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Application of Indices Cp and Cpk to Improve Quality Control Capability in Clinical Biochemistry Laboratories

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Abstract

The traditional criteria for acceptability of analytic quality may not be objective in clinical laboratories. To establish quality control procedures intended to enhance Westgard multi-rules for improving the quality of clinical biochemistry tests, we applied the Cp and Cpk quality-control indices to monitor tolerance fitting and systematic variation of clinical biochemistry test results. Daily quality-control data of a large Taiwanese hospital in 2009 were analyzed. The test items were selected based on an Olympus biochemistry machine and included serum albumin, aspartate aminotransferase, cholesterol, glucose and potassium levels. Cp and Cpk values were calculated for normal and abnormal levels, respectively. The tolerance range was estimated with data from 50 laboratories using the same instruments and reagents. The results showed a monthly trend of variation for the five items under investigation. The index values of glucose were lower than those of the other items, and their values were usually < 2. In contrast to the Cp value for cholesterol, Cpk of cholesterol was lower than 2, indicating a systematic error that should be further investigated. This finding suggests a degree of variation or failure to meet specifications that should be corrected. The study indicated that Cp and Cpk could be applied not only for monitoring variations in quality control, but also for revealing inter-laboratory quality-control capability differences.

Key Words: clinical biochemistry, Cp, Cpk, process capability, quality control

Introduction

Quality of health care has been a much debated issue in recent years. As the healthcare business has long been regarded as rather unique in the service sector, hospital administrators should include both medical and administrative innovations for effective improvement of service processes (18). Clinical biochemistry tests are important for clinical diagnosis and monitoring of treatments in hospitals. The major goals of clinical laboratories are to provide fast and accurate biochemistry test results. Quality-control (QC) and quality-assurance procedures in most hospitals are based on Westgard multi-rules (14) supplemented by QS9000 and D19000 international standards for better laboratory quality. The σ metric is useful for assessing the adequacy of QC procedures and practices. When assessing quality on the σ scale, the higher the σ metric the better the quality. In recent years, the Six Sigma methodology has been widely applied to industrial quality-improvement activities with the aim of monitoring daily operational procedures, reducing

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operation errors and product variations to minimal levels, and promoting quality, efficiency and customer satisfaction. Nevalainen *et al*. (9) demonstrated the application of Six Sigma concepts for characterizing the quality of pre- and post-analytic processes on the σ scale. With the aid of Six Sigma principles and metrics, it is possible to assess the quality of laboratory testing processes and the quality capability that is needed to ensure that the desired quality is achieved. Six Sigma requires that quality tolerance limits be defined, so that poor quality or erroneous test results may be objectively identified. One of methods uses estimates of process variations to predict process performance by calculating a σ metric from the defined tolerance limits and the variations observed for the process. The method is particularly suitable for analytic processes in which the precision and accuracy can be determined by experimental procedures (16).

Montgomery (8) stressed that current engineering techniques and the medical service industry need to instantaneously control every product of the production line by computerized and automated instruments. However, applications of clinical requirements are more complicated for biological variations (15, 17). In the U.S., the Clinical Laboratory Improvement Amendments (CLIA) set a quality requirement and emphasized increased quality assessment for pre-analytic and post-analytic processes (Federal Registration 68, Centers for Disease Control and Prevention). Nonetheless, using performance data evaluated on the σ scale, Westgard and Westgard (16) have concluded that analytic quality is still a problem in U.S. clinical laboratories. The CLIA criteria for acceptability may not be objective and the results are indicative of the quality needed for medical care.

As might be expected, the size of the analytic errors that need to be detected by QC depends on the process capability (2). The process capability index may represent the key index for measuring quality level (7). According to the quality work criteria, the specification width and the width of the natural tolerance are correlated. Statistical process control (SPC), which monitors process conditions by data collection and sampling, is at present widely applied to quality improvement in production lines in the manufacturing industry (5). The process parameter should be adjusted when necessary to reduce variations in quality characteristics, thus prompting preventive quality activities. To develop an SPC strategy that meets European requirements, Beckman *et al*. (1) recently applied statistical process control and the Cpk index to monitor the process capability of blood-component parameters. Other applications of the Cp or Cpk indices may be found in studies of vascular surgery cases (12) and population body mass index (10).

