

Impact of sleep and movement on gastro-oesophageal reflux in healthy, newborn infants

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Abstract

Seventy four normal, healthy newborn babies were studied to examine the relationship between gastro-oesophageal reflux, sleep state, and movement. Multichannel pen recordings were made to determine sleep state, movement, breathing, and reflux. The mean number of reflux episodes per hour was highest in wakefulness, followed by active and indeterminate sleep. In quiet sleep reflux rarely occurred. The mean duration of reflux episodes per hour was longest in active sleep followed by wakefulness, indeterminate and quiet sleep. There was a strong positive correlation between duration of reflux and movement time for wakefulness, active and indeterminate sleep. Movement preceded 88% of all reflux episodes.

Physiological reflux occurs in most newborn infants but is clinically inapparent. The results suggest that state and movement are related to the incidence and duration of reflux. Sleep state is therefore an important variable in determining normal values for reflux in infancy since developmentally the amount of sleep time lessens but quiet sleep proportionally increases.

Gastro-oesophageal reflux is a well known clinical problem in both term and preterm infants. Despite this, there is relatively little information about physiological reflux in the sleeping neonate.

Some information is available for control infants, but this is often deficient in important variables, such as adequate numbers of infants studied at a particular age and the selection criteria. This grouping of data over a wide age range in infancy may ignore developmental changes, while selection of infants from a neonatal special care nursery rather than a healthy, asymptomatic population, may introduce confounding variables to the analysis. The position of both the infant and the pH probe, and the type of milk, are additional variables for which methodological details are frequently incomplete.

Only two studies have examined a large number of neonates. Vandenplas and Sacre-Smits described normal values for reflux from 24 hour pH recording in 92 bottle fed neonates, aged 5-15 days. However, the method of selection and prior health of these infants were not stated.¹ Gouyon *et al* selected 46 control infants from a neonatal unit, 50% of whom were preterm. They were studied at a postnatal age of 2-21 weeks.² The possible impact of develop-

mental changes, however, were not taken into account.

Another variable that has not been adequately explored is sleep state. As young infants spend the major part of the day asleep, this is potentially relevant. Previous studies of sudden infant death, and of those who have had a 'near miss' have suggested that the state of wakefulness or sleep may be important in determining the number of reflux episodes.³⁻⁵

An additional measure that may highlight different underlying mechanisms for reflux is whether or not movement precedes reflux. In older infants, defined as symptomatic controls (with symptoms thought to be related to reflux but with a pH <4.0 for <6% of total monitored time), movement frequently preceded reflux events during sleep (85%). In subjects with pathological reflux (a pH of <4.0 for >6% of total monitored time), movement preceded reflux in only 36% of the events.⁶ While Sondheimer did not describe the mechanisms for these reflux events, others have noted that most asymptomatic reflux in healthy infants is synchronous with swallowing and associated with reflex opening of the lower oesophageal sphincter, which is usually prolonged. By contrast, symptomatic reflux, especially if associated with oesophagitis, is asynchronous with swallowing and usually due to transient relaxation of the lower oesophageal sphincter.^{7,8}

To examine the possible influence of sleep and movement on reflux, variables known to influence the incidence of gastro-oesophageal reflux were controlled. Subjects were then randomly selected from a normal, healthy population of newborn term infants. The aim of the study specifically was to examine the relationship between wakefulness, sleep state, and physiological reflux. The relationship between movement and both the onset and the duration of reflux was also explored.

Methods

SUBJECTS AND SELECTION

Seventy four healthy term infants from the public maternity ward at King George V Hospital were studied between June 1989 and June 1990. The ethics committee of King George V Hospital approved the experimental protocol.

During this 12 month period, 1988 babies were born to mothers in the public ward of the hospital. Estimates from a one month sample period suggested that a total of 454 (23%) babies met the entry criteria, but only 200 infants could be studied (one per day) in the available

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time. Permission was sought from 104 mothers of whom 13 refused. Verbal informed consent was obtained from 91 randomly selected mothers. However, 17 of these studies were unsuccessful due to either limited sleeping or technical difficulties.

Entry criteria required that the infants were: born to English speaking mothers who had no complications of pregnancy, such as drug and alcohol abuse, hypertensive disease of pregnancy and diabetes; at a gestational age of 37–42 weeks; size appropriate for gestational age; not asphyxiated at birth; not treated for jaundice; aged 2–8 days if formula fed and 3–8 days if breast fed, to ensure a milk supply.

