01050

A POINT-OF-CARE ASSAY FOR DIAGNOSIS OF NEUROSYPHILIS

Hemil Gonzalez[1], Igor Koralnik[2], Lauren Tantalo[3], Gregory D. Huhn[4], Zachary Orban[2], Christina Marra[3]
[1]Rush University, Chicago, IL, USA [2] Department of Neurology, Northwestern University, Chicago, IL, USA [3]University of Washington, Seattle, WA, USA [4]Ruth M. Rothstein CORE Center, Chicago, IL, USA

Hemil Gonzalez, MD
hemil_gonzalez@rush.edu
Phone: 312 947 4383
Fax: 312 942 8200

Background

Neurosyphilis (NS) can cause severe disability (1). Globally, the burden of NS remains high, and the ability to diagnose it in resource limited settings (RLS) is restricted (2, 3). We tested whether a point of care test originally developed to detect serum treponemal and nontreponemal antibodies could be used on cerebrospinal fluid (CSF) to diagnose NS.

Methods

CSF obtained via lumbar puncture was retrospectively analyzed in a 1:1 case control study from patients (N=72) with syphilis. Confirmed NS cases (N=36) were defined by: reactive CSF-Venereal Disease Research Laboratory test [VDRL] with or without CSF pleocytosis that normalized after NS therapy. Controls without NS had a nonreactive CSF-VDRL and a CSF WBC ≤5/µL. Cases and controls were matched by age, HIV status and syphilis stage (table 1). CSF was tested with the Dual Path Platform (DPP®) assay (Chembio, Medford, NY) according to the manufacturer's instructions using an electronic reading device that provides units of light intensity. Sensitivity and specificity were calculated using standard formulae. An ROC curve was generated (figure). Using Youden's J statistic, a cutoff of >89 units for the treponemal and >7.7 units for the nontreponemal test was established. Associations between categorical variables were determined by Chi-square and between continuous variables by Mann-Whitney.

Results

Table 1. Participant Characteristics

	Neurosyphilis Cases n=36	Controls n=36	P-values
Male	35 (97%)	36 (100%)	NS
HIV-infected	26 (72%)	27 (75%)	NS
Age	39 (33-47)	39 (31-44)	NS
Syphilis stage Primary Secondary Early latent Late latent/unknown	 1 (3%) 17 (47%) 9 (25%) 9 (25%)	 1 (3%) 15 (42%) 13 (36%) 7(19%)	NS
1/Serum RPR titer	256 (64-512)	128 (64-256)	NS
CSF WBC/µL	66 (34-124)	2 (2-4)	<0.001
CSF VDRL titer	2 (2-7)	0 (0-0)	<0.001

Results are expressed as number (n), percent (%) or median (interquartile range)

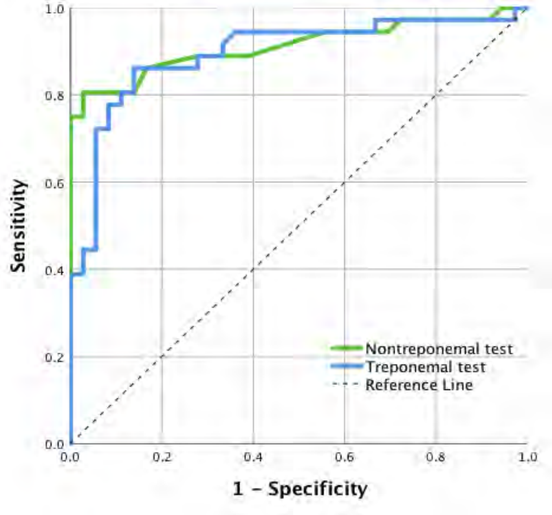
Table 2. False-negative and true positive rates

	Treponemal test			Nontreponemal test		
	False negatives 5/36 (14%)	True positives 31/36 (86%)	P-values*	False negative 7/36 (19%)	True positives 29/36 (81%)	P-values
Median serum RPR titer (IQR)	128 (128-512)	256 (64-512)	NS	128 (64-256)	256 (128-512)	NS
Median CSF VDRL (IQR)	2 (1-8)	2 (2-8)	NS	2 (1-2)	4 (2-8)	NS
Median CSF WBC (IQR)	58 (28-213)	67 (42-131)	NS	31 (29-349)	67 (47-118)	NS

Results are expressed as number (n), percent (%) or median (interquartile range)

Results

Figure. Receiver operator characteristic curve. Area under the curve was .90 for the treponemal antibody and .91 for the nontreponemal antibody



Cases and controls had equal proportions of males, HIV-infected patients and similar age. Cases had a higher serum RPR, CSF WBC and CSF VDRL titer than controls. CSF treponemal antibody POC test result was >89 units in 31/36 cases and 5/36 controls, and CSF nontreponemal antibody POC test result was >7.7 units in 29/36 cases and 1/36 controls. This resulted in a sensitivity of 86% and specificity of 86% for the treponemal test and sensitivity of 81% and specificity of 97% for the nontreponemal test.

Discussion

- A combination of treponemal (high sensitivity) and nontreponemal (high specificity) results could enable NS diagnosis with a high degree of certainty
- Participants with true positive nontreponemal tests had a higher serum RPR and more abnormal CSF. These differences were not significant, likely due to small numbers

Conclusion

The diagnosis of NS in RLS is challenging due to the need for modern laboratory facilities, specialized equipment and trained technicians. The DPP® assay can be an option in the point-of-care diagnosis of NS. Further studies should examine its performance in RLS.

Implications

- The DPP® could be an inexpensive point-of-care tool for the diagnosis of NS
- The test could have widespread application in RLS without need for additional laboratory facilities or highly trained personnel

References

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Financial Support

This work was supported by NIH/NINDS grant #NS34235 to CMM