Monitoring has a vital role to play in demonstrating product conformance and improving processes. However, it is not a substitute for a detailed understanding of the process and its critical control points. Such understanding is essential in order to explain variations or failures to meet specifications and to take effective corrective action (1). For optimal testing, clinical laboratories should design a QC procedure for each individual test to account for the precision and accuracy of their measurement procedures and the quality required for care of their patients. (13) In this study, the use of Cp and Cpk indices was applied to QC sera used by a clinical biochemistry laboratory to improve QC capability.

Materials and Methods

Selected Laboratory Tests

Daily QC data were collected from a large teaching hospital in Taiwan. The hospital's clinical biochemistry laboratory uses an Olympus AU640 automation machine with clinical biochemistry test items including serum albumin, aspartate aminotransferase (AST), total cholesterol, blood glucose level and blood potassium level. Data were collected for the entire year in 2009. The respective reaction principals for the five items are bromocresol green, Tris buffer without pyridoxal 5'-phosphate, cholesterol oxidase/peroxidase, hexokinase and ion-selective electrode. Both normal (Level I) and abnormal (Level II) levels were analyzed two to four times a day for each test item. The monthly mean values and standard deviations were calculated and recorded at the end of each month based on that month's data. The results were compared with those of more than 50 Taiwan's laboratories using instruments of identical brands, the same reagents and QC sera from the same lot. The specific limit (tolerance range) was estimated using the data from the peer laboratories.

Cp and Cpk QC Assessment Tool

The highest and the lowest tolerance ranges were treated as the controlled upper and lower specification limits (USL and LSL, respectively) in the calculation of Cp and Cpk values. The index Cp is given by:

$$Cp = \frac{USL - LSL}{6\sigma} \quad [1]$$

where USL denotes the upper and LSL the lower specification limits. The Cp index describes the relationship between natural tolerance and specification width.

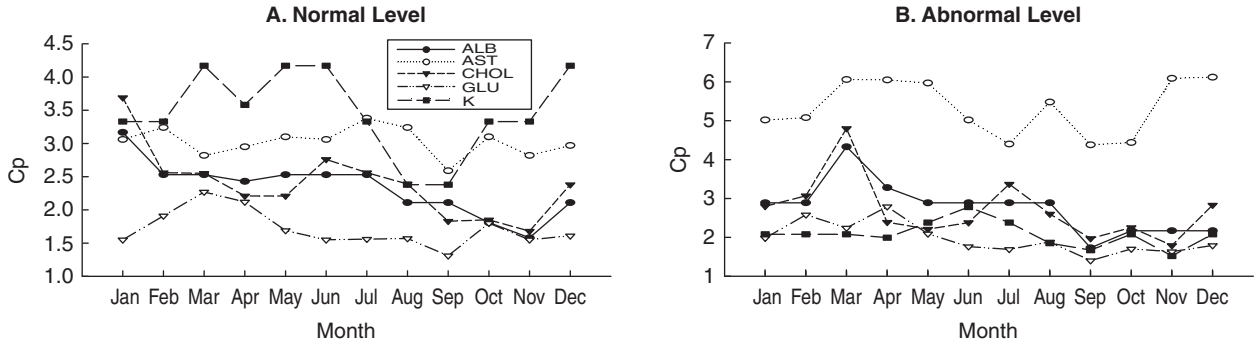

Fig. 1. Monthly variations of Cp value for five biochemical items. (A) Level I and (B) Level II. ALB, albumin; AST, aspartate aminotransferase; CHOL, cholesterol; GLU, glucose; K, potassium.

The Cpk index is given by

$$Cpk = \min\left\{\frac{USL-\mu}{3\sigma}, \frac{\mu-LSL}{3\sigma}\right\} \quad [2]$$

where μ denotes the process mean. Cpk indicates, in addition, how well the distribution is centred about the nominal (target) value, a property that can better reveal the relationship between the mean and objective values. Cp index values fall into three cases:

(a) When Cp < 1, the QC data of the daily sera tend to be unstable or abnormal. This situation corresponds to a lack of process capability, 6σ > (USL − LSL), meaning that products fail to meet the standard specification. In this case, prompt corrective actions and precautions are highly recommended. If this outcome occurs in clinical biochemistry laboratories, it could be viewed as the daily QC data exceeding the pre-set QC limits. Pre-processing procedures should thus be immediately reviewed with the goal of identifying the root causes and carrying out corrective actions and precautions.

