro-oesophageal reflux was demonstrated only by the radionuclide scan. The feasibility of recording physiological variables during periods of reflux was confirmed.

Gastro-oesophageal reflux in infancy may cause oesophagitis with bleeding or stricture formation, recurrent vomiting with failure to thrive, and acute aspiration pneumonia. The accepted method for detecting gastro-oesophageal reflux is the barium swallow with delayed imaging which may detect up to 85% of cases. One limitation of any radiological technique is restriction of exposure time which increases the likelihood of missing delayed or intermittent reflux. Recent interest has concentrated on the possible role of reflux in recurrent aspiration pneumonia in childhood presenting with symptoms of cough and wheeze, and in precipitating prolonged apnoea in the near miss sudden infant death syndrome (SIDS). Both problems require prolonged study, preferably with simultaneous monitoring of physiological variables. We have applied the technique of radioisotope gastro-oesophageal scintigraphy to the investigation of infants with suspected recurrent aspiration pneumonia and of infants who presented as near miss SIDS with suspected apnoea during sleep. We tried to answer two questions. Firstly, is it possible using this technique to detect reflux or aspiration over a prolonged period, preferably during sleep and without the introduction of a foreign body into the oesophagus? Secondly, can the respiratory consequences of reflux or aspiration be studied simultaneously?

Method

Patients. Twenty-six infants, 16 boys and 10 girls, were studied. Their ages ranged from 38 weeks post-conception to 13 months post-delivery. No infant had a history of recurrent vomiting. They could be divided into three groups by clinical presentation.

Group 1. Near miss sudden infant death syndrome
These 17 infants, of mean age 10 weeks with a range of 4–16 weeks, presented with a history that suggested near miss SIDS. Each had been found limp, pale or cyanosed, apnoeic or with apparently abnormal breathing (gasping or almost undetectable breathing efforts), and required resuscitative intervention before returning to clinical normality. In 14 the episode occurred while the baby was thought to have been sleeping and in 2 infants more than one similar episode were described. Three infants were subsequent siblings of SIDS cases but had presented on this occasion as near miss SIDS. These 17 infants had by definition been healthy before their near miss episode and presented with histories of no symptoms or of minor coryza or poor feeding in the 24 hours before presentation.

Initial investigation excluded as far as possible recognised causes for sudden collapse including viral and bacterial infection, hypoglycaemia, seizures, electrolyte imbalance, dehydration, cardiac arrhythmia, and head injury. In addition each of these infants had polygraphic respiratory monitoring on two occasions during investigation.

Group 2. Suspected aspiration between feeds
This group comprised 7 infants ranging in age from 3 weeks to 13 months. Their medical histories were varied and relevant details are shown in the Table.
The radionuclide milk scan was performed because recurrent aspiration was suspected clinically and radiologically.

**Group 3. Suspected aspiration during feeds**

Two infants were studied to exclude reflux as an additional problem in the presence of suspected oesophageal incoordination on swallowing.

**Procedure.** Each infant had a barium swallow and screening with delayed film, performed by one experienced paediatric radiologist. Reflux was graded as described by McCauley et al.\(^3\) The scan was performed over 2 to 4 hours immediately after a feed. The infant was fed his usual volume of milk formula (or expressed breast milk) with \(5.5 \times 10^5\) Bq (150 \(\mu\)Ci) technetium-99m sulphur colloid added. For the first 20 studies we added tracer to the total feed but in one infant (Case 23) failure to complete the feed resulted in low counts. Thereafter we added the tracer to the first 60 ml and completed the feed with unlabelled formula. The baby was then burped and settled for sleep.

Small infants slept on the Gamma camera and larger infants on a trolley with the camera overhead. Sedation or restrictive restraint was avoided. A high sensitivity parallel-hole collimator was used with the camera calibrated for the 140 keV photopeak of \(^{99m}\)Tc using a 15% window. This dose of isotope allowed reliable visualisation and was adequate in all infants regardless of weight or the volume of feed ingested.

Scanning began when the infant was quiet and settled, generally 10–15 minutes after completion of the feed. The stomach and thorax were observed continuously on the monitor oscilloscope and counts accumulated on computer over 30 seconds at 60-second intervals throughout. If reflux was observed the event was recorded as a 60-second cumulative print on polaroid film, noting the time and position. The infant's position was changed by 90° (from supine to lateral to prone) at 15–30 minute intervals. We did not attempt to induce reflux by application of external abdominal pressure. A 'dummy' was offered if the baby was accustomed to one and restless without it.