Of the 74 babies in the final sample, 38 were girls and 36 boys. There were 37 breast and 37 formula fed babies, each being fed until satisfied. Fifteen infants received S-26 formula (Wyeth) and 22 infants Nan formula (Nestlé). The feeds ranged in volume from 15 to 115 ml, the mean (SD) were 57 (23) ml.

POLYGRAPHIC RECORDING OF SLEEP STATE

Multichannel pen recordings were made while the infants were lying supine, in a quiet, warm room for four hours after their morning milk feeds. To determine sleep state, electrodes for recording an electroencephalogram (EEG), electrooculogram (EOG), and submental electromyogram (EMG) were used (EOG and EMG electrodes were only used for the first 20 infants). In the subsequent 54 cases, EOG and EMG electrodes were replaced by piezoelectric transducers, one being positioned on the upper eyelid and one on the laryngeal prominence. As a movement detector, the piezoelectric transducer produced a better signal to noise ratio.

Breathing was recorded by abdominal pneumogram and by nasal flow of end tidal carbon dioxide. The breathing pattern was used to assist in defining sleep state.

MEASUREMENT OF GASTRO-OESOPHAGEAL REFLUX

A pH microelectrode (M1508, Microelectrode Inc, 1.2 mm outer diameter) was introduced nasally in all but two infants, when it was placed orally. It was positioned 6 cm above the lower oesophageal sphincter, according to Strobel's formula, which relates body length to oesophageal length.⁹ A reference electrode (B140249, Beckman Instruments Inc, used on 54 babies and MI402, Microelectrode Inc, used on 20 babies) was attached securely to the infant's leg. The electrodes were connected to a pH meter (Activon, Model 209) through a patient isolation unit and the pH recorded at a paper speed of 100 mm/minute. At the beginning and end of each study, the pH recording system was calibrated in buffers of pH 4 and 7. Recordings were excluded if a calibration drift of 0.3 units occurred after the test. Gastro-oesophageal reflux was defined as a decrease in pH by at least one unit to pH less than 4 for 15 seconds or longer.

ANALYSIS OF RECORDINGS

EEG, EMG, EOG, breathing and oesophageal

pH were recorded continuously on an eight channel pen recorder (Model 78D, Grass Instruments Co). Behavioural observations regarding sleep/wake state and body movement were also recorded continuously on the polygraph paper.

The record was divided into successive epochs of three minutes each by one observer using the method described by Anders *et al.*¹⁰ This defined the sleep state and occurrence of arousal. States were scored as either awake, active, quiet, or indeterminate sleep. If a state occurred for more than half of the three minute epoch, it was considered that this particular state was present.

ANALYSIS OF GASTRO-OESOPHAGEAL REFLUX

The third and fourth postprandial hours were chosen for analysis. This allowed time for the stomach contents to become acidic so that acid reflux could be detected by the pH probe. In addition, differences in milk volume were unlikely to have an effect on reflux frequency more than two hours after feeding.¹¹ To confirm this, the volume of bottle milk feeds was measured and related to both the number and duration of reflux episodes.

A minimum of 90 minutes' recording time was required for analysis. If no reflux was recorded at the end of a study, a gastric pH of <4 was confirmed by advancing the pH electrode beyond the calculated oesophageal length.

The recording was analysed in each state for the following: (1) number of reflux episodes; (2) duration of reflux episodes; (3) number of reflux episodes lasting more than five minutes; and (4) movement time preceding and during each reflux episode. Movement was defined by deflection of the submental EMG or piezoelectrode positioned over the larynx. This detected not only swallowing and sucking but also gross body movements which were also confirmed by interference on other analogue signals. Behavioural observations were also scored on the polygraph paper.

STATISTICAL ANALYSIS

The mean and 95% confidence intervals were generated for all reflux parameters in each state. Regression analysis was performed on duration of movement versus duration of reflux. Correlation coefficients were determined for each sleep state.

Results

SUBJECTS

The mean (SD) for gestational age, birth weight, and postnatal age of the 74 infants studied were 39 (1) weeks, 3436 (472) g, and 4 (1) days respectively.