(b) When Cp = 1, the process capability equals the specification tolerance, or 6σ = (USL − LSL), most quality characteristics meeting the specification requirements. If this situation occurs in manufacturing, an uncontrolled process would lead to unqualified products and relevant staff should identify the causes of defects and make improvements.

(c) When Cp < 1, the process capability is lower than the specification tolerance; 6σ < (USL − LSL), and the process capability is excellent. However, there is a target value within the tolerance, and it is advised that the machines be adjusted and the process be revamped so that the product specification is closer to the target value. This goal of perfection provides a good example for clinical laboratories to follow.

Results

The trend of Cp variations for two levels is illustrated in Fig. 1. Except for glucose, Cp values of which were mostly below 2 in the trend chart of Level I (Fig. 1A), those of the other four items were mostly above 2. The annual average Level I Cp values of the five items were 2.549 ± 0.589 (albumin), 4.108 ± 1.289 (aspartate aminotransferase; AST), 2.546 ± 0.683 (cholesterol), 1.834 ± 0.362 (glucose) and 2.668 ± 0.848 (potassium). Lower Cpk than Cp values were observed (Fig. 2). The annual average Level I Cpk values of the five items were 2.281 ± 0.577 (albumin), 3.134 ± 1.079 (AST), 1.692 ± 0.393 (cholesterol), 1.654 ± 0.299 (glucose) and 2.626 ± 0.827 (potassium). The lowest values were observed for glucose and cholesterol, but the Cpk values of the five items were mostly above 1.7 for the two test levels. The Cp and Cpk values of some test items of Level I were higher than those of Level II (Figs. 1 and 2), that is, the test reports of the normal values were more stable than those of the abnormal values. For instance, the Cp or Cpk values of potassium of Level I were generally above 2.5 while the Cp values of Level II were around 2 (2.081 ± 0.333), and the Cpk values were even lower than 2 (1.951 ± 0.344). However, some test items presented reversed results. For example, the Cp and Cpk values of Level II for AST were generally above 4 (some even above 5) while the Cp values of Level I dropped to around 3 (3.027 ± 0.216) with Cpk values being around 2 (2.139 ± 0.275). This indicated that AST test reports of abnormal values were more stable than those of normal values.

Other trends were apparent in Figs. 1 and 2. The control data of potassium of Level I in August and September tended to drop abruptly, with Level II Cp values lower than 2. In the same trend charts, ALB Cp and Cpk values for either Level I or Level II tended to fall by month and to rise again by De-

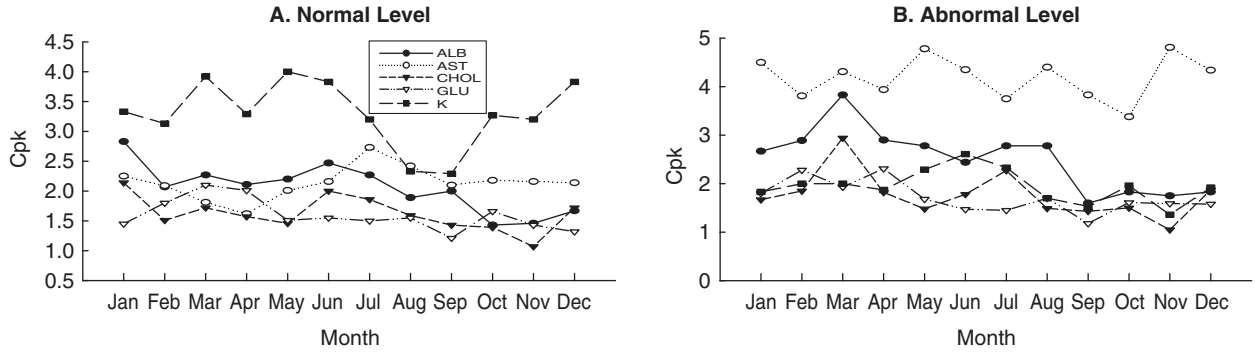

Fig. 2. Monthly variations of Cpk value for five biochemical items. (A) Level I and (B) Level II. Abbreviations are as in Fig. 1.

