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SHORT REPORTS

Impaired immunoreactive secretin release in coeliac disease

Studies using bioassays have suggested that secretion of enteric hormones may be abnormal in coeliac disease.¹ In children with coeliac disease increased numbers of secretin-producing S-cells have been described.² Using radioimmunoassay we have assessed the plasma secretin response to duodenal acidification in coeliac disease.

Patients, methods, and results

After an overnight fast, eight patients with untreated coeliac disease and 12 control subjects had 100 ml 100-mM HCl infused over 15 minutes into the upper duodenum. The position of the tube was checked radiologically. Peripheral venous blood samples for secretin determination were taken at -5, 0, 2½, 5, 7½, 10, 12½, 15, 20, 25, and 30 minutes after the acid infusion was started. Blood was collected into heparinised tubes, plunged into an ice bath, and plasma separated at 4°C. Plasma secretin was immediately extracted by ethanol and assayed in a sensitive and specific radioimmunoassay.³ The sensitivity of the assay was 6 pg/ml with 95% confidence. The statistical significance of differences was estimated using the paired *t* test.

The figure illustrates the results. Fasting immunoreactive secretin (IRS) levels were similar in controls and "coeliacs," all being less than 70 pg/ml.

Mean ($\pm$ SE of mean) plasma secretin (IRS) levels after intraduodenal acid in patients with coeliac disease and in controls.

In controls there was a rapid and significant rise (average $P < 0.005$) in IRS levels during acid infusion, which fell rapidly on termination of the infusion. In the coeliac group as a whole the rise in IRS was not significant. Some coeliac patients, however, showed a response but this was less in magnitude and duration than in the control group; these patients had less severe mucosal abnormalities than the remainder of the coeliac group.

Comment

Children with coeliac disease have increased numbers of secretin-containing S-cells which appear to be full of hormone granules.² The data presented here indicate that IRS release is impaired in coeliac disease and so suggests that the S-cells are full of hormone

because of failure of release rather than as a result of excessive synthesis of the hormone.

The reason for the failure of secretin release is not clear. Possibly the mucosal damaging process, brought about by gluten, also damages the S-cells or their apical projections; or because of the greatly deepened crypts, known to occur in coeliac disease, it may be more difficult for the acid stimulus to reach the S-cells. Gastric acid secretion is reduced in coeliac disease and, possibly owing to the lack of endogenous acid stimulation, S-cell function becomes sluggish and cannot respond even to an adequate exogenous acid stimulus. In view of the partial IRS response in the patients with milder mucosal flattening, it seems likely the degree of impairment of IRS response reflects the severity of the mucosal lesion.

The lack of IRS response to acid may have several consequences. Pancreatic exocrine function may be impaired and this could further aggravate malabsorption. There may also be important metabolic consequences. Secretin has a lipolytic function and during starvation it may play a major part in regulating lipid metabolism.⁴ Secretin may also participate in producing the augmented insulin response to oral glucose as compared with the insulin response to intravenous glucose.⁵ Thus, in coeliac disease where secretin response is abnormal, this may lead to impairment of islet response with consequent widespread effects on glucose, fat, and protein metabolism and also, as outlined, to abnormalities in lipid metabolism directly.

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Biochemical differences between amniotic fluid and maternal urine

Amniocentesis is being used increasingly for the antenatal diagnosis of congenital abnormalities such as open neural tube defects and several chromosomal abnormalities. With this method there is a risk of inadvertently tapping maternal urine instead of amniotic fluid, especially when the placenta is placed anteriorly. Therefore it is important to establish the biochemical differences between these two fluids.

Methods and results

To have a basis for comparison, we measured urea, creatinine, and α -fetoprotein (α -FP) concentrations in maternal urine and amniotic fluid collected from 30 patients undergoing second trimester amniocentesis. Urine samples were midstream specimens collected before the patients underwent transabdominal amniocentesis. After centrifuging both samples at 1000 rpm, we estimated the urea creatinine, and α -FP concentrations.

The different concentration of each substance in amniotic fluid and maternal urine is clearly illustrated in the table.

Urea, creatinine, and α -fetoprotein concentrations in amniotic fluid and maternal urine (means and ranges)

Test	Amniotic fluid	Maternal urine
Urea (mmol/l)	1.83 (0.83-3.49)	47.1 (19.9-106.2)
Creatinine (μ mol/l)	71 (53-97)	3801 (1060-13 437)
α -fetoprotein (mg/l)	18.6 (4.0-34.0)	0.005 (<0.005-0.026)

Conversion: SI to traditional units—Urea: 1 mmol/l $\approx$ 6 mg/100 ml. Creatinine: 1 μ mol/l $\approx$ 0.0113 mg/100 ml.

