Diagnosing Diabetes Mellitus: Performance of Hemoglobin A1c Point-of-Care Instruments in General Practice Offices

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Guest:
Dr. Una Sølvik is an Associate Professor in the Department of Global Health and Primary Care at the University of Bergen in Norway.

Bob Barrett: This is the podcast from *Clinical Chemistry*. I am Bob Barrett.

In making the diagnosis of diabetes, there are several advantages using determinations of hemoglobin A1c rather than glucose measurements. These include the pre-analytics stability of hemoglobin A1c in the sample, a low within-subject biological variation, as well as being free from the dietary restrictions associated with measuring glucose.

Most of the data supporting use of hemoglobin A1c come from measurements performed by laboratories, but what about diagnostic testing performed in point-of-care settings? A paper in the December 2013 issue of *Clinical Chemistry* looks into the matter.

Una Sølvik, an Associate Professor in the Department of Global Health and Primary Care at the University of Bergen in Norway, and at NOKLUS, which is an external quality assurance organization in Norway, was lead author in that study and she is our guest in today's podcast.

Dr. Sølvik, your study examined the quality of hemoglobin A1c results in point-of-care settings. Can you tell us a bit about the study design and what you found?

Dr. Una O. Sølvik: Yes in this longitudinal multicenter study, we have used results from 13 hemoglobin A1c external quality assurance surveys, or EQA surveys, that was performed by NOKLUS from 2006 till 2012 and all the GP offices and hospital laboratories in Norway, that analyze hemoglobin A1c, participated.

So we compared the results for the point-of-care instruments used at the GP offices with analytical performance they refer as the diagnosis of their basis and the performance of hospital laboratory instruments. And the main finding was that between 60% to 90% of the GP's performed measurements, a method followed for specification for both trueness and imprecision on EQA

survey and this was similar to the performance of hospital laboratories in Norway.

Bob Barrett: So it seems that point-of-care instrument measurements of hemoglobin A1c can be used to diagnose diabetes. In what way will this have impact on the patients, and what are the advantages compared to glucose measurements?

Dr. Una O. Sølvik: Well, using the point-of-care instruments at the GP offices; you can have the results during the consultations. Otherwise the blood sample has to be sent for analysis to hospital laboratory, and the patient must wait for the results.

So the test is easier available and this might lead to earlier identification of persons with diabetes. Considering the large number of persons with undiagnosed Type II diabetes, it's a great benefit.

The advantages compared to glucose measurement are that the hemoglobin A1c tests can be performed at any time of the day, and the patient does not need to fast or to be exposed for the metabolic stress test such as the oral glucose tolerance test.

Plus simpler conditions to take the test will lower the threshold to check whether the patient has diabetes. And in addition hemoglobin A1c has less biological variations than glucose, and is to a lesser extent affected by acute changes in the glucose level that can occur during stress or other diseases. It is also less sensitive for a pre-analytical variation.

Bob Barrett: Doctor you emphasized that a stringent quality assurance program is a prerequisite for high quality performance of hemoglobin A1c measurements in physician offices. What are some of the essential elements that should be part of a quality assurance program?

Dr. Una O. Sølvik: Well, in our opinion the essential elements in the quality assurance program are that the participants receive external quality controls on the regular basis, and it is very important that the quality controls are commutable and a fresh native human blood should be used.

A secondary reference laboratory sets the target values for the control and the participants should also receive feedback regarding the EQA results and it is also advised an instruction regarding the measurement should be there, and when they obtain an evaluation of their EQA results outside the quality specification.

In addition the participants should also receive regular guidance in the form of visits and courses from the

laboratory consultants, and have to run internal quality control and a recommendation about what instrument to use.

Recommendation about the quality of point-of-care instruments in NOKLUS is based on evaluation from the Scandinavian evaluation of laboratory equipment for primary health care (SKUP) that performs supplier independent evaluations of the analytical quality and user-friendliness of point-of-care instruments.

