AN ASSESSMENT OF THE "AVERAGE OF NORMALS" QUALITY CONTROL METHOD

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SUMMARY

The "average of normals" laboratory quality control method has been assessed by adding increments to patient results to simulate systematic laboratory errors and applying the control procedure to the erroneous data. Results for eight plasma constituents were examined with simulated errors in the range 3–30%.

In the majority of instances, the "average of normals" quality control procedure failed to detect the error. It is concluded that this procedure is relatively insensitive to shifts in method calibration.

INTRODUCTION

The "average of normals" quality control procedure involves calculation of the average of patients' results falling within the normal range for the test concerned. This average is then compared with pre-determined control limits and any deviation outside these limits taken to indicate a shift in calibration of the method. The procedure has the potential advantage that no special quality control material is required. We have assessed the procedure by testing its ability to detect systematic shifts in method calibration.

METHODS

Blood samples were obtained from healthy persons and from patients. The healthy persons were members of the hospital staff, their relatives and friends. Patients were mainly In-patients of the Alfred Hospital, Melbourne, but a few were Out-patients. The healthy persons fasted overnight before blood collection but only some of the patients fasted.

Blood samples were collected into plastic tubes containing lithium heparin as anti-coagulant. The same persons collected the blood from both groups, and in the laboratory, samples from the two groups were treated identically.

Sodium, potassium, total CO_2, chloride and urea in plasma were measured simultaneously on an Auto-Analyser complex; plasma phosphate and urate were

measured on separate Auto-Analysers; plasma calcium and magnesium were measured by flame atomic absorption.

The "average of normals" quality control procedure was used as described by Hoffmann and Waid[1], except that normal ranges were obtained from the results for healthy individuals. The limits of the normal range were taken to be the mean $\pm 2\times$ standard deviation.

"Average of normals" control limits were calculated by multiplying the standard deviation of patient results falling within the normal range by 1.96 and dividing by 3.16 ($= \sqrt{10}$), since each quality control value was the average of 10 patients' results. To ensure comparability, the patient results used in the study to determine control limits and in the assessment of the quality control method were obtained from the same analytical batches as results for healthy persons. Results were obtained on ten days spread over a period of eight weeks.

RESULTS

A summary of results from healthy persons and patients is given in Table I. Mean plasma urea and urate values were appreciably higher in patients than in healthy persons, whereas the mean plasma calcium was lower. These differences were most likely due mainly to the presence of persons with renal dysfunction in the patient

TABLE I

SUMMARY OF RESULTS FROM HEALTHY PERSONS AND PATIENTS

Test	*Results from healthy persons*			*Results from patients*			*Units*
	No.	*Mean*	*S.D.*	*No.*	*Mean*	*S.D.*	
Calcium	85	10.22	0.71	89	9.09	1.40	mg/100 ml
Chloride	98	100.5	2.89	290	98.1	6.64	mequiv/l
CO_2 (total)	94	23.3	2.77	293	23.9	4.73	mequiv/l
Magnesium	86	1.74	0.13	54	1.62	0.41	mequiv/l
Potassium	98	4.19	0.29	293	4.18	0.83	mequiv/l
Sodium	98	142.1	3.17	293	139.2	6.44	mequiv/l
Urea	98	30.7	7.7	285	72.6	79.5	mg/100 ml
Urate	95	5.54	1.40	119	7.69	3.85	mg/100 ml

TABLE II

"WITHIN NORMAL RANGE" PATIENTS RESULTS

Test	*Normal range**	*"Within normal range" patient results*			*Control limits for "average of normals"***	*Units*
		No.	*Mean*	*S.D.*		
Calcium	8.8–11.6	50	9.82	0.71	9.38–10.26	mg/100 ml
Chloride	94–106	198	99.4	2.92	97.6–101.2	mequiv/l
CO_2 (total)	18–29	249	23.8	2.66	22.2–25.5	mequiv/l
Magnesium	1.50–2.00	27	1.76	0.15	1.67–1.85	mequiv/l
Potassium	3.6–4.8	198	4.09	0.31	3.90–4.28	mequiv/l
Sodium	136–148	211	140.9	3.12	139.0–142.8	mequiv/l
Urea	15–46	146	32.5	8.4	27.3–37.7	mg/100 ml
Urate	2.7–8.3	77	5.66	1.30	4.85–6.47	mg/100 ml

* Mean $\pm$ 2 S.D. for healthy persons.
** For sets of 10 results, *viz.*: Mean of "within normal range" patient results $\pm$ 1.96 $\times$ S.D./$\sqrt{10}$.

group. The spread of results in patients was consistently wider than in healthy persons.

