

Re: Nerli RB, Ghagane SC, Rangrez S, Chandra S, Thakur ML, Gomella L. Detection of bladder cancer using voided urine sample and by targeting genomic VPAC receptors. *Indian J Urol* 2021;37:345-9

We read the article titled “Detection of bladder cancer using voided urine sample and by targeting genomic VPAC receptors” by Nerli *et al.* with interest.^[1] We appreciate the authors’ research on new cytological markers which have found application in bladder malignancy. The authors have shown that the VPAC Combined vasoactive intestinal peptide and pituitary adenylate cyclase activating peptide family of cell surface receptors positivity in low-grade bladder cancer is as high as 83.33%, higher than that of 5-Aminolevulinic acid (ALA) and the cytology group, which is a promising finding. In the methodology, it was mentioned that the suspicious area of the follow-up group ($n = 38$) was biopsied. However, the cystoscopic findings of these patients and characteristics which compelled the investigator to take biopsies to detect the presence or absence of carcinoma *in situ* in these cases were not mentioned. Was mitomycin/Bacillus Calmette-Guerin (BCG) given during the primary treatment in this group?

VPAC receptor is not tissue specific. It is expressed by various tissues such as breast, pituitary, pancreas, and prostate. If VPAC is positive, then how do the authors differentiate whether it is from the bladder or the prostate? It is not mentioned whether the urine samples were examined by the same pathologist and whether the pathologist was blinded. In the result part, there is a disparity regarding the information provided in the text and the table. The text mentions four false-positive results in the 5-ALA group, whereas the table mentions the same in the VPAC group.

In a study conducted by Miyake *et al.*, 614 urine samples were included.^[2] Logistic regression showed

that false-positive results in fluorescent voided urine cytology group may be due to high density of white blood cells and alkaluria. Could there be any such occurrence in this study too? In a similar study based on 5-ALA cytology done by Pytel *et al.*, the study group was further classified based on T stage and grade.^[3]

Another study by the same group as this paper shows 5-ALA urine cytology to have sensitivity of 100% and specificity of 98%.^[4] Its sensitivity is higher than this study’s VPAC cytology group. In the same study, the sensitivity and specificity of 5-ALA cytology is 100% for low-grade bladder cancers. Thus, two studies by the same author have two different implications regarding the superiority of each test.

Overall, the result of this study is admirable as it shows better performance than most of the markers available in the market and the authors should be credited for taking up this new subject. This could avoid repeated check cystoscopies in carcinoma of bladder patients.

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