The Food and Drug Administration (FDA) published recently some recommendations for the best use of the glucose meters that use the enzymatic technology of glucose dehydrogenase pyrroloquinoline quinine (GDH-PQQ)\(^1\). According to these recommendations, such ambulatory glucose monitoring systems might interfere and show results falsely high of glucose in patients who receive therapeutic products by parenteral or intraperitoneal route, that contain substantial quantities of non glycosidic sugars, as galactose, maltose, xylose or icodextrine, a substance that is metabolized in maltose in the body. Under these circumstances, the use of glucose meters with GDH-PQQ, when showing abnormally high values, might mask the presence of serious hypoglycemias and/or induce the inappropriate administration of high doses of insulin, with serious consequences for the patient, including death. Thus, according to the report of the FDA, between 1997 and 2009, a total of 13 deaths due to hypoglycemia have been documented in Health Centers associated to the inappropriate use of strips with GDH-PQQ\(^2\). In most of the cases (n=10), patients were under peritoneal dialysis receiving products containing icodextrine\(^3\).

Table 1 depicts a list of glucose meters with GDH-PQQ that are commercialized in Spain.

Table 1. Glucose meters that use the GDH-PQQ enzymatic technology commercialized in Spain

<table>
<thead>
<tr>
<th>Product</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roche Diagnostics*</td>
<td>Accu-Chek Aviva Freestyle</td>
</tr>
<tr>
<td>Accu-Chek Compact</td>
<td>Accu-Chek Compact Plus FREESTYLE FREEDOM Lite</td>
</tr>
<tr>
<td>Accu-Chek Compact Plus</td>
<td>Accu-Chek Inform System</td>
</tr>
<tr>
<td>Accu-Chek Sensor</td>
<td></td>
</tr>
<tr>
<td>**For further information at:</td>
<td><a href="http://www.roche-diagnostics.com">www.roche-diagnostics.com</a>; www.</td>
</tr>
<tr>
<td></td>
<td>accu-chek.com; <a href="http://www.rochediagnostic">www.rochediagnostic</a></td>
</tr>
<tr>
<td></td>
<td>es.; <a href="http://www.accu-chek.es/">www.accu-chek.es/</a>; Customer</td>
</tr>
<tr>
<td></td>
<td>support: 900-210341.</td>
</tr>
<tr>
<td>**For further information at:</td>
<td><a href="http://www.abbottdiabetescare.com">www.abbottdiabetescare.com</a>; www.</td>
</tr>
<tr>
<td></td>
<td>abbottdiabetescare.es.; Customer</td>
</tr>
<tr>
<td></td>
<td>support: 900 300 119.</td>
</tr>
</tbody>
</table>

Table 2. Products commercialized in Spain that might show false results with the reactive strips based on the GDH-PQQ enzymatic technology*

<table>
<thead>
<tr>
<th>Product</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>ExtraHeal(^5)</td>
<td>In solutions for peritoneal dialysis</td>
</tr>
<tr>
<td>Orencia(^6)</td>
<td>As anti-inflammatory, it is used combined with methotrexate in the treatment of the rheumatoid arthritis</td>
</tr>
</tbody>
</table>

Products administered parenteral or intraperitoneal that contain significant differences of maltose or galactose, or that are metabolized in these substances

Table 2. Products commercialized in Spain that might show false results with the reactive strips based on the GDH-PQQ enzymatic technology*

*This list is updated up to November 16\(^{th}\) 2009.

The list of products commercialized in our country that might potentially interfere with the GDH-PQQ glucose meters is depicted in table 2.
The interferences take place when these substances are administered by parenteral or intraperitoneal route but not when taken orally. In this case, these non-glucidic sugars are previously digested and transformed into monosaccharides at the brush border (enterocytes), as maltose in two glucose molecules. Then, the glucose, the galactose and the fructose will be incorporated into enterocytes using specific transporters, passing finally into the blood. Both galactose and fructose will be metabolized and converted into glucose in the liver. The intake of D-xylose orally has to be pointed out as an exceptional situation. The pentose might be absorbed in the intestine and is not transformed significantly in the liver before its urinary clearance. This sugar was used some years ago in the D-xylose tolerance test in order to evaluate the intestinal absorption of the carbohydrates in the celiac disease. However, at present there are no situations that might imply a relevant oral intake of this substance. Therefore, the consumption of these substances orally, as maltose, lactose (disaccharide which contains glucose and galactose) or rarely, galactose as monosaccharide, will not cause risk situations due to its own digestion process and metabolism in the body.

In spite of the importance of the FDA alert, this problem should be delimited avoiding an excess of alarm among professionals and patients. If the patients are not receiving the above-mentioned products (table 2) by parenteral or intraperitoneal route, the glucose meters with GDH-PQQ are safe and can still be used without any health risk. However, the glucose meters with GDH-PQQ should not be used in the situations that, though specific, might be potentially dangerous for the patients under peritoneal dialysis, those who followed determined treatments for the rheumatoid arthritis, etc. Under these circumstances it is preferable the use of glucose meters with glucose oxidase enzymatic technology, glucose dehydrogenase with nicotinamide adenine dinucleotide (GDH-NAD) or glucose dehydrogenase with flavin-adenine dinucleotide, which do not show a crossed reaction with the mentioned products (table 2) and, therefore, they will not give place to inadequately high values of the capillary glycemia.

In conclusion, the ambulatory glucose monitoring systems of the capillary glycemia in the GDH-PQQ technology are reliable and safe in most of the patients with diabetes, except in those who can be susceptible of receiving substantial quantities of non-glucidic sugared products, such as galactose, maltose, xylose or icodextrines. In these cases, the preventive use of glucose meters based on the oxidase glucose is preferable, as GDH-NAD or GDHAH-FAD, which will not present interferences with the already mentioned substances.

Declaration of potential conflict of interests

Dr. Ampudia-Blasco received fees for conferences and/or consultancy from Abbott, Bristol-Myers-Squibb, GSK, LifeScan, Lilly, Madaus, MannKind Corp., Medtronic, Menarini, Merck Farma and Quimica S.A., MSD, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi-Aventis, Schering-Plough and Solvay. Dr. Ampudia Blasco took part in clinical trials total or partially financed by Astra-Zeneca, Bayer, GSK, Life-Scan, Lilly, MSD, Novo Nordisk, Pfizer, Sanofi-Aventis and Servier.

References

1. Available in: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/PublicHealthNotifications/ucm176992.htm