Pancreatic function testing: serum PABA measurement is a reliable and accurate measurement of exocrine function

A R TANNER AND D P ROBINSON

From the Departments of Medicine and Biochemistry, North Tees General Hospital, Stockton on Tees, Cleveland

SUMMARY A comparison between the NBT-PABA/¹⁴C-PABA test (NBT-PABA, n-benzoyl-tyrosyl para-aminobenzoic acid) using the PABA excretion index (PEI) and serum PABA estimation at 90 minutes has been made in 42 consecutive subjects attending for investigation of possible pancreatic disease to a District General Hospital (DGH). The PEI was unobtainable or incorrect on 38% of occasions compared with 9% for the serum test. Sensitivity, specificity, and efficiency for the PEI (n=33 valid results) were 71%, 88%, and 79% respectively and for the serum PABA (n=41 valid results), 95%, 90%, and 93% respectively. These results confirm that measurement of serum PABA is a simpler, more reliable, and a more accurate method of assessing pancreatic function.

With the advent of simplified methods for measuring pancreatic exocrine function and the widespread availability of ERCP, assessment of pancreatic disease has become commonplace in district general hospitals. The single day NBT-PABA/¹⁴C-PABA has been shown to be a reliable screening test for pancreatic exocrine insufficiency, but has been criticised for a number of reasons.

Drug interference in the assay has been a common problem. Incomplete and contaminated urine collections are frequently encountered, with reported failure rates of between 13% and 30% leading some workers to abandon the test. Using the tracer ¹⁴C-PABA to improve test efficiency incurs a small radiation dose to the subject. Improvements in test performance using HPLC to minimise drug interference have been described, but this methodology is not widely available.

Various investigators have shown that serum measurement of PABA at a fixed time or at intervals after oral ingestion is as accurate as or better than conventional urine collection and measurement. We have evaluated both tests in consecutive patients presenting over a 12 month period to a DGH showing that serum estimation is simpler, more reliable, shows better performance, higher test efficiency and is easily applicable to infirm or very young patients.

Methods

PATIENTS Forty two consecutive patients who were undergoing investigation for possible pancreatic disease were studied. The presence or absence of pancreatic disease was independently established either by surgery with pancreatic histology (n=5), after ERCP (n=25), or by the presence of pancreatic calcification on plain radiography (n=3). In three subjects diagnosis was established at necropsy. In the four subjects with cystic fibrosis, pancreatic disease was assumed on the basis of steatorrhoea, although one had histologically proven pancreatic disease. There were 20 subjects with chronic pancreatitis, two subjects with pancreatic carcinoma and 20 subjects without chronic pancreatic disease. Excluding patients with cystic fibrosis, in only three subjects with pancreatic disease was malabsorption apparent. None has impaired renal function. Of those without pancreatic disease, six were eventually diagnosed as having the irritable bowel syndrome, two unexplained
abdominal pain and there were a variety of other diagnoses in the remaining subjects (Table). This study was approved by the local ethical committee.

**NBT-PABA/C-PABA**
The subjects were fasted overnight and passed urine before drinking the test cocktail. This urine was used as a basal sample to analyse for interference with the PABA estimation. The test cocktail consisted of a standard Lundh meal made to a volume of 300 ml, with 666 mg Bentiromide (NBT-PABA) and 1uCi C-PABA added. The subjects were encouraged to drink freely and allowed a normal lunch at three hours. Ten millilitres of clotted blood were taken at

Table: Study group data. Subjects are grouped according to test results and diagnosis. 1–16, both tests available, no pancreatitis; 17–33, both tests available, chronic pancreatitis; 34–42, only single test available because of technical difficulties.
time 0 and at 90 minutes for estimation of serum PABA.

Urine was collected for six hours and subsequently analysed for PABA and "C-PABA using minor modifications of the Bratton and Marshall method." The PEI is the ratio of the six hour urinary chemical recovery of PABA to the six hour urinary radioisotope recovery of "C-PABA as proportions of the respective oral doses. All analyses were done in duplicate, blanks were used on each specimen and an internal standard routinely used. Completeness of hydrolysis was checked by including a p-acetaminobenzoic acid standard in each batch. Intra-assay and interassay coefficients of variation were 1.5% and 2.9% respectively.

Serum PABA assay involved precipitation of proteins using trichloroacetic acid, acid hydrolysis followed by neutralisation and colour development as with the standard urine assay. The assay was sensitive to a level of 0.1 mg/l and linear to an absorbance representing 20 mg/l serum PABA. Intra-assay and interassay coefficients of variation were 1.3% and 3.5% respectively.

**STATISTICAL ANALYSIS**

Standard calculations for specificity and sensitivity were used. Efficiency is defined as the proportion of correct results (either positive or negative) using the arbitrary thresholds (2 mg/l for serum PABA and 0.65 for PEI). Receiver operating characteristic (ROC) curves were constructed as described by Robertson and Zweig.10

**Results**

In nine of the 42 subjects (21%) the PEI was judged to be unreliable or unobtainable. In two of these subjects the basal urine showed a high 'blank' value, in five subjects the urine collection was incomplete, lost, or contaminated and in two subjects urine collection was impractical because of age or dementia. By contrast only one (2%) serum sample, also from one of the nine subjects (subject 41), was felt to be unsatisfactory because of a high 'blank' serum level at time zero (Table).

