CLINICAL IMPORTANCE OF EVIDENCE BASED THERAPY FOR DIABETES TYPE 2

Mohammad A. bajubair, MD
Faculty of Medicine and Health Sciences, University of Sanaa
Department of Medicine, Althawra Modern Teaching Hospital
Sanaa, Republic of Yemen

ABSTRACT

Objectives: Not all practice guidelines on oral treatment of Type 2 diabetes were consistent with available evidences. Our aim was to explore the necessity of following the new clinical evidences in treatment of diabetes mellitus Type 2 in clinical practice and the availability of randomized controlled trials in literatures used.

Methods: Cross-sectional interview survey of 20 physicians in the Internal Medicine Departments in Althawra Teaching Hospital, University of Sana’a, Yemen, to understand the drug used in Type 2 diabetes in regards to the clinically evidenced trials. The three commonly used literatures were studied for the availability of randomized controlled trials and the systematic reviews.

Results: Examples of drugs to be considered in special correlation and contradiction were metformin and thiazolidinediones (rosi-, pioglitazone). Fear of lactic acidosis was seen in 45% of physicians. Ischemic Heart disease and failure represent the commonest cause of glitazones avoidance, especially for rosiglitazone (100% vs. 50% for pioglitazone).

Example of drugs used were with no agreements of their benefit are gabapentin (35%) and neurobion (30%) for neuropathy prevention. In the side effect consideration, metformin was still considered dangerous, and B-blockers hesitation in ischemic heart disease prevention.

The main source of information used by physicians was Davidson’s Medicine, British national formulary and pharmaceutical marketing leaflets.

Conclusions: Inconsistency between the tested physicians may be improved by better access and implementation of evidence based therapy and guidelines in Type 2 diabetes.

Keywords: Evidence-based therapy, Diabetes Type 2, Yemen.

Address for Correspondence:

Dr. Mohammad A. Bajubair
Faculty of Medicine and Health Sciences
University of Sanaa
Department of Medicine
Althawra Modern Teaching Hospital
Sanaa, Republic of Yemen
masjubair@yahoo.com

Submitted Date: 23/10/2012
MS Approved Date: 27/11/2012
BACKGROUND AND OBJECTIVES

Type 2 diabetes (T2DM) is characterized by insulin resistance accompanied by progressive deficiency in insulin secretion\[^1,2\]. As new classes of oral medications have become available for the treatment of diabetes, clinicians and patients have faced a bewildering array of oral medications with different mechanisms of action\[^3\]. Clinicians may find it difficult to choose between the drug classes that are now in common use\[^4\].

Evidence Based Therapy (EBT) is defined in a generally positive and individualistic way that emphasizes the importance of outcomes and endpoint states, and not surrogate markers (e.g., blood sugar control)\[^5\].

United Kingdom Prospective Diabetes Study, 1998, has demonstrated the progressive nature of T2DM, and as disease progresses, combination oral anti-diabetic drugs and insulin are needed in order to maintain good sugar control\[^6\]. Traditional oral agents like metformin and sulfonylureas have failed to arrest the progression of T2DM\[^6\].

It is critical to evaluate adverse events, since these affect adherence as well as morbidity and mortality\[^7\].

Since the two biggest trials in people with T2DM showed that improved blood glucose alone is not enough to reduce the risk of the disease, we looked for longer-term studies\[^8\].

Not all practice guidelines on oral treatment of T2DM were consistent with available evidence\[^9\].

Our aim was to explore the necessity of following the new clinical evidences in treatment of T2DM in clinical practice, and the availability of randomized controlled trials (RCT) in the used literatures.

METHODS

Cross-sectional interview survey of 20 physicians in the Internal Medicine departments; 10 represented the specialist group of post-graduated physicians and the Arabic board students (4th year) and the other 10 represented the general physicians in Althawra Teaching Hospital, University of Sana’a, Yemen. This survey is to understand the drug use for T2DM on basis of the EBT, this is included in a specially prepared questionnaire. These physicians were randomly selected, in the alternate day’s style, in a cross-section period from August through September 2012. The three most common used sources of drug information by the tested physicians were studied and analyzed for the availability of RCTs and the systematic reviews of the main types of drugs for T2DM, namely biguanides, sulfonylureas, glitazones (thiazolidinediones) and gliptins (dipeptidyl peptidase inhibitors or incretion therapy). The questionnaire was completed by the investigating doctor to ensure that the participating doctors completed and understood the meanings, and to avoid missing responses for some items of the questionnaire.

RESULTS

Eight questions about the drugs used in T2DM have been answered differently by the (20) physicians. Example of hypoglycemic drugs is seen in Table 1 and other drugs used frequently in DM in Table 2.

The three commonly used sources of drug information are Davidson’s Principles & Practice of Medicine\[^10\], drug prescribing marketing leaflets\[^11\] and British National Formulary (BNF)\[^12\].

The new edition of Davidson’s Principles & Practice of Medicine\[^10\] included the recommendation in special boxes that are supported by evidence obtained from meta-analysis of several RCTs, or on one or more RCTs. Recommendations conform to Grade A criteria. In DM section there are only 3 boxes.

Drug prescribing marketing leaflets\[^11\] at the time of research (2012) were last revised at July 2005 (Glucophage® 500, Bristol-Myers Squibb, New York, NY USA), April 2004 (Dialon®, Julphar UAE) and March 2009 (ACTOS®, 4AKEDA® PHARMA, Japan).

Table 1. Baseline knowledge of Physicians and examples of EBM of the oral hypoglycemic drugs use on T2DM.