POLYGRAPHIC SLEEP RECORDING

Figure 1 shows typical recordings for quiet sleep and active sleep. The amount of time spent in each state varied considerably. Over the total study period 12% of time was spent in

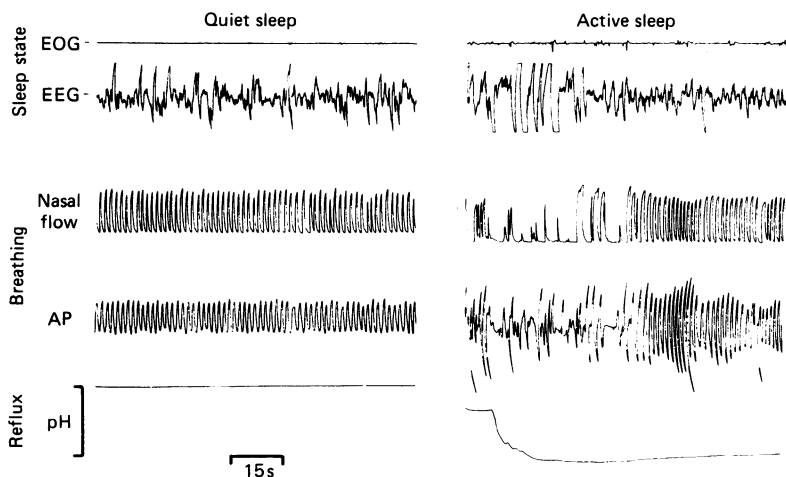


Figure 1 Typical polygraphic trace in quiet and active sleep showing a stable pH usually between 5 and 7, during quiet sleep. A reflux episode is shown in active sleep with a sudden decrease in pH, accompanied by transient body movement, reflected by the movement artifact on the EEG trace. AP, abdominal pneumogram.

wakefulness, 53% in active sleep, 14% in indeterminate sleep, and 21% in quiet sleep.

GASTRO-OESOPHAGEAL REFLUX

A total of 227 episodes of reflux were recorded by the pH meter in the 74 infants. Only 13 of these episodes were clinically apparent.

Fifty six of the 74 infants studied (76%) demonstrated at least one reflux episode during the third and fourth postprandial hours: 52 (70%) had one or more reflux episodes in the active sleep state, 11 (15%) demonstrated reflux in indeterminate sleep, while three babies (4%) had a total of five episodes in quiet sleep.

The mean number of reflux episodes per hour was highest in wakefulness, followed by active sleep, and then indeterminate sleep. Reflux was a rare occurrence in quiet sleep (table). Although more reflux episodes per hour occurred in wakefulness, reflux was most prolonged during active sleep, followed by wakefulness, indeterminate and quiet sleep. The same trend was observed for the mean number of reflux episodes lasting five minutes or more per hour (table).

In all states there was a positive correlation between the duration of reflux and the duration of movement. Figure 2 shows the regression line for duration of reflux versus duration of movement for active sleep. The correlation coefficients were 0.88, 0.84, 0.86, and for wakefulness, active sleep, and indeterminate sleep respectively. Movement preceded 88% of all reflux episodes.

The volume of the milk feed was unrelated to either the number or duration of reflux episodes

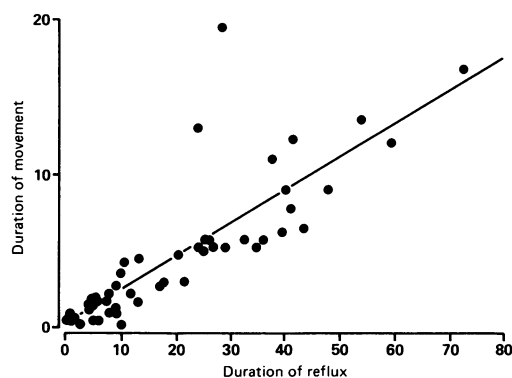


Figure 2 Regression line for duration of reflux (minutes) versus the duration of movement time (minutes) in active sleep. The correlation coefficient is 0.84.

during the third and fourth postprandial hours. The amount of milk consumed/kg of body weight/day (ml/kg/day) was calculated for the 37 infants who were fed formula milk. Correlation coefficients for milk consumed versus episodes and duration of gastro-oesophageal reflux were not significant, being 0.16 and 0.18 respectively.

Discussion

This study provides new information on the frequency and duration of reflux during sleep and wakefulness in healthy newborn infants at term, after normal pregnancies. These data confirm a relationship between gastro-oesophageal reflux, sleep state, and movement.