In the remaining 33 subjects (17 chronic pancreatitis/16 other) a direct comparison was made between the urine and serum estimations. For the PEI there were two false positives and five false negatives giving a specificity of 88%, sensitivity 71%, and efficiency of 79%; for the serum PABA estimation there were two false positives and one false negative giving a specificity of 88%, sensitivity of 94%, and efficiency 91%. Test results are shown in the Table and Figure, where the overlap can be clearly seen to be less using the serum test. If the further reliable serum results are included (n=41), the specificity of the serum PABA is 90%, sensitivity 95%, and efficiency 93%. Taking all the results, the PEI was unobtainable or incorrect on 38% (16/42) of occasions compared with 9% (4/42) for the serum test.

The one false negative serum PABA also had a normal PEI (0.98) with only minimal changes at ERCP. There were two patients with carcinoma of the pancreas, one situated distally and not detected by either test. In the other patient with a proximal lesion the serum test was abnormal but urine was not obtained.

Because arbitrary thresholds have been applied and relatively small numbers of patients involved, receiver operating characteristic curves (ROC's) have been constructed (plotting true positive rate against the false positive rate at all decision levels). This allows the different tests to be compared under equivalent conditions and at all decision levels. The closer the curve approaches the vertical and superior horizontal axes the better the clinical performance. Serum estimation of PABA at 90 minutes is shown to be superior to PEI estimation (Fig. 2).
Pancreatic function testing

Pancreatic exocrine failure is an insidious process and there is a very large reserve of exocrine function, so
that more than 90% of activity needs to be lost before disease is apparent. No diagnostic procedure is likely
to be efficient in establishing the presence of early disease. Even histology can be difficult to interpret at
an early stage. At present, assessment of pancreatic disease depends on established clinical skills,
measurement of exocrine activity and the use of a variety of imaging techniques. Measurement of
exocrine activity has been greatly simplified with the introduction of tubeless tests and these tests are as
accurate as the Lundh test meal. As outlined in the introduction, the NBT-PABA test has been criticised
because of a high technical failure rate and 21% of tests proved unreliable in the present study. Measure-
ment of serum PABA was far more reliable (2% unreliable), more efficient, easier to carry out and
would be without radiation exposure.

A previous pilot study by ourselves in 18 subjects
had established that the 90 minutes sampling time
provided the best discrimination between disease and
no disease with a test efficiency of 90%. Sampling
times were every 30 minutes for four hours and then
hourly to six hours. Other methods of analysis such as
estimating areas under curve for different time
periods did not improve discrimination. Other
workers have also recommended a 90 minutes, 120
minutes, or 150 minutes sampling time. In fact
most previous studies have concluded that serum
sampling is as accurate as the urine excretion and may
indeed be superior. The present study showed a
very high sensitivity and specificity for the serum
PABA, but combining results from previous studies
without including the present results still shows a high
efficiency for the test with overall sensitivity 82% and
specificity 84%.

There were five subjects where the serum estima-
tion appears more sensitive than the PEI, two with
pancreas divisum (subjects 17 and 18), one with only
minimal changes at ERCP (subject 31), one with an
alcoholic aetiology (subject 19) and one subject with
hypercalcaemia (subject 21). Another subject (38)
with pancreas divisum had a diagnostic serum level
and an unreliable PEI estimation. It may be that
serum estimation at 90 minutes is a more sensitive
indicator of early disease than PEI estimation. A
further patient (32) with minimal changes at ERCP
had completely normal test results probably indicating
well maintained exocrine function. One patient
classified as having unexplained abdominal pain
(subject 7) had both tests abnormal, but other
imaging investigations of the pancreas have so far
proved normal.

The use of ROC curves has been previously
recommended for the comparison of different tests
under equivalent conditions or when analytical
improvements are made to the test procedure. With-
out recourse to sophisticated statistics, test perform-
ance can easily be compared. We believe this form of
analysis should be encouraged.

Lankisch and coworkers' have concluded that the
use of serum tests will simplify the test procedure and
could be used in the elderly, the severely ill and in
outpatients. Our results support this conclusion, but
we would go further and recommend that serum
estimation (91% reliable) replace urine collection
(62% reliable).

References

1 Braganza JM, Kay GH, Tetlow VA, Herman KK.
Observations on the BT-PABA/C-PABA tubeless test
47.

2 Tanner AR, Fisher D, Ward C, Smith CL. An evalua-
tion of the one day NBT-PABA/C-PABA in the
assessment of pancreatic exocrine insufficiency.

3 Faulder GC, Strange RC. Brief study of the urinary
PABA test for assessment of pancreatic exocrine


Pancreatic function testing: serum PABA measurement is a reliable and accurate measurement of exocrine function.

A R Tanner and D P Robinson

*Gut* 1988 29: 1736-1740
doi: 10.1136/gut.29.12.1736

Updated information and services can be found at:
http://gut.bmj.com/content/29/12/1736

**Email alerting service**
Receive free email alerts when new articles cite this article.
Sign up in the box at the top right corner of the online article.

**Topic Collections**
Articles on similar topics can be found in the following collections
Pancreas and biliary tract (1949)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/