Relevancy of serum ionized magnesium in clinical chemistry

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Chapter 5

Serum Ionized Magnesium:
Comparison of Results Obtained with Three Ion-Selective Analyzers
Chapter 2

Serum/Ionixed Measurement

Comparison of Results Obtained with Three Ion-Sieve Analyzers
Comparison of three Mg ion-selective analyzers

Serum Ionized Magnesium:
Comparison of Results Obtained with Three Ion-Selective Analyzers

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Summary

In a two-center (Academic Medical Center, The Netherlands, and National Institutes of Health, USA) study, we compared ionized magnesium results in serum determined with the AVL 988/4, KONE Microlyte 6 and NOVA CRT, which are the currently available analyzers equipped with a magnesium ion-selective electrode. The comparison was performed with frozen serum samples from healthy volunteers and patients. Imprecision and reference intervals were established.

We found the best agreement between the KONE (x) and AVL (y) magnesium ion-selective electrodes ($y = 0.972x - 0.013; n = 138$) with samples from patients. With samples from healthy volunteers, all three analyzers reported significantly different results ($p < 0.05$). Best precision was found using the NOVA; coefficients of variation established at three levels were all <4.0%. Coefficients of variations for the AVL and KONE were <5.0% at normal and high ionized magnesium concentrations, but 10.7% and 9.4%, respectively, at a concentration of about 0.30 mmol/L. The reference intervals (mean ± standard deviation) based on measurements in fresh serum samples were different for each analyzer: 0.55-0.63 mmol/L for AVL, 0.47-0.57 mmol/L for KONE and 0.43-0.55 mmol/L for NOVA.

Thus, significant differences among the ionized magnesium concentration obtained with the three analyzers, limit comparison of results in clinical practice, and need to be resolved (e.g. improvement of specificity and standardization of calibrators).
Introduction

Since 1980 several studies have been published about the development of ionophores selective for magnesium (Mg). In 1990 this research resulted in two papers about the measurement of the ionized Mg concentration (iMg\(^{2+}\)) in human serum \{1,2\}. Hereafter evaluation reports about commercially available analyzers equipped with an ion-selective electrode (ISE) were published \{3-5\}, followed by studies on Mg fractions in serum \{6,7\}, establishment of reference intervals, and influence of pH, heparin and other pre-analytical factors \{8-13\}.

In these studies, Mg ion-selective electrodes (Mg-ISE's) obtained from three different manufacturers were used: AVL, KONE, and NOVA.

Comparison of two of the Mg-ISE's was done by Altura et al. in 1994 \{14\}. In a small study they measured serum iMg\(^{2+}\) (iMg\(^{2+}\)) from 13 healthy volunteers and 21 hospitalized patients using the KONE and the NOVA analyzers. The AVL and NOVA analyzers were compared in four studies by the coauthors of the present study from the National Institutes of Health (NIH), Bethesda, MD, USA \{13,15-17\}. However, until now no study has compared all three commercially available Mg-ISE's.

We report a two-center comparison study comparing the three currently commercially available Mg-ISE's. Serum obtained from both patients and healthy volunteers was collected, and iMg\(^{2+}\), determined at two different locations: the Academic Medical Center (AMC) (Amsterdam, The Netherlands) provided the AVL 988/4 and KONE Microlyte 6 results, and the NIH (Bethesda, USA) provided the NOVA results.

Material and Methods

Analyzers

The AVL 988/4 (AVL Medical Instruments AG, Schaffhausen, Switzerland), KONE Microlyte 6 (KONE Instruments, Espoo, Finland), and NOVA CRT (NOVA Biomedical, Waltham, MA, USA) analyzers were described previously \{4,15\}. Briefly, the ion-selective membrane of the Mg electrode contains a neutral carrier ionophore (ETH 7025 for AVL, ETH 5220 for KONE, proprietary for NOVA) dispersed in a polyvinylchloride (PVC) matrix. The electrode is calibrated with aqueous calibrators at the following Mg/Ca concentrations: 0.30/0.90, 0.30/1.25, 0.90/0.90, 0.30/0.90 mmol/L for AVL, 0.30/0.75, 0.30/1.75, 0.60/1.25 mmol/L for KONE, and 0.50/1.00, 0.50/2.00 and 1.50/1.00 mmol/L for NOVA. The manufacturer warrants the analytical range of 0.1 to 3.0 mmol/L for AVL, 0.2 to 3.0 mmol/L for KONE and 0.1 to 2.5 mmol/L for NOVA Mg-ISE. Each analyzer
automatically corrects for the response of the Mg-ISE to the free calcium in the sample (chemometric correction). The KONE and NOVA analyzers automatically provide the i\(Mg^{2+}\), result corrected to pH of 7.40 (i\(Mg^{2+}_{\text{pH=7.4}}\)). The NOVA analyzer reports these results only for samples with pH between 6.9 and 7.8; for KONE no pH restriction was specified.