Bob Barrett: Doctor you looked at some specific instrumentation for hemoglobin A1c measurements. What did you find, and did all instrument types perform satisfactorily in their ability to diagnose diabetes?

Dr. Una O. Sølvik: Yes, that's right we looked at point-of-care instruments Afinion, and different levels of DCA which were merged into one group, and Nycocard, and we found that the Afinion and DCA--and not Nycocard--fulfilled analytical quality specification for hemoglobin A1c measurements and diagnosis on their basis.

Also another study from 2010 investigated the performance of six other point-of-care instruments in a hospital environment, but these instruments did not fulfill the quality criteria, so currently only these two instruments are recommended to use to diagnose diabetes.

However, new instruments are already coming into the market after this study was performed and probably there will be even more instruments in the future, but it's of course important that the GP offices using these new instruments also participate in quality assurance program and that they can show that the quality is in with the specifications.

In Norway, the point-of-care instruments Quo-Test A1c and HemoCue 501, came into the market from autumn 2012 and spring 2013 respectively, but the number in the EQA surveys are currently too low to determine if GP offices using these instruments fulfill the quality specifications.

Bob Barrett: Are there any situations were Hemoglobin A1c should not be used to diagnose diabetes?

Dr. Una O. Sølvik: Oh yes. In a condition that shorten erythrocyte survival or decreases mean erythrocyte age have impact on the hemoglobin A1c test results. Like after acute blood loss, certain anemias like hemolytic anemia and iron deficiency anemia, and chronic malaria.

The most common important factor worldwide affecting hemoglobin A1c levels are hemoglobinopathies, for example, where hemoglobin A1c is replaced by other hemoglobin variants.

In some cases, A1c can be measured depending on the measurement method. In addition, gestational diabetes and diabetes I who develop very fast cannot be diagnosed by hemoglobin A1c. In all these situations the diagnosis of diabetes should be based on glucose measurement.

Bob Barrett: Wouldn't those situations also affect laboratory measurements of hemoglobin A1c as well?

Dr. Una O. Sølvik: Yes, of course hospital laboratory measurements can also – must -- be used in these situations.

Bob Barrett: So if measurements of hemoglobin A1c should not be used in such patients, can glucose point-of-care instruments be used to diagnose, and are the quality specifications for glucose as strict as those for hemoglobin A1c?

Dr. Una O. Sølvik: In principle, any instruments fulfilling the quality specifications in hands of the user can be used for diagnosing diabetes. Currently, however, there is no consensus for what analytical performance of glucose meters that is necessary to use them for diagnostic purpose.

So results from SKUP have shown that there are several glucose point-of-care instruments that have very good analytical quality. One main problem with using glucose for diagnosing is the pre-analytical considerations.

Bob Barrett: Well finally, doctor, in the discussion section of your paper you mention that the NOKLUS Quality Assurance Program has recently started to also monitor *within* laboratory day-to-day variation. Do you have preliminary results, and has there been any negative reaction to this practice?

Dr. Una O. Sølvik: Well, unfortunately it's too early to comment on the results on internal quality assessments from the participants that we so far have too few data. We did experience that it is difficult to have the results from some internal quality control from the GP offices.

The recommendation (from NACB) is to include two control materials with different mean values at both the beginning and the end of each day's run. In Norway there are many small GP offices and they find it too expensive and time-consuming to perform internal quality control twice a day, and furthermore, the Norwegian Hemoglobin A1c Working Group finds it unnecessary to analyze controls so

frequently, and they recommend that the controls are run everyday the hemoglobin A1c instrument is used.

Bob Barrett: Dr. Una Sølvik is an Associate Professor in the Department of Global Health and Primary Care at the University of Bergen in Norway, and at NOKLUS, an external quality assurance organization in Norway. She has been our guest in today's podcast from *Clinical Chemistry*.

I am Bob Barrett. Thanks for listening.