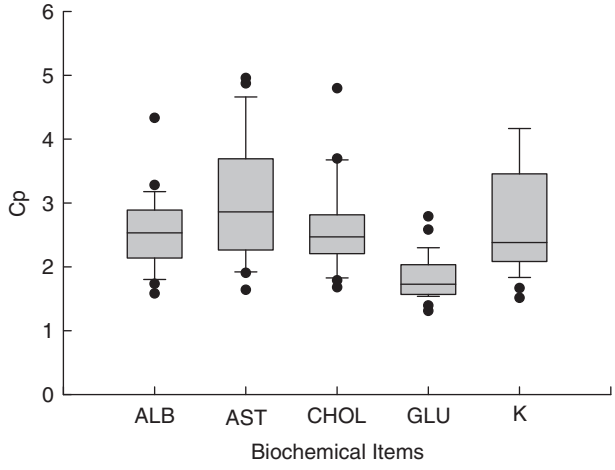

Fig. 3. Distribution of Cp values of five biochemical items. Abbreviations are as in Fig. 1.

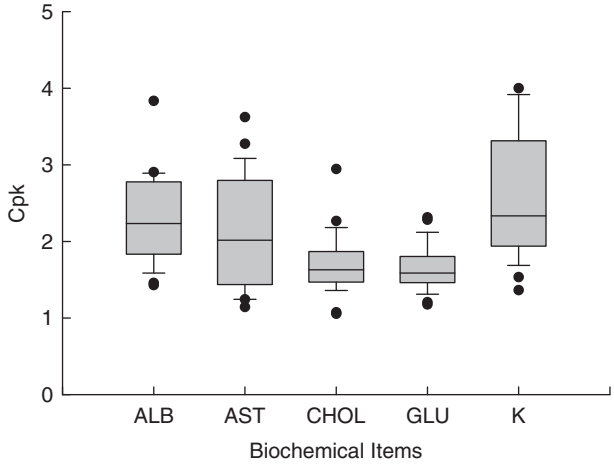

Fig. 4. Distribution of Cpk values of five biochemical items. Abbreviations are as in Fig. 1.

cember. These results suggested a decline in process quality.

The means and standard deviations of the two indices collected over one year are shown in Figs. 3 and 4. Here, more Cp and Cpk variations for AST and potassium appeared, with mean values above 2. However, while cholesterol and glucose showed less Cp and Cpk variations, their means were lower, especially for glucose, Cp and Cpk values of which were both below 2 (but still around 1.8). In contrast to the Cp value for cholesterol, Cpk of cholesterol was lower than 2, indicating a systematic error that should be further investigated. Cp and Cpk values were compared with the QC data of other hospitals that used the same instrument models and QC sera from the same lot before being analyzed according to the QC data compiled monthly by every hospital. Accordingly, the tests that showed greater variations tended to be more unstable than those of the peer hospital laboratories. The items the mean values of which were lower tended to present lower quality capability and report quality compared with the peer hospital laboratories.

Discussion

The application of Cp and Cpk values to quality process monitoring has historically favoured higher values (1, 8). A lower value would signal a defect in pre-laboratory or post-laboratory processing and would require immediate identification of factors threatening patient safety. In this research, the Cp index values of potassium in August and September tended to drop sharply. Inspection revealed that the defect resulted from the replacement of the reverse osmosis water processor's filter, usually done in late September. Following its replacement, the Cp values rose above 3 after September. In the same trend charts, the ALB Cp value tended to drop monthly and to rise again by December. This could be attributed to the vendor's regular instrument maintenance in November, which included reaction plate cleaning, bulb checking and bulb replacing. Because the colour and the reaction color of reagents used in the ALB biochemistry test were darker, worn or unclean reaction plates would affect the quality of test report. However, Cp values were unable to demonstrate systematic de-

viation upward or downward, while Cpk values could do so. The monitoring of Cpk values revealed that worn bulbs or colour comparators of automatic clinical biochemistry instruments might result in systematic variations in daily QC data.

