Journal Scan:

Closed-loop insulin delivery during pregnancy in women with type 1 diabetes

Complication of type 1 diabetes during pregnancy are related to poor glycemic control around the time of conception leading to congenital anomalies and maternal hyperglycemia that persists during pregnancy is responsible for other complications. In patients with type 1 diabetes who are not pregnant, closed-loop (automated) insulin delivery has been shown to provide better glycemic control than sensor-augmented pump therapy. The authors explored the feasibility of closed-loop therapy during pregnancy. For this, the authors performed an open-label, randomized, crossover study comparing overnight closed-loop therapy with sensor-augmented pump therapy, followed by a continuation phase in which the closed-loop system was used day and night. Sixteen pregnant women with type 1 diabetes completed 4 weeks of closed-loop pump therapy (intervention) and sensor-augmented pump therapy (control) in random order. During the continuation phase, 14 of the participants used the closed-loop system day and night until delivery. The primary outcome was the percentage of time that overnight glucose levels were within the target range (63 to 140 mg per deciliter [3.5 to 7.8 mmol per liter]). The percentage of time that overnight glucose levels were in the target range was found to be higher during closed-loop therapy than during control therapy (74.7% vs. 59.5%; absolute difference, 15.2 percentage points; 95% confidence interval, 6.1 to 24.2; P = 0.002). The overnight mean glucose level was found to be lower during closed-loop therapy than during control therapy (119 vs. 133 mg per deciliter [6.6 vs. 7.4 mmol per liter], P = 0.009). No significant difference was noted between closed-loop and control therapy in the percentage of time in which glucose levels were below the target range (1.3% and 1.9%, respectively; P = 0.28), in insulin doses, or in adverse event rates. During the continuation phase (up to 14.6 additional weeks, including antenatal hospitalizations, labor, and delivery), glucose levels were found to be in the target range 68.7% of the time [the mean glucose level was 126 mg per deciliter (7.0 mmol per liter)]. No episodes of severe hypoglycemia requiring third-party assistance were reported during either phase.

Comment

The study demonstrates the usefulness of a closed-loop system, as compared with sensor-augmented pump therapy with improved glycemic control, without increases in hypoglycemic episodes or the insulin dose which supports the findings observed in non pregnant women with type 1 diabetes. However, trials assessing the effect of this therapy on maternal and neonatal outcomes needs to be assessed before this can be used in clinical practice.

Stewart ZA, Wilinska ME, Hartnell S, Temple RC, Rayman G, Stanley KP, Simmons D, Law GR, Scott EM, Hovorka R, Murphy HR. Closed-loop insulin delivery during pregnancy in women with type 1 diabetes. N Engl J Med.2016;375:644-54.

Timeliness “at a glance”: assessing the turnaround time through the six sigma metrics

The turnaround time (TAT) is a “fundamental dimension” within the clinical laboratory paradigm and is recognized as a mandatory quality indicator (level 1) for the post-analytical phase by the

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http://svimstpt.ap.nic.in/jcsr/oct-dec16_files/js16.pdf

Working Group for Laboratory Errors and Patient Safety of the International Federation of Clinical Chemistry and Laboratory Medicine.The TAT analysis is aimed to assess the tendency of the laboratory system to meet a certain goal of timeliness. This in turn assumes quality as a natural consequence of speed ("the faster, the better"), so that efficiency and speed are thought synonyms.

Several indicators are to date available to assess and report quality with respect to timeliness, but they sometimes lack the communicative immediacy and accuracy. The six sigma is a paradigm developed within the industrial domain for assessing quality and addressing goal and issues. The sigma level computed through the Z-score method is a simple and straightforward tool which delivers quality by a universal dimensionless scale and allows handling non-normal data. In this article, the authors report their preliminary experience in using the sigma level to assess the change in urgent (STAT) test turnaround time for cardiac troponin-I (CTNI) tests ordered by the Emergency Department (ED) in the regular morning shift due to the implementation of total automation. The median and 90th percentile of TAT was found to be 35 and 60 minutes respectively after automation compared to 55 and 95 minutes respectively before automation. The tolerance limit was set to 60 minutes as recommended by the American College of Cardiology Foundation and American Heart Association (ACCF/AHA) guidelines. They found the Z-score method to be a valuable and easy to use method for assessing and communicating the quality level of laboratory timeliness, providing a good correspondence with the actual change in efficiency which was observed retrospectively.

