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The Effect of Breast Feeding on Plasma Cholecystokinin in Neonates

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Objectives: Prospective study was conducted to evaluate the effect of breast feeding on cholecystokinin in neonates.

Settings: This study was conducted in King Abdul-Aziz University Hospital.

Method: Plasma concentration of cholecystokinin (CCK) was estimated in 41 neonates (19 boys, 22 girls). The study was done in the neonates on the third day after delivery. Serum CCK was estimated by radioimmunoassay.

Results: It was found that CCK rises immediately after breast feeding and declines 10 minutes later.

Conclusion: CCK rises immediately after breast feeding.

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Cholecystokinin (CCK), a gastrointestinal hormone, is secreted by the duodenum in response to the presence of gastric acid, amino acids and nutrients in particular fat in the duodenal lumen (1). The half life of this hormone is about 2.5 minutes and the kidney is considered the major site of its uptake from the systemic circulation[1]. Cholecystokinin is responsible for stimulating gallbladder contraction and pancreatic secretion[2]. Gallbladder function is under the control of various neural and hormonal actions[3]. In dogs, truncal vagotomy reduces the sensitivity of the gallbladder to CCK[3]. However, truncal vagotomy may not alter the rate of gallbladder emptying[3]. In man, the post contraction volume of the gallbladder is greater after complete vagotomy, suggesting a parasympathetic role in emptying[4]. Vagal stimulation may also regulate the response of gallbladder to CCK[7].

Various hormones and peptides have action on the gallbladder. These include cholecytokinin, gastrin 17, secretin, substance P, and pancreatic polypeptides[5]. Gastrin 17 causes gallbladder muscle contraction in some species but not in man[5]. Secretin potentiates the action of CCK on the gallbladder[5]. Substance P directly stimulates gallbaldder contraction in both dogs and rabbit[6]. Pancreatic polypeptides cause relaxation of the gallbladder and decreased intraluminal pressure, which encourages refilling after contraction[6]. However, the most important gastrointestinal

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hormone in the control of gallbladder contraction is CCK[6]. The gallbladder by contracting plays a role in the negative feedback suppression of CCK release by the upper intestine[7]. In 1987, Linden et al estimated the plasma concentration of CCK in response to feeding and during pregnancy in dogs[8]. In 1989, Linden et al estimated the plasma concentration of CCK in male rats in response to food intake[9]. In 1990, Linden et al estimated CCK in lactating female rats in response to suckling[10]. The aim of this study is to estimate CCK level in the neonatal period and to evaluate the effect of breast feeding on cholecystokinin release.

METHOD

Estimation of plasma CCK was done in forty one neonates. The blood samples were collected on the third day after delivery. All the neonates were full term and were delivered by spontaneous vaginal delivery with good Apgar scores. There was good antenatal care for their mothers during pregnancy. The neonates enrolled in this study were in good condition and were not suffering from any problem which could be observed in the nursery (eg. respiratory distress syndrome, hypoglycemia, birth injuries hypocalcemia, diarrhoea or vomiting). Informed consent was taken from the parents. The birth weight of the neonates in this study ranges between 3.153 to 3.650 Kg with an average weight of 3.395 Kg. Blood was collected before feeding, immediately after breast feeding, 10 minutes and 30 minutes after feeding. High pressure liquid chromatography was used in order to separate CCK from gastrin. The samples taken from the noenates were added to a mixture of 50% distilled water and 50% of 0.1% trifluoroacetic acid. High pressure liquid chromatography was applied by injecting each of the above samples into a TSK-T column (4.6 × 250 mm, with 5 mm particle size) using an isocratic system using 34% acetonitrite in 1% trifluoroacetic acid at a flow rate of 1 ml/minute. The samples were collected, frozen and lyophilized before the radioimmunoassay. The radioimmunoassay was done using an antiserum labeled 2717, Copenhagen which detects CCK-8, 9, 33 and 39. The total concentration of CCK was calculated.

RESULTS

The results of the study are shown in Table 1. Plasma CCK immediately before feeds was 73 pmol/*l*. It rises to 541 pmol/*l* immediately after feeding. Ten minutes after feeding, it drops to 95 p pmol/*l* to rise again in 30 minutes after feeding to 368 pmol/*l*.