If counts persisted in the nasopharynx after reflux, a chaser swallow of liquid was given to clear the pharynx. In two infants (Cases 18 and 21) with suspected aspiration, late follow-up screening was repeated 6 hours after the feed to observe the lung fields for late aspiration.

**Dosimetry.** The isotope was \(^{99m}\)Tc sulphur colloid prepared by the Department of Medical Physics, Royal Infirmary of Edinburgh. The calculated dose for this study is maximally:

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Table **Results**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (weeks)</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>26</td>
<td>Reflux</td>
<td>Aspiration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Barium</td>
<td>GS</td>
</tr>
<tr>
<td>19</td>
<td>26</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>20</td>
<td>54</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>21</td>
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<tr>
<td>22</td>
<td>3</td>
<td>Negative</td>
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<tr>
<td>23</td>
<td>12</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>24</td>
<td>8</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

**IPPV = intermittent positive pressure ventilation, BPD = bronchopulmonary dysplasia, TOF = tracheo-oesophageal fistula, GS = gastrointestinal scintigram.**

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Whole body $4.8 \times 10^{-6}$ Ckg$^{-1}$
Bowel $19.35 \times 10^{-6}$ Ckg$^{-1}$
Thyroid Negligible

These doses compare favourably with the exposure in a routine barium fluoroscopy and are lower than the dose in a radioisotope liver scan.

The gastro-oesophageal scintigram was combined with respiratory monitoring and documentation of sleep stage in group 1 infants. Respiratory movement was detected by an adapted respiratory monitor sensor (Grasby Dynamics MR10) attached to the abdominal wall skin. Airflow through nostrils and mouth was detected by sensitive thermocouples. These respiratory variables were continuously recorded on paper (Mingograph 81 recorders). Apnoea was defined as central if respiratory movements and airflow were absent for longer than 6 seconds. Obstructive apnoea was recorded if airflow was absent but respiratory movements continued or increased in the absence of gross body movement during sleep.7 Sleep stage was assessed behaviourally8 and was noted on the recording together with the occurrence of any reflux9 or aspiration, its timing, and the infant's position. Because of the limitations of the behavioural criteria only definite active sleep and quiet sleep were categorised as such, with other stages combined as indeterminate sleep.

Results

The results for group 1 are shown below (groups 2 and 3 are summarised in the Table) with relevant clinical comments. In Group 1 the use of gastro-oesophageal scintigraphy increased the detection rate of reflux compared with barium studies. In addition, the practicality of recording respiration simultaneously during 'scans' was confirmed. In group 2 infants in whom aspiration between feeds was suspected, this was identified more frequently by the milk scan than by barium.

Twenty-five of the 27 infants slept throughout the scan whereas all were awake during barium oesophagography. The changes of position seldom roused the infant. Each infant in our study spent 30–45 minutes in each of the four positions; supine, prone, left and right lateral. Reflux was most often seen when the infant was in the left lateral position but was occasionally observed in all positions. We did not attempt to scan in the semi-upright position used in treatment of reflux. Neither the occurrence of spontaneous movement nor sucking a 'dummy' led to reflux. In most infants the reflux cleared spontaneously within 5–10 minutes, but a chaser swallow was needed for one near miss SIDS infant (Case 8) to clear the nasopharynx. The timing of reflux varied between 15 minutes and longer than 2 hours after the feed, stressing the need for prolonged continuous observation.

In group 1 gastro-oesophageal reflux was identified by barium swallow in two cases, one (Case 7) a sibling of SIDS aged 6 weeks, the other (Case 4) an infant born at 34 weeks' gestation aged 4 weeks at presentation. Using the radionuclide gastro-oesophageal scintigram 8 infants were shown to have reflux including the 2 with positive barium swallows and an infant aged 8 weeks who had been delivered at 30 weeks' gestation but had no significant neonatal problems. No aspiration was seen in any infant presenting as near miss SIDS. One near miss SIDS infant who remained awake during the radionuclide scan had a negative scan and went on to develop bronchiolitis (Case 8). In group 2 infants (Cases 18, 19, 21) who had had oesophageal atresia with distal tracheo-oesophageal fistula repaired, persistent counts were seen after reflux at the level of the mid oesophagus.

In several infants the 'possetting' of a mouthful of milk or fluid occurred during the scan. This small quantity did not appear as oesophageal counts but in two cases there was subsequent evidence of tracer in the nasopharynx. These events have not been interpreted as reflux. In no infant was the reflux visualised on screen accompanied by overt vomiting.

