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Comparison of the automated Roche Elecsys Cobas Anti Mullerian Hormone (AMH) assay with the Beckman AMH Gen II ELISA

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Anti Mullerian Hormone (AMH), traditionally used to investigate gonadal development and abnormal sexual differentiation in newborns, is increasingly being used as a biochemical marker for the assessment of the growing ovarian pool and thus a surrogate marker for the ovarian reserve and female fertility (1,2). Current existing AMH assays exhibit limitations with respect to throughput and have been reported to demonstrate a high degree of between-laboratory variability (3,4). For example Zuvela et al. (4) showed that for the Beckman AMH Gen II assay (the most common in the Netherlands) when samples were send to different laboratories for AMH measurement, while each laboratory showed good reproducibility, there was a wide range of average values relative to the consensus value from -24.0% to +22.7%. Recently a fully automated AMH assay has been developed on the Roche Elecsys/Cobas electrochemiluminescence immunoassay platform which is claimed to be an more reliable alternative (5). In this study we tested this newly introduced AMH assay from Roche Diagnostics and compared the outcome with the Beckman AMH Gen II assay, currently used in het University Medical Center Groningen.

Materials and methods

Precision analysis (according to EP5 protocol), linearity and analytical sensitivity were determined for both assays. Passing-Bablock method comparison was carried out using serum samples from 44 patients. The Roche Cobas 6000 was used for the Roche assay and the Beckman AMH Gen II assay was performed using a DS2 ELISA robot system, both according to manufacturers instructions. Within run and between run precision analyses were performed using three pooled serum AMH levels. Independent quality control samples were not available at the time of analysis.

Results

The within run and between run precision results of both methods are presented in Table 1. Both the intra-assay variation as the inter-assay variation, measured at 3 serum levels, of the Roche assay were smaller than the Beckman assay. Both assay showed good linearity.

Table 1. The within run (upper) and between run (lower) precision results of the evaluated Beckman and Roche AMH assays.

Beckman		**Roche Cobas**	
Measured concentration (ng/mL)	CV (%)	Measured concentration (ng/mL)	CV (%)
0.29	4.7	1.73	0.71
3.08	4.3	5.11	0.73
8.88	3.4	8.93	0.49

Beckman		**Roche Cobas**	
Measured concentration (ng/mL)	CV (%)	Measured concentration (ng/mL)	CV (%)
1.29	5.54	1.66	1.99
7.37	6.87	4.87	2.58
15.22	8.01	8.40	4.92

The limit of quantitation (estimated minimum concentration achieved at 20% total imprecision) was < 0.01 ng/mL for the Roche assay and approximately 0.03 ng/mL for the Beckman assay. Both assays showed good linear correlation in the physiological range and the overall comparison of the two assays (Figure 1) resulted in the following equation: Cobas = 0.82 * Beckman + 0.05 (ng/mL).

Conclusions

In this method comparison study both the new Roche assay as the current Beckman Gen II ELISA should be suitable for clinical application. However, both the intra-assay variation as the inter-assay variation, measured at 3 serum levels, for the Roche assay were profoundly smaller than for the Beckman assay. We found a good correlation between the two methods. Overall, the Roche values were approximately 20% lower than the Gen II assay.

Interestingly, the Roche reference values differ more than the expected 20% from the Beckman reference values (Table 2). Since the Roche values are based on relatively small numbers per group (N=28-149) these ranges need more extensive series. However, in 2015 a study by Anderson et al. (6) showed that the Roche AMH assay shows good correlation with age and antral follicle count in women of reproductive age, providing a reproducible measure of the total follicle pool. Nevertheless, more extensive clinical validation studies are necessary to strengthen the clinical utility of the Roche AMH assay. Moreover, contrary to the well studied Beckman reference values (7) the Roche reference values do lack subgroup ranges for men.

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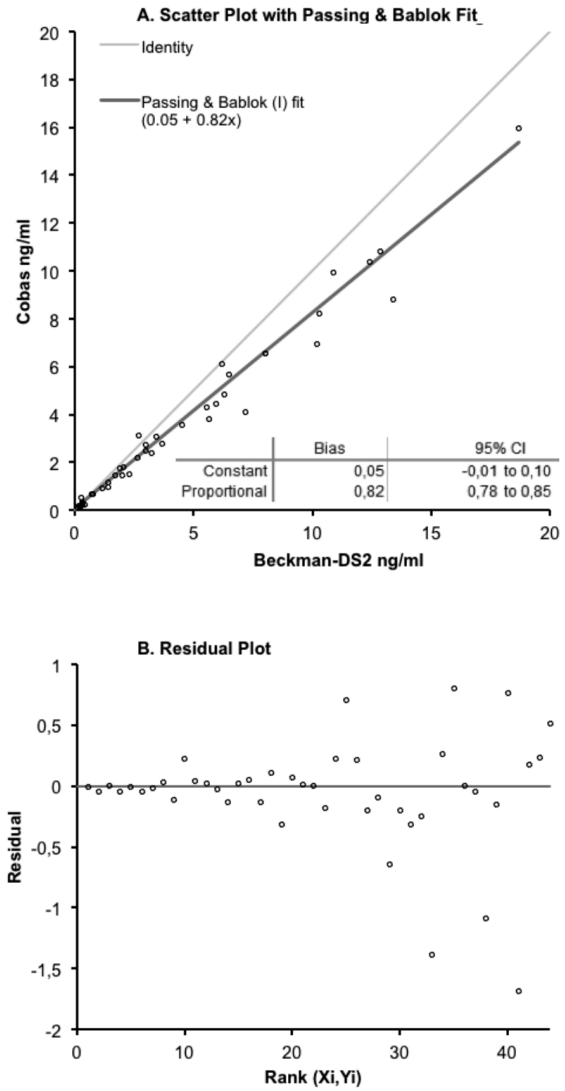

Figure 1. (A) Scatter plot with Passing- Bablock fit and (B) Residual plot of the two assays

Eventually, both assays are suitable for AMH measurement with the new Roche assay showing better analytical performance. Furthermore, the fully automated Roche assay allows access to in house AMH measurement for more centers compared to the Beckman method.

Table 2. Manufacturers reference values.

Beckman Gen II

Women	ng/mL
< 30 jaar	0,52 - 12,01
31 - 35 years	0,35 - 11,84
36 - 40 years	0,33 - 9,68
41 - 45 years	0,26 - 8,78
46 - 50 years	0,22 - 6,34
Post-menopausal	< 0,1

Men	ng/mL
Umbilical cord	7 - 48
2 - 6 months	105 -270
6 months - 4,5 years	55 - 196
4,5 - 6 years	45 - 187
G1	42 - 156
G2	6 -157
G3	3-103
G4	2-16
G5	3-18
>21 years	2-14

Roche

Women	ng/mL
20 - 24	1.66 - 9.49
25 - 29	1.18 - 9.16
30 - 34	0.672 - 7.55
35 - 39	0.777 - 5.24
40 - 44	0.097 - 2.96
45 - 50	0.046 - 2.06
PCOS pts	2.41 - 17.1

Men	ng/mL
>21 years	1.43 - 11.6

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