Table II lists the calculated normal range (mean $\pm$ 2 $\times$ standard deviation) for healthy persons and the number, mean and standard deviation of patient results falling within this range. It also lists calculated control limits for the "average of normals" patient results taken in groups of 10.

Table III shows that when the patient results falling within the normal range were grouped in sets of 10, the average results in most instances fell within control limits. However, when a positive (or negative) increment was added to every patient result to simulate a systematic method error and new "average of normals" calculated, a high proportion of the averages still fell within control limits (Table III).

TABLE III

EFFECT OF ERROR ON "AVERAGE OF NORMALS" PATIENT RESULTS

Test	*"Averages of normals"—Actual results*		*Simulated error*	*"Averages of normals"—Adjusted results*	
	Total	*No. within control limits*		*Total*	*No. within control limits*
Calcium	5	4	+0.5 mg/100 ml	6	6
Chloride	19	18	+5 mequiv/l	19	9
CO_2 (total)	24	21	+2 mequiv/l	22	18
Magnesium	2	2	−0.2 mequiv/l	2	2
Potassium	19	18	−0.4 mequiv/l	14	12
Sodium	21	18	+5 mequiv/l	18	8
Urea	14	13	−5 mg/100 ml	16	13
Urate	7	7	−1 mg/100 ml	8	7

DISCUSSION

The "average of normals" quality control procedure is attractive in that it requires no material other than the specimens from patients being analysed and provides quality control based on much larger numbers of results than with conventional procedures. Our assessment, however, indicates that it is relatively insensitive to shifts in method calibration, for in most tests, errors of 3–30% failed to produce consistent deviation of the "average of normals".

The failure of this procedure to detect consistently errors of this magnitude is inherent in the method. In every test, results from patients had a wider spread (as reflected in the standard deviation—Table I) than those from healthy persons. When a small difference is added systematically to all patient results, some results at the top end of normal range come to exceed the upper normal limit, while some below the lower normal limit are brought into the normal range. As a consequence, the "average of normals", *i.e.* the average of those patient results within the normal range, is not necessarily affected by the systematic error. The reverse happens when a small difference is subtracted from all patient results.

The considerably greater spread of results in patients than in normals makes it unlikely that our findings result from a failure to obtain an appropriate normal range on which to base quality control limits. Hoffmann and Waid[1] used normal ranges computed from patient results but we feel that this procedure is invalid because this

method of obtaining normal ranges involves subjective decisions. It must be admitted that the normal ranges used in this study were obtained from a population having almost certainly a different age structure to that of the patients, that the healthy persons were consistently fasted before samples were taken whereas the patients were not, and that the healthy persons were ambulatory whereas the patients were mostly in bed. However, the effect of age[2] or posture[3] on most plasma components is slight and we know of no evidence that fasting affects the components studied sufficiently to invalidate our findings.

In this assessment, we deliberately restricted patient results to those obtained on the same days as results from healthy persons in order that the two sets of results should not be subject to methodological differences. This meant that the quality control parameters for "averages of normals" were derived from less than the 500 results recommended by Hoffmann and Waid[1]. However, comparison of the parameters used with those derived from two larger groups of patient results (Table IV)

TABLE IV

OTHER "WITHIN NORMAL RANGE" PATIENT DATA

Each series consisted of 500 results. Data refer to "within normal range" results.

Test	*Series "A"*			*Series "B"*			*Units*
	No.	*Mean*	*S.D.*	*No.*	*Mean*	*S.D.*	
Calcium	345	9.88	0.20	—	—	—	mg/100 ml
Chloride	320	98.4	3.05	349	98.6	3.00	mequiv/l
CO_2 (total)	406	24.5	2.66	418	24.2	3.03	mequiv/l
Magnesium	310	1.78	0.16	—	—	—	mequiv/l
Potassium	333	4.13	0.34	320	4.17	0.35	mequiv/l
Sodium	309	140.1	3.19	307	140.1	2.98	mequiv/l
Urea	249	31.8	8.18	243	33.0	7.27	mg/100 ml
Urate	302	5.51	1.49	—	—	—	mg/100 ml

failed to reveal any indication that the control parameters used were inappropriate for this reason.

The failure of the "average of normals" quality control procedure to detect consistently appreciable shifts in method calibration, make this procedure unsuitable for detecting shifts in single analytical batches, and, in our assessment, of limited value in detecting shifts over a period. It is conceivable that a quality control system based on some other parameter of patient results, such as the average of results in the interquartile range, would be more sensitive to method calibration shift. However, it seems likely that inclusion of a suitable number of control samples in each analytical batch would provide a much more certain means of detecting method calibration shifts, though this entails additional work for the laboratory.

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