An atomic absorption spectrometer (AAS) (PE 2100, Perkin Elmer, Gouda, The Netherlands) was used to determine serum total Mg concentration (tMg\(_s\)).

**Samples**

Samples were collected at both locations from 138 presumably healthy volunteers (AMC: 25 males, 44 females, median age 37.5 years, range 21-61 years; NIH: 26 males, 43 females; median age 37 years, range 20-62 years) and patients (AMC: n=90, NIH: n=8). Healthy volunteers had their breakfast and did not use Mg supplements. Patients with both a normal and abnormal tMg\(_s\), (e.g. hemodialysis patients or patients treated by cisplatin) were included in the study.

The same three-level lyophilized human-based control sera, produced in one batch (Nycomed AS, Diagnostics, Oslo, Norway), were used at both institutes as a control.

**Procedures**

The blood was drawn anaerobically in silicone-free tubes (Vacutainer ref. 362745, Becton Dickinson BV, Leiden, The Netherlands). The separated serum was analyzed within 1 hour of drawing (fresh samples) on AVL, KONE (both at AMC) and NOVA (NIH). Two aliquots of each sample (#1 and #2) were stored in air-tight capped plastic tubes (Microtubes, Sarstedt BV, Etten-Leur, The Netherlands) at -20 °C (frozen samples). The tubes were filled completely and the aliquotting was performed with minimal exposure of sample to air. The #1 aliquots were stored at the location of drawing and the #2 aliquots were shipped on dry ice to the other location. The aliquots were stored for up to 9 months. The subsequent determinations of pH, i\(Mg^{2+}\), and tMg\(_s\), were coordinated so that the same frozen aliquots were analyzed at both locations on the same day, #1 at initiating laboratory and #2 at the other laboratory. The capped tubes were allowed to stand at room temperature for 1 hour, the samples were mixed, and immediately analyzed.

All samples were analyzed for i\(Mg^{2+}\), pH and tMg\(_s\), and when provided by the analyzer, the i\(Mg^{2+}_{\text{pH=7.4}}\) was recorded. The measurements were performed in duplicate and the data were analyzed using the calculated mean of duplicates.

Because comparison of the i\(Mg^{2+}\), results was based on frozen samples, we evaluated the effect of storage at -20 °C on the i\(Mg^{2+}\) results of each analyzer by comparing i\(Mg^{2+}\) of fresh and #1 frozen aliquots. Differences between the fresh and frozen i\(Mg^{2+}\)
results were analyzed using the paired t-test. The effect of transport on dry ice was evaluated by comparing the pH of 1# frozen aliquots stored in Amsterdam with pH values from the #2 aliquots after shipping to NIH. Differences were analyzed by the paired t-test.

Method imprecision was determined by daily measurement of the three control sera and was expressed as the coefficient of variation (CV) of the calculated mean iMg$^{2+}$. The reference interval for the iMg$^{2+}$ was calculated as the mean ± SD using the results for the fresh samples from healthy volunteers. Comparison of the results obtained with the three analyzers and the correlation between iMg$^{2+}$ and tMg, was calculated by debiased regression according to Passing and Bablok \{18\}. The mean difference between the iMg$^{2+}$ results was calculated by the paired t-test. Statistical analysis was done with SPSS, version 6.1.3 (SPSS Benelux BV, Gorinchem, The Netherlands) and Evalkit, version 3.1 (Tilburg, The Netherlands). Values of p<0.05 (two-tailed) were considered significant.

All procedures were in accordance with the ethical standards laid down in the Helsinki Declaration of 1975, as revised in 1983.