During sleep, both the occurrence and duration of reflux was most frequent in the active sleep state: 70% of babies demonstrated reflux in this sleep state. By contrast, reflux in quiet sleep was very uncommon. The pH trace in quiet sleep was characteristically stable and usually between pH 5 and 7.

This difference in state related reflux events has been observed for other physiological variables such as respiratory reflexes in the newborn. For example, the ventilatory response to hypoxaemia,¹² the inhibition of intercostal muscles leading to paradoxical movement of the rib cage,¹³ and the laryngeal response to stimulation in the adult dog,¹⁴ differ greatly depending on the state of active or quiet sleep. It has been proposed that different neural pathways operate in the various sleep states.¹⁵

Some indirect evidence supports this concept with regard to reflux. Primary peristalsis, which is initiated by swallowing, and increased gastric pressure secondary to movement are two common mechanisms associated with reflux in healthy infants.⁸ In this study movement commonly preceded reflux (88%) in the awake state

Results as mean (95% confidence intervals) for gastro-oesophageal reflux episodes in all states of sleep and wakefulness

	Wakefulness	Active sleep	Indeterminate sleep	Quiet sleep
State time (min/hour)	7:00 (5:34 to 8:66)	32:00 (30:00 to 34:00)	8:50 (7:43 to 9:57)	12:50 (10:97 to 14:03)
Episodes/hour	2.65 (1.56 to 3.74)	1.87 (1.45 to 2.29)	0.77 (0.17 to 1.37)	0.22 (-0.03 to 0.47)
Duration (min/hour)	8:40 (5:20 to 11:60)	12:10 (9:04 to 15:16)	7:55 (4:18 to 10:92)	5:25 (2:13 to 8:37)
No of episodes >5 min/hour	0.54 (0.16 to 0.92)	0.90 (0.63 to 1.17)	0.37 (0.11 to 0.63)	0.30 (0.07 to 0.50)

and during active and indeterminate sleep. Although swallowing was not recorded, swallowing,¹⁶ peristaltic activity,¹⁷ and movement are uncommon in quiet sleep as opposed to active sleep. The rare occurrence of reflux in quiet sleep is consistent with these observations. It may suggest that neural pathways that underlie programmed swallowing do not operate in quiet sleep.

In infancy, increasing time is spent in quiet sleep with advancing age, the average being 24% in the first week, 44% at 3 months, and 50% at 6 months.¹⁸ The values for active sleep are 58%, 42%, and 34% respectively. Physiological reflux in sleep is therefore likely to be less frequent with increasing age during infancy. The striking difference in state related reflux in this study suggests that the total duration of active sleep during pH monitoring is an important variable in calculating the frequency and duration of reflux in infants.

The extent to which reflux occurs and is unrecognised in the newborn was reflected in the few clinically evident refluxes. Thirteen of the 227 refluxes were clinically apparent as milk in the mouth or nares. Thus conclusions as to possible effects of reflux on heart rate, breathing, and aspiration are valid only with continuous pH monitoring. The difficulty in interpreting any effect of reflux on these events, however, is complicated by the observation that movement and reflux are closely related. Movement itself frequently interferes with the usual analogue recordings of heart rate and breathing. This observation, that body movement is correlated with the duration of reflux, has not been previously published. However, both Ariagno *et al* and Paton *et al* have observed that reflux is frequently preceded by movement in older infants presenting with either acute life threatening episodes or significant reflux.^{19 20} The reason as to why the duration of body movement is correlated with the duration of reflux in all states is unclear. Other physiological recordings of EEG, EOG, and EMG did not suggest this represented arousal when the infant was in active sleep. Whether body movement represents a stimulus or a response to reflux might be aided by oesophageal manometry.

An attempt was made to control the known variables which influence both the rate and duration of reflux. The results indicate a wide intersubject variance of reflux in healthy, newborn infants. Recent studies in healthy adults,²¹ and adults and children,²² with symptomatic reflux also indicate a large intrasubject variance with 24 hour pH recordings.

In conclusion, these data indicate that physiological gastro-oesophageal reflux is a common but not usually evident event in both wakeful-

ness and sleep in healthy, newborn infants. Both the occurrence and duration of reflux appears to be related to sleep state and movement.

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