Stability of BUN and Creatinine Determinations on the Siemens Advia 1800 Analyzer

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Background: Serum creatinine values of patients tend to change as a result of the use of different blanks used for creatinine determinations on the Advia 1650. After upgrading the analyzer to the Advia 1800, creatinine values tended to be more reproducible. As part of a quality assurance investigation to test the reproducibilities of creatinine values, we determined serial creatinine values in the sera of 13 patients whose initial values were either in the reference range or elevated (range 0.58–7.8 mg/dl). These values were determined concurrently with serum blood urea nitrogen (BUN) determinations (range 6.0–84.4 mg/dl) as these two analytes are used together in evaluation of renal function. **Methods:** We determined BUN and creatinine values, using the glutamate dehydrogenase lined enzyme assay system and the Jaffe method, respectively. **Results:** We

find that all values for creatinine on samples stored at 4°C were reproducible as were the corresponding BUN values, which is revealed by low values for the coefficients of variation (CVs), that is, mean CV of 4.55% for creatinine and 2.52% for BUN. One sample with relatively high CV (10.6%) for creatinine was found to have an initial value of 1.1 mg/dl, in the reference range; but, on repeat determinations, the obtained levels were as high as 1.5 mg/dl, above the reference range. BUN values for this sample remained in the reference range, suggesting that no renal disease was present. **Conclusion:** We conclude that creatinine and BUN determinations are stable, but occasional spurious creatinine values can occur on the Advia 1800 analyzer. J. Clin. Lab. Anal. 27:435–437, 2013.

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INTRODUCTION

As part of a general quality assurance program in clinical chemistry, we have been following the stabilities of determinations on what are commonly known as stat analytes. These include electrolytes (sodium, potassium, chloride, bicarbonate, calcium), glucose, urea (blood urea nitrogen [BUN]), and creatinine. This quality assurance activity is motivated by the requests made to the Laboratory Service at our hospital for repeated determinations of one or more of these analytes in particular patients. While these requests are infrequent, they are critical since there may be doubt as to their validity, and the need for assurance of reproducibility is high.

Several years ago, the Bayer 1650 Advia chemistry analyzer utilized a blank for creatinine determinations that gave somewhat higher values than those of other manufac-

turers. This resulted in lower values for serum creatinine determinations. After approximately 1 year, the higher blanks were replaced by more conventional ones, giving creatinine values that were comparable to the ones obtained on other chemistry analyzers. During the transition time, there were discrepancies on serum creatinine value in patients, which resulted from the change in blanks.

After Bayer was replaced by the Siemens Corporation, which then upgraded our Advia 1650 analyzers to the

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Advia 1800 analyzers, as a check on creatinine reproducibility we endeavored to examine the reproducibility of serum creatinine values. Since serum urea determinations are performed concurrently with serum creatinine determinations, we have also explored the stabilities of urea (BUN) determinations.

In separate studies, we have examined the reproducibility on the Siemens Advia 1800 chemistry analyzer for electrolyte (1) and glucose determinations (2). In both areas, we have found quite low coefficients of variation for all of these analytes measured on groups of patients over extended time periods. We now present our findings on the reproducibility of determinations for serum creatinine and BUN.

METHODS

Thirteen serum samples at the Brooklyn Campus of the New York Harbor VA Medical Center that were within 1 day of disposal (i.e., the samples had been retained for 6 days) were selected such that assay results for BUN and creatinine fell either within or above the normal reference range for these analytes. The respective values were determined and recorded over an additional 9-day period at 24-hr intervals. The total time span for these determinations was therefore 15 days, that is, 6 days after the initial determination plus an additional 9 days of daily assays. The specimens were stored in the specimen refrigerator at 4°C during the duration of this study. As far as we are aware, there are no studies on the stabilities of these two analytes over the extended time period of 15 days as in this current study. Determination of all values was performed on the Siemens Advia 1800 chemistry analyzer using the Jaffe method (formation of a complex of creatinine with picric acid) for creatinine and urease-catalyzed release of

ammonia measured by the glutamate dehydrogenase system (3) (Siemens Corp., Tarrytown, NY, USA).

RESULTS

- (1) **Urea (BUN).** The values of BUN over the 15-day period are summarized in Table 1. Mean BUN values for each patient sample ranged from 6.0 to 84.4 mg/dl over the course of the study, with seven samples (53%) falling within the normal reference range (6.0–22.0 mg/dl), and the remaining six samples above the normal reference range. The values obtained on the first day of the study, day 6 (column 2 in Table 1), are almost exactly the same as those initially found for each sample on day 1 (column 1 in Table 1). The coefficient of variation (CV) for each sample ranged from 0 to 5.0%, with an average CV of 2.52%. Samples 4 and 12 showed no deviation in BUN values. Thus, the precision for serum BUN determination on the Advia 1800 analyzer is quite high.
- (2) **Creatinine.** As shown in Table 2, for creatinine, mean values ranged from 0.58 to 7.8, with seven samples (53 percent) falling within the normal reference range (0.4–1.2 mg/dl) and six above the normal reference range (see table 2). The CV for each creatinine sample ranged from 1.4 to 10.6% with an average CV of 4.55%. As with the BUN results, the values for creatinine on day 6, the first day of the sequential stability study (column 2 in Table 2), were quite similar to those found initially for each sample (column 1 in Table 2) with the exception of the creatinine value in sample 2 that increased from 0.8 to 1.0 mg/dl and the creatinine value in sample 6 that decreased from 1.3 to 1.1 mg/dl.