Results

Imprecision
The results from the daily measurements of the three control sera are summarized in Table 1. The imprecision (expressed as percentage of CV) of the NOVA measurements at all three iMg$^{2+}$ levels was <4%. For the AVL and KONE analyzers, the imprecision was <5.0% at iMg$^{2+}$ ≥ 0.65 mmol/L, but at iMg$^{2+}$ close to 0.30 mmol/L, the imprecision was 9.4% and 10.7%, respectively.

<table>
<thead>
<tr>
<th>Analyzer</th>
<th>Days</th>
<th>Level 1</th>
<th>Level 2</th>
<th>Level 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n)</td>
<td>Concentration (mmol/L)</td>
<td>CV (%)</td>
<td>Concentration (mmol/L)</td>
</tr>
<tr>
<td>AVL</td>
<td>20</td>
<td>0.32</td>
<td>9.4</td>
<td>0.65</td>
</tr>
<tr>
<td>KONE</td>
<td>20</td>
<td>0.28</td>
<td>10.7</td>
<td>0.65</td>
</tr>
<tr>
<td>NOVA</td>
<td>19</td>
<td>0.21</td>
<td>3.6</td>
<td>0.53</td>
</tr>
</tbody>
</table>

Comparison study
Data from the method comparison study for iMg$^{2+}$ results of the frozen samples are summarized in Table 2 and Figure 1. The table shows the slope, intercept and mean
Table 2. Comparison of the AVL, KONE and NOVA magnesium ion-selective electrodes

<table>
<thead>
<tr>
<th>X vs. Y</th>
<th>Number</th>
<th>Slope</th>
<th>Intercept</th>
<th>Mean diff. X minus Y</th>
<th>p-value</th>
<th>Number</th>
<th>Slope</th>
<th>Intercept</th>
<th>Mean diff. X minus Y</th>
<th>p-value</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Healthy volunteers</td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>iMg^{2+} at actual pH:</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KONE vs. AVL</td>
<td>138</td>
<td>0.765</td>
<td>0.134</td>
<td>-0.01</td>
<td>&lt;0.001</td>
<td>98</td>
<td>0.972</td>
<td>-0.013</td>
<td>0.03</td>
<td>0.003</td>
</tr>
<tr>
<td>(0.667-0.875)</td>
<td>(0.073-0.187)</td>
<td>(-0.015-0.005)</td>
<td></td>
<td></td>
<td>(0.917-1.033)</td>
<td>(-0.042-0.026)</td>
<td>(0.011-0.052)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AVL vs. NOVA</td>
<td>138</td>
<td>1.667</td>
<td>-0.43</td>
<td>0.07</td>
<td>&lt;0.001</td>
<td>98</td>
<td>0.688</td>
<td>0.095</td>
<td>0.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(1.333-2.000)</td>
<td>(-0.620-0.247)</td>
<td>(0.058-0.074)</td>
<td></td>
<td></td>
<td>(0.636-0.750)</td>
<td>(0.065-0.124)</td>
<td>(0.060-0.098)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KONE vs. NOVA</td>
<td>138</td>
<td>1.111</td>
<td>-0.107</td>
<td>0.06</td>
<td>&lt;0.001</td>
<td>98</td>
<td>0.676</td>
<td>0.094</td>
<td>0.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(1.000-1.333)</td>
<td>(-0.225-0.050)</td>
<td>(0.048-0.064)</td>
<td></td>
<td></td>
<td>(0.605-0.750)</td>
<td>(0.053-0.133)</td>
<td>(0.086-0.136)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

iMg^{2+} at pH between 6.9 and 7.8 only:

| KONE vs. NOVA | 88 | 1.000 | -0.040 | 0.05 | <0.001 | 83 | 0.698 | 0.098 | 0.09 | <0.001 |
| (0.667-1.333) | (-0.232-0.152) | (0.037-0.059) | | | (0.611-0.788) | (0.050-0.145) | (0.068-0.112) | | |

Results for debiased regression (Passing and Bablok) and the paired t-test. Values of slope and intercept printed bold were not significantly different from 1.0 and 0.0, significantly (p>0.05). 95% confidence intervals of slope and mean difference are printed in parentheses.
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difference including their 95% confidence interval (CI) for the healthy volunteers and patients. The figure shows the relationship between tMg_s (x) and iMg^{2+}_s (y) for the normal and patient population. Based on iMg^{2+} (not pH corrected) obtained in patient samples, the AVL and KONE results are not significantly different, but in samples from healthy volunteers all analyzers gave different iMg^{2+}. However, the mean difference between the KONE and AVL iMg^{2+} results was only 0.0097 mmol/L (paired t-test, p < 0.001). When using iMg^{2+}_{pH=7.4} values, the KONE and NOVA reported comparable iMg^{2+} in samples from healthy volunteers, but significantly different values in samples obtained from patients.