Respiratory monitoring (group 1 cases only) was readily applicable to the milk scan. We limited our recording of respiratory movements and upper airway airflow to minimise disturbance of the infant. This monitoring revealed associated prolonged mixed central/obstructive apnoea during active

*Details of individual patients are available on request from authors. Address as for reprints.
sleep in only one (Case 4) (Figure). The apnoea lasted 16 seconds and the infant recovered spontaneously. In 2 other infants (Cases 6 and 7) reflux occurred during periods of periodic breathing with long inter-period pauses of 5–10 seconds, during quiet sleep. These were the only respiratory abnormalities observed during the total near miss SIDS scan time of about 45 hours.

All infants with gastro-oesophageal reflux were treated with thickened feeds (0·2% Carobel) and 24-hour semi-upright positioning. Only two repeat scans were performed during treatment and in neither was reflux demonstrated.

Discussion

Prolonged monitoring of intraoesophageal pH has provided the only extended observations on reflux in infants to date. Both distal and proximal placements of pH probes have shown that the fall in pH is of longer duration and at longer intervals after feeds in symptomatic infants (known by other methods to have reflux) than in asymptomatic infants thought to be normal. Jolley reports infants who developed wheeziness in association with a decline in intraoesophageal pH, while Herbst et al. recorded central apnoea with cyanosis in 5 infants during pH troughs. These findings led to the suggestion that apnoea induced by reflux might explain the clinical presentation—near miss SIDS.

Because of a possible association of sleep apnoea and SIDS, Jeffery et al. studied intraoesophageal pH during polygraphic recording of sleep stage and respiration in siblings of SIDS or infants presenting as near miss SIDS. They found acid reflux in active sleep and postulated that this results from sphincter relaxation in active sleep such as occurs in adults. Although they did not report the respiratory events associated with reflux in active sleep, they suggested that prolonged apnoea in active sleep secondary to gastro-oesophageal reflux may be a cause of SIDS. In contrast, Walsh et al. found no difference between reflux and non-reflux periods with respect to apnoea of 3 seconds or more. We have not regarded such pauses as abnormal.

Although the pH probe evidence linking reflux with apnoea suggests cause and effect, reservations must be made. pH electrode studies introduce a foreign body into the nasopharynx. Awake adult studies suggest that the presence of a tube assembly in the oesophagus does not alter the occurrence of reflux but comparable studies have not been reported in sleeping infants. The possible effect of the pH probe on oesophageal dynamics and the work of breathing is therefore unknown. Further, pH probe studies detect only acid reflux generally to pH 4 or less. Gastric acidity in young infants is less than in older children, and may be partially neutralised by milk feeds so that reflux after feeds may not be acidic. Gastric acid output is also lower in quiet than inactive sleep. The findings of Jeffery may therefore be more directly related to sleep state characteristics than to the occurrence of reflux. The use of the gastro-oesophageal scintigram avoids these potential difficulties.

Cardiac dysrhythmias have been reported in animals in association with introduction of acid into the lower oesophagus. Their possible role in the pathogenesis of SIDS has been extensively studied although the aetiology is unclear. Preterm infants after the newborn period, in whom the risk of SIDS is increased, show ‘silent arrhythmias’ with and without apnoea on long-term screening. Such infants may have episodes of apnoea for which theophylline is prescribed. This use of theophylline in late onset apnoea has not been extensively validated. Our findings indicate that a thorough search for gastro-oesophageal reflux should be made in any such infant before using a drug known to relax the gastro-oesophageal sphincter thereby potentially contributing to reflux and recurrent aspiration.

Reports of the effect of position on reflux have concentrated on prone or supine and semi-upright, the last as a form of therapy. It is relevant to consider lateral positioning as this is frequently recommended to a mother as the optimal sleep position for the young infant. Our work suggests that this advice may warrant reassessment if gastro-oesophageal reflux is accepted as a potential hazard in infancy.

Questions about the significance of reflux and of possetting which we elected to ignore, as do most radiologists, may be answered with further comparative long-term studies of normal infants and suspected reflux subjects. Meantime we suggest that any infant diagnosed as near miss SIDS or with unexplained apnoea warrants extensive search for reflux, and this study supports the use of the gastro-oesophageal scintigram for this purpose. The scintigram is also useful in the investigation of infants suspected to have recurrent broncho-pulmonary aspiration during reflux. In particular infants who have undergone tracheo-oesophageal fistula repair and have required prolonged intermittent positive pressure ventilation may present with recurrent respiratory symptoms. Such infants have been shown to have a high incidence of gastro-oesophageal reflux. The milk scan allows the identification of pulmonary aspiration as a contributor to respiratory difficulties which may be...
more amenable to intervention than the after effects of ventilation. Our study suggested that the known oesophageal dysmotility after tracheoesophageal fistula repair may predispose to persistence of refluxed material in the oesophagus.

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References


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