TABLE 1. Patients' BUN Values

Patient	BUN values, mg/dl (reference range 6–22)										SD	CV(%)
	Day 1	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 14	Day 15	Mean		
1	15	15	16	15	15	15	15	16	15	15.22	0.44	2.90
2	22	23	24	24	23	23	23	24	23	23.22	0.67	2.87
3	46	45	47	47	46	46	45	47	46	46.11	0.78	1.70
4	21	21	21	21	21	21	21	21	21	21.0	0.0	0.0
5	11	10	11	11	10	10	10	11	10	10.44	0.53	5.05
6	11	11	11	10	10	11	10	11	11	10.67	0.50	4.69
7	35	36	37	37	36	36	35	37	36	36.11	0.78	2.16
8	25	26	27	26	26	26	25	26	26	25.89	0.60	2.32
9	83	84	85	85	85	85	84	86	83	84.44	1.01	1.20
10	8	9	9	9	9	9	9	9	9	8.89	0.33	3.75
11	55	55	55	56	56	56	55	57	55	55.56	0.73	1.31
12	6	6	6	6	6	6	6	6	6	6.0	0.0	0.0
13	9	9	10	9	9	9	9	10	9	9.22	0.44	4.78

BUN, blood urea nitrogen; SD, standard deviation; CV, coefficient of variation.

TABLE 2. Patients' Creatinine Values

Patient	Creatinine values, mg/dl (reference range 0.4–1.2)										SD	CV(%)
	Day 1	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 14	Day 15	Mean		
1	0.9	0.9	0.9	0.9	1.0	0.9	0.9	1.0	0.9	0.92	0.04	4.78
2	0.8	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.98	0.07	6.82
3	4.7	4.7	4.6	4.8	4.8	4.7	4.6	4.7	4.8	4.71	0.08	1.66
4	1.4	1.4	1.3	1.4	1.4	1.4	1.4	1.4	1.4	1.39	0.03	2.4
5	0.9	0.9	0.9	0.9	1.0	0.9	0.9	0.9	1.0	0.92	0.04	4.78
6	1.3	1.1	1.2	1.5	1.5	1.5	1.3	1.3	1.3	1.33	0.14	10.61
7	3.3	3.3	3.3	3.4	3.4	3.4	3.3	3.4	3.5	3.37	0.07	2.10
8	0.7	0.7	0.7	0.7	0.8	0.7	0.7	0.7	0.8	0.72	0.04	6.11
9	7.7	7.8	7.6	7.9	7.9	7.8	7.7	7.9	7.9	7.80	0.11	1.43
10	1.1	1.1	1.1	1.1	1.2	1.1	1.1	1.1	1.2	1.12	0.04	3.93
11	4.1	4.2	4.1	4.2	4.3	4.2	4.1	4.3	4.3	4.20	0.09	2.06
12	0.5	0.6	0.5	0.6	0.6	0.6	0.6	0.6	0.6	0.58	0.04	7.63
13	0.7	0.7	0.6	0.7	0.7	0.7	0.7	0.7	0.7	0.69	0.03	4.84

SD, standard deviation; CV, coefficient of variation.

The one sample, highlighted in entry 6, Table 2, for which we found the highest CV of 10.6% gave results that ranged from 1.1 to 1.5 mg/dl or 0.4 mg/dl. The actual values for creatinine were found to be initially elevated at 1.3 mg/dl which then fell to a value of 1.1 mg/dl within the reference range as can be seen in the highlighted row 6 in Table 2. A value within the reference range (1.2 mg/dl) was found on the next day; however, all subsequent values were found to be elevated and reached values of 1.5 mg/dl on days 9–11 that decreased to 1.3 mg/dl (still elevated) thereafter. Importantly, the BUN for the same sample remained within the reference range with a relatively low CV of 4.7% as highlighted in Table 1.

DISCUSSION

For both BUN and creatinine, the CVs were low, indicating a high degree of stability for these analytes. Overall, the average CV for creatinine was higher than that for BUN as might be expected by the lower absolute values of the former, rendering minor changes more significant. Thus, the samples with lower absolute creatinine values showed a higher CV and vice versa.

The maximum CV obtained was 10.6% for creatinine (sample 6, highlighted in Table 2) which is about five times higher than that for sample 4 that had the lowest CV of 2.4%. While other samples were found to have higher CVs, such as sample 12 (7.6%), the actual value changes were relatively low, and the values remained in the reference range. Only in the case of sample 6 did the values for creatinine change in such a manner as to affect its occurrence in or above the reference range. The reasons for the high CV found for this sample are not clear. Further investigation of this issue is warranted.

Thus, for sample 6, based strictly on the creatinine values, it would be impossible to determine whether renal pathology is present. While the second and third values were within the reference range, the first value and values after day 8 were either mildly elevated or significantly elevated to 1.5 mg/dl on days 10 and 11 as seen in the highlighted row in Table 2. The fact that the BUN was always within normal limits suggests that renal pathology was not present. Thus, borderline values of creatinine, that is, ones that lie close to the upper limit of the reference range, may show some imprecision (here a CV of more than 10%) and may render results that are nondiagnostic.

CONCLUSION

The precision of the serum BUN assays on the Advia 1800 analyzer is quite high over the prolonged time period of 15 days. The same conclusion applies to serum creatinine assay results on this analyzer with the caveat that borderline values can show less precision-making evaluation of renal function more difficult.

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