The mean difference (frozen minus fresh) between iMg^{2+} in fresh and iMg^{2+} in stored frozen serum samples was calculated for each analyzer. AVL (69 healthy volunteers plus 90 patients): mean -0.02 mmol/L, 95% CI -0.025--0.007 mmol/L, p < 0.001; KONE (69 healthy volunteers plus 90 patients): mean +0.01 mmol/L, 95% CI -0.007-0.018 mmol/L, p=0.367 and NOVA (69 healthy volunteers plus 8 patients): mean -0.03 mmol/L, 95% CI -0.036--0.021 mmol/L, p< 0.001. The mean difference (shipped minus non-shipped) between the pH of frozen shipped and pH of frozen non-shipped serum samples was -0.006, 95% CI -0.012--0.001, p=0.02.

Reference interval

Table 3 shows the AVL, KONE and NOVA reference intervals for iMg^{2+}, and the mean value for serum tMg_s. For comparison, the table also shows reference intervals that have been published previously. The highest mean iMg^{2+}_s in this study with samples from healthy volunteers was obtained with the AVL (0.59 mmol/L), while the mean value measured by both the KONE and NOVA were substantial lower, 0.52 and 0.49 mmol/L, respectively.

Discussion

Reproducibility

The imprecision of the iMg^{2+}, measurement in the middle and high range (0.65-1.10 mmol/L) is comparable for all three analyzers (Table 1). AVL and KONE showed greater imprecision at low iMg^{2+} (=0.30 mmol/L), whereas the NOVA analyzer performed better (3.6% at iMg^{2+} 0.21 mmol/L). The high CV (10.7%) of level 1 measured with the KONE may be explained by the lower limit of linearity found by van Ingen et al. (0.30 mmol/L) {4}, which is higher than that specified by the manufacturer (0.20 mmol/L). Maj-Zurawska et al. {2} reported a CV of 3.6%, but their lowest control level had a Mg concentration of 0.44 mmol/L. However, a CV of 3.0%, obtained using a human serum sample with iMg^{2+}
of 0.35 mmol/L, has also been reported \{21\}. In previously published studies \{11,15,20\} better results for the AVL were found. However, in all those studies AVL control material was used, which is a bovine albumin-based electrolyte solution; our results were based on lyophilized human-based serum. The characteristics of the control material seem to have less influence on the NOVA Mg-ISE. Hristova \textit{et al.} \{15\} used NOVA controls (bovine albumin-based electrolyte solution) and reported a CV of 4.5\%, which is even higher than our value of 3.6\% with lyophilized human-based serum.

\textbf{Comparison study}

The best agreement among the three analyzers was between the KONE and AVL (Table 2, Figure 1) where the measured iMg$^{2+}$, did not differ significantly with patient specimens. The results obtained using the NOVA analyzer showed iMg$^{2+}$ in these specimens that was significantly lower than the AVL and KONE iMg$^{2+}$. In sera obtained from healthy volunteers, all analyzers gave different results. When studying healthy volunteers (Figure 1), a large scatter of points and thus a wide 95\% CI of the slope and intercept, for the KONE and NOVA analyzers can be seen. The large variation of iMg$^{2+}$ in healthy volunteers with a similar tMg is probably the cause of the lack of correlation between these two analyzers and the AVL. Calculations based on iMg$^{2+}$, pH=7.4 values showed that the KONE and NOVA analyzers gave comparable results in the group of healthy volunteers (Table 2), but the 95\% confidence interval of the slope and intercept was large. Because only samples with pH between 6.9 and 7.8 were included, this comparison was based on 88 samples instead of 138 samples. When comparing KONE and AVL iMg$^{2+}$ (both not pH corrected) based on these 88 sera, slope and intercept (0.857 and 0.073 mmol/L, respectively) were also not significantly different from 1.0 and 0.0, respectively.

