Urol Res (193) 11:167–170

Urological Research


# Zinc in Post Prostatic Massage (VB3) Urine Samples: A Marker of Prostatic Secretory Function and Indicator of Bacterial Infection

J. P. Kavanagh, C. Darby, C. B. Costello and S. D. Chowdhury

Department of Urology, University Hospital of South Manchester, Manchester, UK

Accepted: April 25, 1983

**Summary.** The value of biochemical examination of post-prostatic massage (VB3) urine samples has been investigated. Measurement of zinc levels provides a good marker of prostatic secretory function. In the absence of prostatic carcinoma findings of $\geqslant$ 100 $\mu$g zinc in VB3 urines is strong evidence (2% false negatives) of an absence of infectious or inflammatory prostatic disease. Less than 40 $\mu$g of zinc is suggestive (14% false positives) of prostatitis. There is little need to consider the endogenous urinary zinc levels. This simple test should be of particular value in cases where an expressed prostatic secretion is not obtained (about 40% of this series of patients), when it would be a valuable adjunct to cytological and bacteriological examination of split urine samples.

**Key words:** Zinc, VB3 urines, Prostatitis.

## Introduction

Bacteriological and cytological examination of expressed prostatic secretion (EPS) and voided bladder urine samples (VB1, VB2 and VB3) are of great importance in the diagnosis and management of prostatitis patients [2, 3, 8]. Biochemical examination of the EPS has also been shown to be of value, particularly the raised pH and lowered zinc and citric acid concentration associated with inflammatory disease [1, 4, 6]. In many cases prostatic massage fails to elicit an EPS sample of sufficient volume for any or all of these tests to be performed. This paper examines the potential for biochemical examination of VB3 samples to give indirect evidence of the secretory function of the prostate.

Many constituents of the EPS are good indicators of prostatic secretory capacity, with a diagnostic value [6, 7]. In order to be useful as a marker of prostatic function in urine any such constituent should fulfil the following conditions. It must be present in the EPS in very much greater concentrations than in urine, the assay method must be capable of detecting the component at much lower concentrations than found in the EPS and there must be no interference in the estimate by urine. Zinc fulfils all these requirements and in addition is stable, easing problems of sample handling and storage. Of seven prostatic secretion constituents investigated zinc and citric acid were the best indicators of secretory function [5]. Zinc therefore appears to be the marker of choice.

There are four factors which will influence the amount of zinc recovered in VB3 urines. The concentration of zinc in the EPS, the volume of EPS flushed out by the urine, the endogenous urinary zinc concentration and the volume of the VB3. In order to evaluate the usefulness of VB3 zinc measurements we must consider whether the volume of EPS flushed out falls into a sufficiently narrow range and whether the amount of endogenous urinary zinc need be taken into account. Similar considerations also apply to the measurement of bacteria and leucocytes in VB3 urines and presumed to be prostatic in origin.

## Materials and Methods

*Collection of samples:* Initial and midstream urine samples (VB1 and VB2) were obtained, followed shortly by prostatic massage and collection of any expressed prostatic secretion (EPS). A post massage urine (VB3) was then passed. The volume of the urine samples was noted and aliquots taken for routine bacteriological, cytological and biochemical analysis.

*Biochemical Analysis.* Methods for EPS analysis are fully described elsewhere [5]. Urinary zinc was measured by atomic absorption spectroscopy (Pye-Unicam SP192, sensitivity 0.009 $\mu$g/ml). Samples were measured undiluted, or were diluted with 0.1 M $HNO_3$ as required to give concentrations in the range 0–1.0 $\mu$g/ml. The recovery of added zinc to urine was 95% and the coefficient of variation was about 5%.

*Classification of Patients.* The patients were classified on the basis of history, clinical findings, histology and bacteriological and cytological examination or urine samples (and EPS samples when available). They were divided into three groups. 1) Prostatitis (P), with