Table 1. **Plasma CCK level in 41 neonates**

	Plasma CCK level pmol/litre	± *SD*
Immediately before feeds	73 pmol/l	12
Immediately after feeding	541 pmol/l	190
10 minutes after feeding	95 pmol/l	14
30 minutes after feeding	368 pmol/l	144

DISCUSSION

This study aimed at evaluating neonatal plasma CCK level and its relation to breast feeding. Various studies were conducted to estimate the CCK level and its relation to feeding. In 1982, Walsh et al estimated CCK in adults and its relation to feeding[11]. In 1988, Salmenpera et al studied the effects of feeding regimen on blood glucose and plasma concentration of various gastrointestinal hormones including CCK in children at the age of nine months[12]. The difference between our study and the study conducted by Salmenpera et al is that this study was conducted at an earlier age group. We found that plasma CCK immediately before breast feeding was 73 pmol/l ± 12 (±2 SD). This level is higher than that found in adults by Walsh et al and in 9 months old babies by Salmenpera et al[11,12]. The cause of the high difference in plasma pre-feeding level of CCK in neonates and the plasma CCK in other studies is unknown.

The serum level of CCK just immediately after breast feeding was 541 pmol/*l*. This peak cannot be explained by the mechanism that milk caused this through its action on the duodenal lumen as that occurs later. The decrease (95 pmol/*l*) 10 minutes after breast feeding, also indicates that the peak is not related to the presence of nutrients in the duodenum. The mechanisms of this elevation is probably neural. It is known that insulin secretion increases and somatostain decreases when infants sucks a pacifier[13]. As the release of both these hormones is controlled by the vagus nerve, we conclude that the sucking stimulus triggers an activation of the vagus nerve. Similarly, as CCK is also under the control of the vagus nerve. The CCK elevation is more likely to be due to vagal stimulation induced by sucking rather than by food itself. The second peak which appears 30 minutes after breast feeding with a level of 368 pmol/*l* is due to the presence of nutrient in the duodenal lumen. Antin et al produced sleep in rats via the injection of the cholecystokinin[14]. The post parandial sleep in infants could be due to the second peak of CCK. We observed that CCK is increased twice in relation to breast feeding. The first peak could be due to sucking while the second peak of CCK could be the presence of nutrients in doudenal lumen.

CONCLUSION

It is concluded that cholecystokinin in neonates rises immediately after breast feeding. The CCK level rises again 30 minutes after breast feeding.

REFERENCES

1. Alfven G, Unvas Moberg K. Elevated cholecystokinin concentrations in plasma in children with recurrent abdominal pain. Acta Paediatr. 1993;82:967-70.
2. Stern HP, Stroh SE, Fiedorek SC. Increased plasma levels of pancreatic polypeptide in encopretic children. Pediatrics 1995;9:111-7.
3. Chung KS, Kim JW, Lee CH. Colonic transit patterns and cholecystokinin levels in children with recurrent abdominal pain. Yonsei Med J 1999;40:349-54.

4. Jansen JB, Lamers CB. Radioimmunoassay of Cholecystokinin in human tissue
and plasma. Clin Chim Acta 1993;131:305-16.

5. Liddle RA. Integrated actions of cholecystokinin on the gastrointestinal tract. Gastroenterol Clin North Am 1989;18:735-56.
6. Cantor P, Petrojijevic L, Pederson JF. Cholecystokinetic and pancreozymic effect of sulphated gastrin compared with non-sulphated gastrin and cholecystokinin. Gastroenterology 1997;72:639-43.
7. Jansson R, Svanik J. Effects of intravenous secretion and cholecystokinin on gallbladder. Gastroenterology 1997;72:639-43.
8. Linden A, Uvnas Moberg K. Plasma levels of cholecystokinin in response to feeding and during pregnancy in dogs. Scand J Gastroenterol 1987;22:859-64.
9. Linden A, Unvas Moberg K, Forsberg G. Plasma concentrations of cholecystokinin octapeptide and food intake in male rats treated with cholecystokinin octapeptide. J Endocrinol 1989;121:59-65.
10. Linden A, Eriksson, Hasen S. Suckling-induced release of cholecystokinin into
plasma in lactating rats. J Endocrinol 1990;127:257-63.
11. Walsh JH, Lamers CB, Valenzuela JE. Cholecystokinin immunoreactivity in human plasma. Gastroenterology 1982;82:438-44.
12. Salmenpera L, Perheentupa J, Sime MA. Effects of feeding regimen on plasma
concentrations of pancreatic hormones and gut regulatory peptides at 9 months of age. J Ped Gastroentero Nutr 1988;7:651-6.
13. Widstrom AM, Marchini G, Matthiesen AS. Non-nutritive sucking in tube fed
infants. J Ped Gastroenterol Nutr 1988;7:517-25.
14. Antin J, Gibs J, Holt J. Cholecystokinin elicits the complete behavioural sequence of satiety in rats. J Comp Psychol 1985;89:784-90.