<table>
<thead>
<tr>
<th>Type 2 Diabetes mellitus</th>
<th>Drug Therapy</th>
<th>Specialist 10</th>
<th>General 10</th>
<th>Total 20 Physicians</th>
</tr>
</thead>
<tbody>
<tr>
<td>First line drug</td>
<td>- Use of metformin</td>
<td>80%</td>
<td>40%</td>
<td>60%</td>
</tr>
<tr>
<td>Why not use and precaution of metformin?</td>
<td>- Lactic acidosis</td>
<td>60%</td>
<td>30%</td>
<td>45%</td>
</tr>
<tr>
<td></td>
<td>- Gastrointestinal upsets</td>
<td>70%</td>
<td>30%</td>
<td>50%</td>
</tr>
<tr>
<td>Sensitizers use Precautions</td>
<td>- Pioglitazone</td>
<td>60%</td>
<td>40%</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>- Rosiglitazone</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>- Heart failure</td>
<td>80%</td>
<td>30%</td>
<td>55%</td>
</tr>
<tr>
<td></td>
<td>- Liver toxicity</td>
<td>20%</td>
<td>0%</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>- Expensive</td>
<td>60%</td>
<td>20%</td>
<td>40%</td>
</tr>
<tr>
<td></td>
<td>- Bladder cancer</td>
<td>20%</td>
<td>0%</td>
<td>10%</td>
</tr>
</tbody>
</table>
DISCUSSION

Textbooks and manufacture leaflets are the main sources of drug information by the tested physicians Davidson’s Principles & Practice of Medicine[10], drug manufacture literature leaflets[11] and BNF[12]). These are the traditional sources in comparison to the newly developing internet based literatures.

Examples of oral hypoglycemic drugs to be considered in special correlation and contradiction were metformin and thiazolidinediones (rosi- or pioglitazone).

Metformin still considered dangerous (renal-lactic acidosis), although, it could not be recorded in RCT[10,13]. Still, there is a fear of lactic acidosis in nearly half of the participants which is mostly in the specialist group (60% vs. 30%).

Pooled data from 347 comparative trials and cohort studies revealed no evidence from prospective comparative trials or from observational cohort studies that metformin is associated with an increased risk of lactic acidosis, or with increased levels of lactate, compared to other anti-hyperglycemic treatments[13].

Thiazolidinediones or glitazones are insulin sensitizers. Theoretical benefits of the peroxisome proliferators activated receptor gamma activator rosiglitazone on endothelial function and cardiovascular risk factors might result in fewer macrovascular disease events in people with T2DM[14]. The large RCT, A Diabetes Outcomes Progression Trial (ADOPT) suspected increased cardiovascular risk, and hence, subsequent trials and meta analysis confirmed this association[14,15].

The avoidance of rosiglitazone may indicate late response (100%) after market withdrawal. Bladder cancer is relatively new precaution for pioglitazone and known only by 10% of the physicians.

Data from the placebo-controlled PROactive® trial of pioglitazone suggested a higher incidence of bladder cancer among pioglitazone users than among controls[16]. Subsequent RCTs and observational studies have reported various studies reporting a significant increase[17-19] and a non-significant increase[20-22] of bladder cancer. More recently long-term TZD therapy (≥ 5 years) in patients with T2DM was found to be associated with an increased risk of bladder cancer[23,24].

Some medications used frequently in DM with no clinical agreements of their benefit. An example of this was found in vitamin B (Neurobion) and gabapentin (50% vs. 20%) use for neuropathy prevention, (40% vs. 20%), B-blockers use for hypertension in DM without ischemic heart disease (40% vs. 0%) and antihypertensive use in DM, Amlodipine 25%.

The hesitation in belief about the drugs (unclear or unmonitored evidences) may be reflected to the patients as omission of the drugs.

The three sources of drug information are traditional sources, which are not quickly updated and non-internet based.

In BNF even unlicensed use is reported[24].

CONCLUSIONS

The non-agreement and contradictions between the tested physicians may be improved by better access and implementation of evidence based therapy and guidelines in DM.

Results showed a necessity for following clinical evidences (EBT-RCT). Including the RCTs in most commonly used in textbooks with familiarity to benefit from as it may help to relieve some of the confusion about clinical practice of drug therapy for diabetes type 2.

- Internet based drug information and following the newly clinical evidences has to be encouraged.

- Drug prescribing information leaflets have to be revised and updated more frequently e.g., annually.

  - No conflict of interest.

Table 2. Baseline knowledge of physicians and examples of EBM of non-hypoglycemic drugs used frequently on T2DM.

<table>
<thead>
<tr>
<th>Type 2 Diabetes mellitus</th>
<th>Drug Therapy</th>
<th>Specialist 10</th>
<th>General 10</th>
<th>Total 20 Physicians</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic neuropathy prevention</td>
<td>- Neurobion</td>
<td>40%</td>
<td>20%</td>
<td>30%</td>
</tr>
<tr>
<td></td>
<td>- Gabapentin</td>
<td>50%</td>
<td>20%</td>
<td>35%</td>
</tr>
<tr>
<td></td>
<td>- No Evidence</td>
<td>20%</td>
<td>30%</td>
<td>25%</td>
</tr>
<tr>
<td>B-blocker for hypertension in DM</td>
<td>- Only in ischemic heart disease</td>
<td>60%</td>
<td>40%</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>- No precaution</td>
<td>40%</td>
<td>0%</td>
<td>20%</td>
</tr>
<tr>
<td>Antihypertensive use in DM</td>
<td>- ACEI</td>
<td>60%</td>
<td>30%</td>
<td>45%</td>
</tr>
<tr>
<td></td>
<td>- Amlodipine</td>
<td>20%</td>
<td>30%</td>
<td>25%</td>
</tr>
</tbody>
</table>
REFERENCES