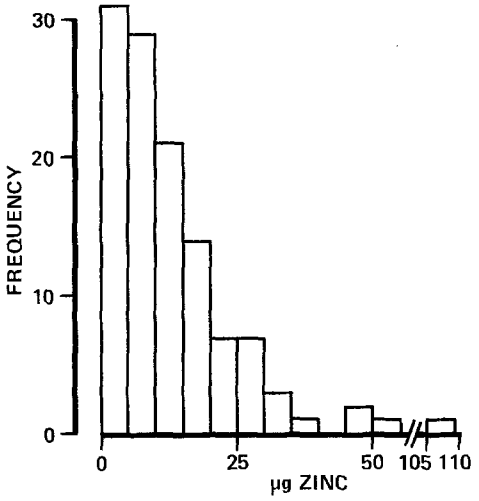



Fig. 1. The distribution of endogenous urinary zinc found in VB3 urine samples

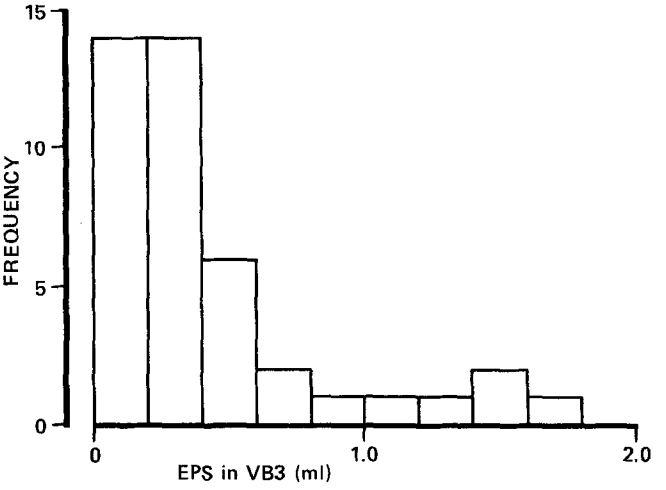
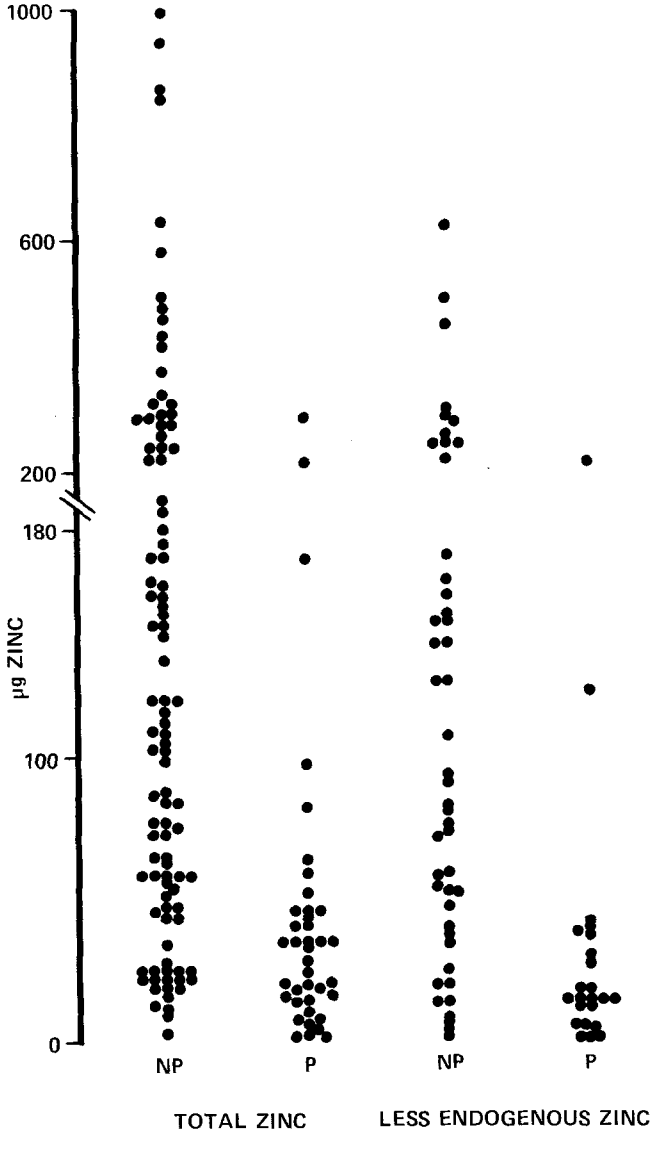



Fig. 2. The distribution of volumes of EPS contained in VB3 urine samples




◀ Fig. 3. The amount of zinc found in VB3 urines (total and prostatic-only). *NP*, non-prostatitis; *P*, prostatitis

clear evidence of infectious or inflammatory prostatic disease. 2) Non-prostatitis (NP), absence of infectious or inflammatory prostatic disease or carcinoma. This group comprised those with apparently healthy prostates, BPH patients and prostatodynia cases (defined in [6]). 3) Resolving Prostatitis (RP), with evidence of a recent, but not completely subsided episode of prostatitis. When EPS samples were available this group was subdivided according to whether or not the EPS had returned to normal. The criteria used were, for samples returned to normal, a pH of $\leqslant 6.8$ or a pH of 7.1 with either zinc $\geqslant 0.325$ mg/ml ($\geqslant 5$ mM) or citric acid $\geqslant 75$ mM or both. These samples are referred to as RP ("NP"). Continued abnormal prostatic secretory function (RP ("P")) was defined as pH $\geqslant 7.4$ or pH 7.1 with either $\leqslant 0.130$ mg/ml of zinc ($\leqslant 2$ mM) or citric acid $\leqslant 45$ mM or both. Justification for the choice of these values is given in [6].