Discussion

Since, irrespective of the reason for amniocentesis, all amniotic fluid is routinely tested for α -FP, an abnormally low level of this protein leads to suspicion that the specimen is in fact urine. Urea and creatinine concentrations are then estimated for confirmation and when necessary the patient recalled for another amniocentesis.

In our series of over 500 second trimester amniocentesis seven specimens of urine were inadvertently collected. A low α -FP concentration (<0.100 mg/l in each sample) led to further testing. Urea and creatinine concentrations were, respectively, >16.6 mmol/l (100 mg/100 ml) and >530 μ mol/l (6.0 mg/ml), which fell within the maternal urine range (see table). Two fetuses out of the seven had neural tube defects. One had an open meningomyelocele and one was an anencephalic.

Hence in view of the short time interval between diagnosis and any subsequent termination of pregnancy it is imperative to ascertain rapidly the nature of fluid along the lines we have suggested.

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Reservoir of group B streptococci in women in labour

Streptococci of Lancefield's Group B (*Streptococcus agalactiae*) are a major pathogen in perinatal infections.^{1,2} This study aimed at establishing whether a routine screening of women in labour for this organism would help in making an early diagnosis leading to successful treatment of the disease in the neonate.

Methods and results

High vaginal and rectal swabs were taken from 125 women in labour in the maternity unit at Hammersmith Hospital just before artificial rupture of membranes. The vaginal swabs were plated on blood agar plates with and without 25 mg/l neomycin. The vaginal and rectal swabs were then cultured by a modification of the technique of Baker *et al*³ involving initial enrichment in selective nutrient broth containing nalidixic acid, 10 mg/l; gentamicin, 4 mg/l; and 4% defibrinated horse blood. The enrichment cultures were incubated at 37°C aerobically overnight, after which they were subcultured on Columbia blood agar (Oxoid CM 331) plates with and without nalidixic acid, 15 mg/l; gentamicin, 4.5 mg/l; and polymyxin B 50 000 units/l. All the plates were incubated anaerobically overnight using the "Gas Pak" system. Any orange or brown colonies showing small hazy zones of beta-haemolysis were presumed to be group B streptococci after

Proportion of 125 women in labour from whom group B streptococci were isolated from either vagina and rectum, or both

Type of specimen	Proportion positive for group B streptococci	
	No	%
High vaginal swabs only	9	7.2
Rectal swabs only	5	4.0
Both high vaginal and rectal swabs	9	7.2
Total	23	18.4

staining by Gram's method. Confirmation was by Lancefield's grouping using the autoclave antigen extraction method. Only rectal swabs which grew faecal flora on MacConkey agar were included in the survey, to avoid isolates of group B streptococci from the perineal skin, which could have originated from either vagina or rectum.

The isolation rates of group B streptococci from the vagina and the rectum are shown in the table. Overall, group B streptococci were present in the rectum in 11.2% of the women sampled and in the vagina in 14.4%. Taken together, 18.4% of the women had group B streptococci at either or both sites. The organism was found in the vagina in 8.8% of the women before enrichment culture and no isolates were detected before enrichment which could not be found by the selective enrichment technique. During the study a full-term newborn baby died of group B streptococcal pneumonia with septicæmia. This was despite treatment with penicillin and gentamicin after the early diagnosis of the infection, but only after the baby was already clinically ill. The diagnosis of group B streptococcal septicæmia in this child was expedited by the results of the mother's screening cultures which indicated presence of beta-haemolytic streptococci in the mother's vagina seven hours after the baby's birth and one day before the streptococcus was isolated from the baby's blood cultures.

Discussion

The results indicate that group B streptococci are present in the faeces and vagina of women in labour; this poses a problem to obstetricians who may wish to give prophylactic antibiotics to pregnant women harbouring these organisms in order to avoid infection of the neonate. There are no controlled studies showing that administration of antibiotics to such pregnant women will prevent neonatal infection or will eradicate the carrier state for the duration of pregnancy. Moreover, antibiotic prophylaxis of colonised neonates does not always eradicate the streptococcus and may not prevent recolonisation.⁴ While in most women it is possible temporarily to eradicate the organism from the vagina with parenteral penicillin,⁵ it is unlikely that such treatment will eradicate the organism from the faeces because penicillinase-producing coliforms in the faeces will destroy penicillin. Whether dangerous colonisation of the baby during labour can be prevented by giving the mother penicillin during labour is not clear and may require controlled study of over 10 000 deliveries for any statistical evidence to emerge. Knowledge that the mother had been a group B streptococcal carrier did not help the paediatricians in successfully treating the baby here described once it became ill immediately after birth. In view of the low attack rate of colonised babies (about 1%),¹ routine chemoprophylaxis is not recommended. Nevertheless, early treatment of at risk babies after taking appropriate specimens for culture is probably the best method of management at present.

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