临床生化酶类测定应用保证西格玛与长期缺陷率在统计质量控制策略中的应用

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摘 要:目的 应用实验室生化酶学测定项目的短期西格玛($Sigma_{short\text{-}term}$)估算其保证西格玛 $Sigma_{Assured}$,并依据系统误差功效图得出相应的统计质量控制(statistical quality control,SQC)规则,估计生化酶学测定项目的长期缺陷率(defects per million, DPM),确保实验室生化酶学测定项目结果的可靠。**方法** 计算公式 Sigma = (TEa - Bias)/*CV*;$Sigma_{long\text{-}term}$ = $Sigma_{short\text{-}term}$ - 1.5 ;$Sigma_{Assured}$ = $Sigma_{Observed}$ - $Sigma_{SQC}$, $Sigma_{Assured}$ = 1.65,SQC 规则为 $1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$,$N=2$。**结果** 计算得到实验室丙氨酸氨基转移酶(ALT)的 $Sigma_{short\text{-}term}$ = 3.6,DPM = 274 253;天门冬氨酸氨基转移酶(AST)的 $Sigma_{short\text{-}term}$ = 7.9,DPM < 3.4;谷氨酰基转移酶(GGT)的 $Sigma_{short\text{-}term}$ = 5.6,DPM = 4 661;碱性磷酸酶(ALP)的 $Sigma_{short\text{-}term}$ = 7.4,DPM = 5;淀粉酶(AMY)$Sigma_{short\text{-}term}$ = 17.7,DPM < 3.4;肌酸激酶(CK)$Sigma_{short\text{-}term}$ = 9.3,DPM≤3.4;乳酸脱氢酶(LDH)的 $Sigma_{short\text{-}term}$ = 6.1,DPM = 968;脂肪酶(LPS)的 $Sigma_{short\text{-}term}$ = 5.3,DPM = 10 724。**结论** 实验室生化酶学测定项目期望的长期缺陷率在误差检出率(Ped)达到90%,其 $Sigma_{Assured}$ 在1.65,相同的 SQC 规则 $1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$,$N=2$,的情况下,其 $Sigma_{short\text{-}term}$ 越大,长期 DPM 越低,才能确保生化酶学测定项目的结果可靠。

关键词:西格玛;统计质量控制;短期西格玛;保证西格玛;长期缺陷率
中图分类号:R446 **文献标志码:**A **文章编号:**1671-7414(2020)01-143-03
doi:10.3969/**j. issn.** 1671-7414.2020.01.038

Use of Assured Sigma and Defects Per Million in Statistical Quality Control Strategies in Clinical Enzymes Measurements

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Abstract: Objective To estimate the assured Sigma by using the short term Sigma, obtain the statistical quality control (SQC) procedure according to the power function graph, and estimate the defects per million (DPM) of those items. These procedures can ensure reliable results in the laboratory. **Methods** The computationalformula were: Sigma = (TEa - Bias)/*CV*;$Sigma_{long\text{-}term}$ = $Sigma_{short\text{-}term}$ - 1.5 ;$Sigma_{Assured}$ = $Sigma_{Observed}$ - $Sigma_{SQC}$, $Sigma_{Assured}$ = 1.65, and SQC procedure was $1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$,$N=2$. **Results** For alanine aminotransferase (ALT), $Sigma_{short\text{-}term}$ = 3.6, DPM = 274 253. For aspartate amino transferase (AST), $Sigma_{short\text{-}term}$ = 7.9,DPM < 3.4. For gamma-glutamyl transpeptidase (GGT), $Sigma_{short\text{-}term}$ = 5.6,DPM = 4661. For alkaline phosphatase (ALP), $Sigma_{short\text{-}term}$ = 7.4, DPM = 5. For amylase (AMY), $Sigma_{short\text{-}term}$ = 17.7,DPM < 3.4. For creatine kinase (CK), $Sigma_{short\text{-}term}$ = 9.3, DPM≤3.4. For lactic dehydrogenase (LDH), $Sigma_{short\text{-}term}$ = 6.1, DPM = 968. For lipase (LPS), $Sigma_{short\text{-}term}$ = 5.3,DPM = 10 724. **Conclusion** When the probability of error detection (Ped) was ≥90% ,assured Sigma was 1.65 and the SQC procedure was $1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$,$N=2$. It was found that the long term DPM was lower when the $Sigma_{short\text{-}term}$ was higher, and this enabled reliable results in clinical enzymes measurements.

