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CSF biomarker method comparison in dementia patients

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PURPOSE / OBJECTIVES

Neurodegenerative dementias are becoming an increasingly significant burden in the developed world; a battery of clinical, imaging, psychological and laboratory tests are used to diagnose cognitive impairment and mood/behavioral/language disturbances and differentiate from other non-degenerative causes [1]. They comprise a spectrum of diseases; mainly, are classified in one of four categories such as **Alzheimer's (AD**, the majority of cases ~60-70%), **Frontotemporal dementia (FTD), Lewy-body dementia and Vascular dementia** (although mixed cases are not uncommon).

CSF proteins **amyloid beta1-42 (Ab), tau and p-tau** are now considered reliable biomarkers of amyloid plaque formation, neurodegeneration and tau aggregation resulting in neurofibrillar tangles according to the recent AT(N) 2018 classification of neurodegenerative dementias [2]. The automation of these immunochemical measurements will increase both accuracy, turnaround time and widespread application.

MATERIALS & METHODS

35 CSF samples from patients from the neurodegenerative spectrum (Alzheimer's disease, Frontotemporal Dementia etc.) were analyzed for all CSF biomarkers with the gold-standard Innotest ELISA methods from Fujirebio and in parallel, with the new CE-IVD Roche reagents that employ Elecsys/Cobas automated platforms. **An external quality assessment sample** was also included (Instand, Oct 20).

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CSF lab biomarkers (amyloid beta 1-42, tau and p-tau) are increasingly being used for diagnosis and classification of dementia patients.

Automation of these immunochemical measurements will increase both accuracy, turnaround time and widespread application.

Method comparison was performed between the gold-standard Innotest ELISA methods from Fujirebio and the new CE-IVD Roche reagents that employ Elecsys/Cobas automated platforms.

Efforts for standardization and harmonization of these CSF parameters should continue worldwide.

RESULTS

The new Roche reagents are easy to implement, rapid (results within 19 min compared to 20 hours for the ELISA manual procedures) and showed excellent precision results (CV% of internal low and high quality controls <5% compared to 8-12% for ELISA).

Regression, correlation and concordance statistical analysis showed the following results:

a) $Ab_{Roche} = 1.18 \times Ab_{Fujirebio} - 104$ (r=0.91, concordance 72%),

b) $tau_{Roche} = 0.65 \times tau_{Fujirebio} + 7$ (r=0.97, concordance 97%),

c) $p\text{-}tau_{Roche} = 0.55 \times p\text{-}tau_{Fujirebio} - 9$ (r=0.97, concordance 80%).

In order for a fair method comparison to be performed, normal/abnormal concordance was evaluated according to literature universal cut-off values for Fujirebio measurements (550, 375, 52 pg/ml for Ab, tau, p-tau although the manufacturer provides age-specific cut-offs) and to suggested cut-off values for Roche (800, 300, 27 pg/ml for Ab, tau, p-tau correspondingly). The Roche suggested Ab cut-off of 1000 pg/ml was changed arbitrarily to 800 in order to improve concordance.

SUMMARY/CONCLUSION

Our results showed high correlation for the tau and p-tau methods; the Roche tau cut-off seems appropriate for correct classification of the cases and the Roche p-tau cut-off needs slight adjustment in order for the concordance to improve. Ab values seem to converge with acceptable correlation but the cut-off value of the two methods need to be re-examined in light of the new certified Ab reference material [3].

Final and correct adjudication of the cases should be examined during patient monitoring.

Efforts for standardization and harmonization of these CSF parameters should continue worldwide.