At present, general clinical biochemistry laboratories use mostly control charts showing daily values for QC sera as indicators of the data quality of the daily-issued test reports. The control charts provide only information on the relative stability of the test procedure. Most laboratories employ Westgard multi-rules to decide whether the daily QC items can be accepted and the test report can be issued. Although this QC procedure could be applied to monitoring the trend of test quality variations, the procedure is limited to internal comparisons of the laboratories. More reliable estimates might be available from peer-comparison programs, in which laboratories submit all QC data for analysis and comparison with peer groups (16). Cp or Cpk values whose quality is evaluated by specification limits determined under identical analytical conditions could be used in process-capability monitoring. The relative quality process capability could then be compared among laboratories that used the same instruments and reagents of the same lots and specifications.

This study illustrated that when Cp and Cpk values were included in comparisons of a laboratory's five test items, the mean values for glucose and cholesterol were low. This trend was especially marked for the Cpk values of cholesterol, which dropped sharply to a level close to those of glucose and tended to be lower than the Cp values of the test items. This result indicates that, despite the relatively stable values of cholesterol, systematic variations might start to occur. Although this condition is usually not detectable in daily Westgard multi-rules control charts, a gradual systematic upward or downward trend might appear in the test reports. In this case, laboratory supervisors should further track, analyze and understand the given item in order to identify the causes and make improvements. This study has shown that the Cp and Cpk QC indices usually used in the manufacturing industry, may also be applied to QC in the clinical biochemistry laboratory. The merit of this research consists in the application of the two new QC indices. Laboratories conventionally evaluate their own internal QC data. The indices employed in this study afford comparison with laboratories using the same instrument models and QC sera. When Cp or Cpk values tend to drop sharply, laboratories should immediately review and examine each process of the pre-procedure. Reagent quality, instrument factors and human factors must all be considered for a prompt diagnosis and response, leading to an improvement in the quality and variation of test results.

The level at which an index's reference value should be set requires studies. In the manufacturing industry, Cp values should be above 1.33. In the high-precision QC process of the electronics manufacturing industry, Cp values are usually controlled to above 2 and Cpk values to above 1.7. Nonetheless, He *et al*. (6) considered that adjustment of tolerance should be made after the variation effect is sufficiently reduced. They conducted an improved approach with process capability index providing more flexibility for designing for manufacturability. In particular, specimen quality requirements, such as biological goals for imprecision and bias, are more complicated. Owing to biological variations, the requirement may be converted into biologically allowable total errors (11). Clinical outcome criteria such as a decision interval for test interpretation require that pre-analytic variables as well as biological variations be taken into account (15, 17). Beckman *et al*. (1) have also indicated that wide physiological variations in cellular and plasma content in donated blood make tight control over parameter yields in the intermediate and final components difficult to achieve. This is apparent from the wider SPC control limits and lower process capabilities than for non-biological manufacturing processes. Thus, medical laboratories should use data from more laboratories at the same time before establishing the data thresholds or reference ranges. In healthcare, measurement tools should be developed in order to come up with useful instruments to measure the process orientation of the employees (4). A system for assessing and improving healthcare organizations should be applied for promoting service quality (3). It is advised that large medical biochemistry laboratories or those that conduct quantitative analysis of trace elements or high-precision quantitative tests should apply Cp and Cpk values extensively to promote quality process capability.

In summary, this study considers that the two quality indices could contribute to the timely monitoring of clinical variation factors. Cp and Cpk values can be applied not only to monitoring a laboratory's quality capability variations in clinical biochemistry tests, but also to revealing the relative QC capability of different laboratories that use the same machines and reagents. Quality-capability comparisons with other laboratories that use the same instruments and reagents could be made, based on the two indices, in an attempt to initiate peer group review for constantly improving the quality indices of test reports. We propose that medical test quality could approach perfection if all results were shared among laboratories.

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