Keywords: Sigma; statistical quality control (SQC); short term sigma; assured sigma; long term DPM

临床实验室需要获得可靠的测定结果以支持临床作出正确的决策,降低患者风险。实验室通常根据检测项目的允许总误差(TEa)来确定质量目标,超过 TEa 的检测结果即为错误结果或缺陷,而结果的可靠性是由检测方法产生不可靠结果的比率决定的,即缺陷率(defect rate),缺陷率定义为每百万次机会的错误结果(defects per million opportunities,DPMO)[1],缺陷率越高,检测结果的可靠性越低。而西格玛(Sigma)又是一种衡量缺陷率的指标。工业中的长期西格玛($Sigma_{long\text{-}term}$)是采用短期西格玛($Sigma_{short\text{-}term}$)值减去1.5来估算其长期缺陷率[2]。在医学实验室估算保证西格玛($Sigma_{Assured}$)可通过观察西

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格玛($Sigma_{observed}$)减去1.65来估算长期缺陷率,$Sigma_{Assured}$的大小决定了统计质量控制(statistical quality control,SQC)策略,所以$Sigma_{Assured}$是衡量实验室结果可靠性的更好指标。

SQC广泛应用于医学实验室,实验室分析阶段长期DPM取决于质量控制程序的能力,长期可靠性的结果又取决于所选择的质量控制程序,WESTGARD等[3]介绍了当实验室内$Sigma_{Assured}$为1.65和质量控制程序为$1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$,$N=2$时,估算长期DPM的方法。本研究以生化酶学测定项目,包括丙氨酸氨基转移酶(ALT)、天门冬氨酸氨基转移酶(AST)、谷氨酰基转移酶(GGT)、碱性磷酸酶(ALP)、淀粉酶(AMY)、肌酸激酶(CK)、乳酸脱氢酶(LDH)和脂肪酶(LPS)为例,在误差检出率Ped≥90%,其$Sigma_{Assured}$在1.65,以及相同的SQC规则$1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$,$N=2$的情况下,通过缺陷率表估算期望的长期DPM。

1 材料与方法

1.1 研究对象 生化酶学检测项目丙氨酸氨基转移酶(ALT)、天门冬氨酸氨基转移酶(AST)、谷氨酰基转移酶(GGT)、碱性磷酸酶(ALP)、淀粉酶(AMY)、肌酸激酶(CK)、乳酸脱氢酶(LDH)和脂肪酶(LPS)。仪器为罗氏Cobas 702,试剂为配套试剂。允许总误差(TEa)与偏倚(Bias)、变异系数(*CV*)来自于Westgard sigma VP性能验证报告。

1.2 方法 Sigma计算公式:Sigma=(TEa-Bias)/*CV*[4];$Sigma_{observed}=Sigma_{short\text{-}term}$;工业$Sigma_{long\text{-}term}$计算公式:$Sigma_{long\text{-}term}=Sigma_{short\text{-}term}-1.5$;医学临界系统误差SEcrit=[(TEa-Bias)/*CV*]-1.65;医学保证Sigma计算公式:$Sigma_{Assured}=Sigma_{Observed}-Sigma_{SQC}$。采用相同的SQC规则,即$1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$,$N=2$。

2 结果

当采用相同的SQC规则,即$1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$,$N=2$时,计算和查表得到本实验室生化酶学检测项目的$Sigma_{Assured}$与长期DPM,结果见表1。