Comment

The authors describe the application of the industry-born concept of six sigma to suit the TAT quality level assessment of a core laboratory and found it to be a valuable tool for delivering "at a glance" the quality level of the clinical laboratory TAT, due to its immediacy and the correspondence with the perceived level of proficiency. However, it should be noted that the sigma level strictly depends on the tolerance limit set, and therefore the appropriate specification limit value should be established with respect to analytes and operative conditions through consensus conferences in order to grant standardization. Further, it is mandatory to check data for normality and eventually transform them before applying the Z-score method in order to obtain a reliable sigma level.

Ialongo C, Bernardini S. Timeliness "at a glance": assessing the turnaround time through the six sigma metrics. Biochem Med (Zagreb) 2016;26:98-102.

Portraying breast cancers with long noncoding RNAs

Emerging evidence suggests that long noncoding RNAs (lncRNAs) may play a role in cancer development, but this role is not yet clear. The authors performed a genome-wide transcriptional survey to explore the lncRNA landscape across 995 breast tissue samples. They identified 215 lncRNAs whose genes are aberrantly expressed in breast tumors, as compared to normal samples. Unsupervised hierarchical clustering of breast tumors on the basis of their lncRNAs revealed four breast cancer subgroups that correlate tightly with PAM50-defined mRNA-based subtypes. Using multivariate analysis, the authors identified around 210 lncRNAs prognostic of clinical outcome. By analyzing the coexpression of lncRNA genes and protein-coding genes, they inferred potential functions of the 215 dysregulated lncRNAs. The authors then associated subtype-specific lncRNAs with key molecular processes involved in cancer. A correlation was observed, on the one hand, between luminal A–specific lncRNAs and the activation of phosphatidylinositol 3-kinase, fibroblast growth factor, and transforming growth factor–â pathways and, on the other hand, between basal-like–specific lncRNAs and the activation of epidermal growth factor receptor (EGFR)–dependent pathways and of the epithelial-to-mesenchymal transition. Finally, they showed that a specific lncRNA, which the authors termed CYTOR, plays a role in breast cancer. The authors confirmed its

predicted functions, showing that it regulates genes involved in the EGFR/mammalian target of rapamycin pathway and is required for cell proliferation, cell migration, and cytoskeleton organization. This work provides the most comprehensive analyses for lncRNA in breast cancers and the findings suggest a wide range of biological functions associated with lncRNAs in breast cancer and provide a foundation for functional investigations that could lead to new therapeutic approaches.

Comment

Breast cancer is a major public health issue and the second leading cause of cancer related mortality in India. Breast cancer is a heterogeneous disease, and different subtypes have been described including a classification based on protein and gene status. Clinically, breast tumors are subclassified into three main subgroups on the basis of estrogen receptor (ER) and human epidermal growth factor receptor 2 (HER2) gene expression: Recently, because of whole-transcriptome sequencing [RNA sequencing (RNA-seq)], this classification has been refined, with the identification of 12 breast tumor subgroups. Despite these advances, there is a lack of understanding in breast cancer heterogeneity because tumors of the same subtype can respond differently to therapy and can have different outcomes. The findings of this study can be useful in understanding the molecular mechanisms that underlie breast cancer heterogeneity and help in designing potential targets for future therapies.

Van Grembergen O, Bizet M, de Bony EJ, Calonne E, Putmans P, Brohée S, Olsen C, Guo M, Bontempi G, Sotiriou C, Defrance M, Fuks F. Portraying breast cancers with long noncoding RNAs. Science Advances *2016;2:e1600220.*

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