Another study found similar results to ours. Hristova \textit{et al.} \{15\}, who compared the pH, Na, Ca and Mg results of the NOVA analyzer with those of the AVL, reported a significant different for iMg$^{2+}$ in specimens from healthy volunteers. In specimens from 51 patients, the AVL and NOVA analyzers were found to correlate ($r$=0.837, $p<0.001$). However, after excluding the results of the five samples with the lowest iMg$^{2+}$ (iMg$^{2+}$<0.35 mmol/L) the correlation coefficient decreased to 0.741. In our study the same phenomenon was observed. When comparing AVL and NOVA with samples from patients with an iMg$^{2+}$, below the mean reference value ($n=41$), a slope (0.870) and intercept (0.026 mmol/L) were found that did not differ significantly from 1.0 and 0.0 mmol/L, respectively. In a second study of Hristova \textit{et al.} \{17\}, iMg$^{2+}$, was measured with both analyzers in chronic alcoholics, and the difference in the iMg$^{2+}$, was significantly. But, in this specific patient population the correlation between NOVA and AVL at low iMg$^{2+}$, ($\leq$0.38 mmol/L) was worse than at normal and high iMg$^{2+}$. In one preceding study the
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KONE analyzer was compared with the NOVA analyzer. Serum obtained from only 12 healthy volunteers and 21 randomly-selected hospitalized patients was first measured in Germany (KONE) and then sent to the USA for measurement on the NOVA analyzer. In this small study, a comparable mean iMg$^{2+}$, was found for both analyzers \{14\}.

The comparison study was performed on frozen specimens since two different institutes were involved. Transport of the frozen aliquots on dry ice between the two institutes compared to the initial frozen aliquots effected a minimal change of pH (-0.006, shipped minus non-shipped), which has an undetectable influence on iMg$^{2+}$. Because iMg$^{2+}$ was measured in both fresh and frozen samples at the institute of collection, fresh vs. frozen comparisons were done with all specimens for each analyzer. Based on measurements performed with the AVL and NOVA analyzers, a significantly different iMg$^{2+}$ was found. However, these differences (frozen minus fresh) were comparable and minor, -0.02 and -0.03 mmol/L, respectively. The mean difference determined with the KONE analyzer was even smaller (+0.01 mmol/L), but the 95% CI, which enclosed 0.0, was larger than that of the AVL and NOVA analyzers.

This suggests that the influence of freezing on a serum sample
measured by the KONE analyzer has greater imprecision, while for the AVL and NOVA analyzers freezing seems, as expected, to induced a relative constant negative bias in the iMg\(^{2+}\), due to a decreased H\(^+\) concentration. The KONE finding corresponds to the results published by Sanders et al. {12} who investigated the influence of storage at +4\(^{\circ}\)C, -20\(^{\circ}\)C and -80\(^{\circ}\)C. They also found a positive and negative deviation with the KONE. Based upon their data they advised a maximum period of storage of 3 months at -20\(^{\circ}\)C, after this period of storage the pH of all their samples exceeded 7.8. However, in our population the pH of only a limited number of samples, measured by the KONE, increased due to storage up to >7.8, and exclusion of these values did not influence the mean difference between fresh and frozen iMg\(^{2+}\), (mean difference 0.10 mmol/L, p >0.05, n=145).

**Reference interval**

In addition to the differences between the analyzers noted above, also different reference intervals for healthy volunteers were obtained with each instrument. From the overview in Table 3, it can be concluded that the iMg\(^{2+}\), reference interval not only depends on the manufacturer of the Mg-ISE, but also on the reference population tested. For example, the mean iMg\(^{2+}\), for the AVL analyzer ranges from 0.52 mmol/L {15} to 0.60 mmol/L {11}. The mean iMg\(^{2+}\), reference value for the NOVA analyzer ranges from 0.49 mmol/L (this study) to 0.58 mmol/L {3}. When studying all results presented in Table 3, it is striking that the difference between the highest and lowest reported mean iMg\(^{2+}\), is even larger than the difference between the highest and lowest reported mean tMg, (0.11 and 0.09 mmol/L, respectively), while for the biologically active iMg\(^{2+}\) fraction a more narrow range would be expected.