表1 生化酶学检测项目的$Sigma_{Assured}$与长期缺陷率

项目	Sigma值		临界值	保证Sigma	缺陷率
	长期	短期			
ALT	3.60	2.10	1.95	1.65	274 253
AST	7.90	6.40	6.25	1.65	<3.4
GGT	5.60	4.10	3.95	1.65	4 661
ALP	7.40	5.90	5.75	1.65	5
AMY	17.70	16.20	16.05	1.65	<3.4
CK	9.30	7.80	7.65	1.65	<3.4
LDH	6.10	4.60	4.45	1.65	968
LPS	5.30	3.80	3.65	1.65	10 724

3 讨论

预期长期最大DPM是由分析系统长期性能决定的,然而实际工作中没有办法估算长期DPM,但可以估算短期内的DPM来估算长期预期最大DPM,以保证分析系统长期结果可靠。Bayat[5]介绍了估算临床实验室长期DPM的方法。$Sigma_{Observed}$定义为方法验证实验得到短期性能指标,估算得到的Sigma。$Sigma_{Assured}$则取决于SQC策略检测漂移的能力,Ped≥90%的情况下,选择多规则$1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$,$N=2$。若SQC策略较宽松,大的漂移则不会轻易检测到,因此预期长期最大DPM将远远大于短期DPM。当SQC策略可以立即检测到非常小的系统漂移,那么预期的长期最大DPM与短期DPM大致相同。但在实际工作中,没有SQC策略可以立即检测到系统小的变化,因此,$Sigma_{long\text{-}term}$质量总是会比短期的质量要差。长期最大DPM取决于SQC策略的误差检出率(Ped),当Ped=100%时SQC策略是最理想,但同时会增加错误拒绝的概率(Pfr),实验室工作中普遍预期的实验结果是至少保证有95%的结果可靠。5%的缺陷率(50 000 DPM)被认为是长期性能的最大可接受的DPM,长期期望的最小Sigma可以计算为:$Sigma_{Assured}=Sigma_{Observed}-Sigma_{SQC}$。超过5%漂移为临界错误结果,那么SEcrit=[(TEa-Bias)/CV]-1.65,其中1.65为单边z值,产生错误结果的概率为5%,SQC应当选择Ped≥90%的SQC策略以保证长期的缺陷率<5%。通常情况下,SQC策略的目的是检测那些足以产生超过5%的错误结果的漂移,在SQC策略目标小于5%的缺陷率下,不管$Sigm_{Observed}$大小如何,要保证长期质量至少是1.65 Sigma以上。当系统稳定状态下,$Sigma_{Observed}$与产生不可靠患者结果的预测概率直接相关,而在失控期间,最大预期错误结果由SQC策略决定,因此建议评估SQC策略时必须包括分析过程中长期性能。CLSI-C24指南提出了实验室的质量控制实践中的方法长期性能与病人伤害风险原则[6],临床实验室应该建立不同的$Sigma_{Assured}$的SQC策略,使用更严格的SQC策略。如果需要通过简单SQC策略提供高水平的$Sigma_{Assured}$,$Sigma_{Observed}$应该远远大于所需的$Sigma_{Assured}$来满足Ped≥90%。表1中生化酶学检测项目的SQC策略在达到Ped≥90%的情况下的所用质控规则,如要应用这个SQC策略,$Sigma_{Observed}$至少需高出1.65,估算分析性能的长期DPM,如表中AST,

ALP,AMY,CK,实验室SQC策略规则为$1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$,$N=2$,长期DPM为<3.4,即这台仪器在长期使用中可产生3.4个错误结果。由此可见,为确保长期结果的可靠,需检测项目的$Sigma_{short\text{-}term}$越大,才能确保长期DPM越低。

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收稿日期:2019-08-08
修稿日期:2019-10-12

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收稿日期:2019-01-14
修回日期:2019-10-30