Mann Whitney U tests were used for statistical evaluation of the results.

## Results

*Endogenous Urinary Zinc.* Comparison of the zinc concentration in VB1 and VB2 samples showed no significant difference (mean values 0.355 and 0.358 µg/ml respectively, $p > 0.6$, $n = 118$). The endogenous urinary zinc concentration of each VB3 was taken to be the mean of its corresponding VB1 and VB2 values. The amount of endogenous zinc in the VB3 could then be calculated. The median value was 9.90 µg, with a range of 0.8–110 µg ($n = 118$). The distribution of values is shown in Fig. 1.

*Volume of EPS Flushed Out by VB3.* This could only be estimated when an EPS sample was obtained of sufficient volume for a zinc determination to be made. We had 44

**Table 1.** The zinc content of VB3 urines

| Condition | Total zinc | | | | Less endogenous zinc | | | |
|---|---|---|---|---|---|---|---|---|
| | *n* | median (μg) | range (μg) | *p* | *n* | median (μg) | range (μg) | *p* |
| NP | 98 | 110 | 4-989 | | 47 | 91 | 0-620 | |
| P | 39 | 36 | 2-278 | < 0.001 | 23 | 15 | 0-208 | < 0.001 |
| RP | 58 | 56 | 5-894 | 0.02 | 32 | 51 | 0-504 | > 0.1 |
| RP ("NP") | 20 | 116 | 15-894 | > 0.1 | 13 | 79 | 13-504 | > 0.1 |
| RP ("P") | 6 | 15 | 5-32 | < 0.001 | 1 | 0 | – | – |

*NP* = non prostatitis, *P* = prostatitis, *RP* = resolving prostatitis, *RP ("NP")* = resolving prostatitis (normal EPS), *RP ("P")* = resolving prostatitis (abnormal EPS)

**Table 2.** The effect of choosing different cut-off values of VB3 zinc in distinguishing prostatitis and non-prostatitis

| Samples[a] considered | Cut-off values (μg) | Total Zinc | | | Less Endogenous Zinc | | |
|---|---|---|---|---|---|---|---|
| | | *n* | False + ve | False – ve | *n* | False + ve | False – ve |
| | 100 | 137 | 32% | 2% | 70 | 36% | 3% |
| NP | 75 | 137 | 27% | 4% | 70 | 29% | 3% |
| P | 50 | 137 | 18% | 6% | 70 | 19% | 3% |
| | 40 | 137 | 14% | 10% | 70 | 16% | 6% |
| | 100 | 26 | 31% | 0% | 14 | 50% | 0% |
| RP ("NP") | 75 | 26 | 27% | 0% | 14 | 43% | 0% |
| RP ("P") | 50 | 26 | 19% | 0% | 14 | 36% | 0% |
| | 40 | 26 | 12% | 0% | 14 | 29% | 0% |
| NP | 100 | 163 | 32% | 2% | 84 | 38% | 2% |
| P | 75 | 163 | 27% | 3% | 84 | 31% | 2% |
| RP ("NP") | 50 | 163 | 18% | 5% | 84 | 21% | 2% |
| RP ("P") | 40 | 163 | 13% | 9% | 84 | 18% | 5% |

[a] *NP* = non-prostatitis, *P* = prostatitis, *RP ("NP")* = resolving prostatitis (normal EPS), *RP ("P")* = resolving prostatitis (abnormal EPS)

such samples. The median volume was 0.285 ml and the range was 0.006 to 1.65 ml. The distribution of values is shown in Fig. 2. These values were calculated assuming that all the VB3 zinc originated from the prostate. In the 12 cases where VB1 or VB2 samples were available to calculate the endogenous VB3 zinc the mean decrease in the calculated volume of EPS was only 0.038 ml.

*VB3 Zinc.* 195 VB3 samples obtained from patients attending urology clinics are considered here. In 38% of these cases no EPS was obtained. 98 samples were from patients without prostatitis or carcinoma, 39 from men with prostatitis and 58 from resolving prostatitis cases. The values of total VB3 zinc for the prostatitis and non prostatitis groups are presented in Fig. 3, also shown are the values obtained after subtraction of the endogenous VB3 zinc, when available. Details of these results together with those of the resolving prostatitis patients are given in Table 1. The numbers of false positives and negatives using different cut-off values are considered in Table 2.