Some results in this study are difficult to explain. The KONE and NOVA analyzers give comparable iMg\(^{2+}\), \(\text{pH}=7.4\) results in the group of healthy volunteers but significantly different iMg\(^{2+}\), \(\text{pH}=7.4\) results in the patient population. When comparing the KONE and AVL iMg\(^{2+}\), results, the opposite was found (Table 2). Moreover, the KONE and AVL analyzers measured comparable iMg\(^{2+}\) in control level 2 (0.65 mmol/L), but did not show a similar reference interval. The mean iMg\(^{2+}\) of control level 3 measured by the NOVA and AVL analyzers was similar (1.03 mmol/L and 1.01 mmol/L, respectively) but the between-analyzer difference in patient samples increased with increasing iMg\(^{2+}\), (Figure 1).

Therefore, it can be concluded that not only different calibration methods or incomplete chemometric correction for the iCa\(^{2+}\) interference are responsible for the discrepancies between the analyzers {16}, but also the characteristics of the Mg ion-selective membranes. The most important component, the ionophores, used in the KONE and AVL Mg ion-selective membranes, are both developed at the Swiss Federal Institute of Technology (ETH
Comparison of three Mg ion-selective analyzers

Table 3. Mean total and ionized magnesium concentrations and the reference interval of ionized magnesium in serum from healthy volunteers. Literature overview.

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of tested samples</th>
<th>Mean magnesium concentration</th>
<th>Reference interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>tMg(_s), (mmol/L)</td>
<td>iMg(^{2+}), (mmol/L)</td>
</tr>
<tr>
<td>AVL analyzer:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sachs et al. {19}</td>
<td>91</td>
<td>0.88</td>
<td>0.57</td>
</tr>
<tr>
<td>Hristova et al. {15}</td>
<td>50</td>
<td>0.82</td>
<td>0.52</td>
</tr>
<tr>
<td>Filos et al. {20}</td>
<td>100</td>
<td>0.79</td>
<td>0.54</td>
</tr>
<tr>
<td>Zoppi et al. {11}</td>
<td>103</td>
<td>0.85</td>
<td>0.60</td>
</tr>
<tr>
<td>Hristova et al. {17}</td>
<td>40</td>
<td>0.85</td>
<td>0.56</td>
</tr>
<tr>
<td>This study*</td>
<td>70</td>
<td>0.85</td>
<td>0.59</td>
</tr>
<tr>
<td>KONE analyzer:</td>
<td></td>
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</tr>
<tr>
<td>Ingen van et al. {4}</td>
<td>76</td>
<td>0.86</td>
<td>0.56</td>
</tr>
<tr>
<td>Ising et al. {8}</td>
<td>79</td>
<td>0.85</td>
<td>0.55</td>
</tr>
<tr>
<td>Huijgen et al. {6}</td>
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<td>0.88</td>
<td>0.56</td>
</tr>
<tr>
<td>This study*</td>
<td>68</td>
<td>0.85</td>
<td>0.52</td>
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<td>NOVA analyzer:</td>
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<tr>
<td>Altura et al. {3}</td>
<td>60</td>
<td>0.81</td>
<td>0.58</td>
</tr>
<tr>
<td>Hristova et al. {15}</td>
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</tr>
<tr>
<td>Hristova et al. {17}</td>
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<td>0.50</td>
</tr>
<tr>
<td>This study*</td>
<td>72</td>
<td>0.82</td>
<td>0.49</td>
</tr>
</tbody>
</table>

In reference 8 and 15 the reference interval was defined by a non-parametric method, in all other studies the reference interval was defined as mean ± SD; *samples collected at the AMC; b samples collected at the NIH 5220 and ETH 7025, respectively). These molecules show certain similarity in their structures; they are both built of units of malondiamides bridged by octanes \{22,23\}. Of course the characteristics of an ion-selective membrane is not only determined by the structure of the ionophore, but also by the concentration of anionic sites (e.g. potassium tetrabutyl-borate) and plasticizers used. However, similar structure of the ionophores used in the AVL and KONE membrane could be the explanation for the concordance found in the comparison study. Unfortunately, the composition of the NOVA Mg-ISE is still proprietary.

In conclusion, this study shows that iMg\(^{2+}\) concentration measured in serum samples depends on the analyzer used. Here it is demonstrated that, based on serum samples obtained from patients, best agreement was found between the AVL 988/4 and KONE...
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Microlyte 6. The NOVA CRT iMg$^{2+}$ results were lower on average. The reference intervals were different for each analyzer. Therefore, we conclude that the Mg-ISE's can be used for patient care only if accessory reference intervals are established. We recommend improvements to the specificity of electrodes, research on interference of common drugs, and standardization of calibrators and control materials.

References