It was also noted that the zinc content of VB3 urines from carcinoma patients was consistently low (96% of cases contained < 100 μg). This will be considered in a separate communication.

## Discussion

The pre-prostatic massage urinary zinc levels are similar to those reported elsewhere for healthy individuals [9] and more than a thousand times less than the concentration of zinc found in normal EPS [5]. 81% of the VB3's contained < 20 μg of endogenous zinc. When more than this was found it was attributable, almost equally, to comparatively high urinary zinc concentrations (≥ 0.75 μg/ml) or comparatively large VB3 volumes (≥ 50 ml), or both.

In order for the VB3 samples to be perfectly representative of the prostatic secretion they should all contain the same volumes of EPS. This clearly will not be the case, but Fig. 2 shows that two thirds of the samples contained < 0.4 ml of EPS and that large volumes are much less frequent. It is evident from this that VB3 samples containing low volumes of EPS with normal to high zinc concentrations may not be easily distinguishable from VB3's con-

taining about average volumes of EPS with low zinc concentrations. However, there are likely to be many fewer cases of confusion between VB3's containing large volumes of EPS low in zinc and VB3's with average volumes of EPS and normal zinc concentrations. Despite these limitations our results demonstrate that zinc determinations of VB3 urines can be diagnostically useful.

Figure 3 and Table 1 show that, as expected, the zinc content of VB3 urines from prostatitis patients is significantly lower than most of those without prostatitis. Taking into account the endogenous VB3 zinc does not affect this conclusion. Table 2 shows the effect of choosing different cut-off values for distinguishing these two groups, indicating that VB3 samples containing 100 $\mu$g of zinc are very unlikely to come from patients suffering from prostatitis. Values of $< 40$ $\mu$g are suggestive of abnormal prostatic secretory function, which is evidence of infectious or inflammatory prostatic disease. Again, taking into account endogenous zinc does not greatly affect these conclusions. However, if VB1 or VB2 samples were routinely available then further experience might suggest slightly lower cut-off values. The main value of measuring the endogenous urinary zinc lies in identifying patients with raised urinary zinc levels. This condition may arise in nephrosis, post alcoholic hepatic cirrhosis and hepatic porphyria [9].

The resolving prostatitis group falls roughly between the non-prostatitis and prostatitis groups (Table 1). When other evidence was available to classify the EPS of these patients it was clear that a return of normal prostatic secretory activity was frequently associated with $> 100$ $\mu$g of zinc in the VB3 (Table 2). Thus this test can provide an indication of a patients response to treatment.

In conclusion, it is clear that the measurement of the zinc content of VB3 urines would be a useful member of the battery of tests available to the urological clinician. It would be particularly useful when little or no EPS is obtained (about 40% of this series of patients), being a valuable adjunct to the bacteriological and cytological examination of VB3 samples. A finding of $> 100$ $\mu$g of zinc would be very strong evidence that the patient was not suffering from inflammatory prostatic disease. In such cases there should be no need for an early return of the patient for another attempt to obtain an EPS sample.

## References


1. Blacklock NJ, Beavis JP (1974) The response of prostatic fluid pH in inflammation. Br J Urol 46:537–542
2. Drach GW (1974) Problems in diagnosis of bacterial prostatitis: Gram negative, gram-positive and mixed infections. J Urol 111: 630–636
3. Drach GW, Fair WR, Meares EM, Stamey TA (1978) Classification of benign diseases associated with prostatic pain: prostatitis or prostatodynia? J Urol 120:266
4. Fair WR, Crane DB, Schiller N, Heston WDW (1979) A reappraisal of treatment in chronic bacterial prostatitis. J Urol 121: 437–441
5. Kavanagh JP, Darby C (1982) The interrelationships between acid phosphatase, aminopeptidase, diamine oxidase, citric acid, $\beta$-glucuronidase, pH and zinc in human prostatic fluid. Int J Androl 5:503–512
6. Kavanagh JP, Darby C, Costello CB (1982) The response of seven prostatic fluid components to prostatic disease. Int J Androl 5:487–496
7. Meares EM (1980) Prostatitis syndromes: New perspectives about old woes. J Urol 123:141–147
8. Meares EM, Stamey TA (1972) The diagnosis and management of bacterial prostatitis. Br J Urol 44:174–179
9. Underwood EJ (1977) Trace elements in human and animal nutrition. 4th ed, Academic Press, New York London, pp 196–242



Dr. J. P. Kavanagh
Department of Urology
University Hospital of
South Manchester
Manchester M20 8LR
U.K.