Case report discussed by experts

Type 2 diabetes and other comorbidities in an elderly patient

Diabetes tipo 2 y otras comorbilidades en un paciente anciano

Male aged 83 with T2D of 16 years evolution, who showed a good general condition and an HbA1c of 8.6%.

Personal history
The patient received the diagnosis of non-proliferative retinopathy and cataracts, undergoing surgery in the left eye. Moreover, he shows mild distal polyneuropathy, incipient nephropathy without renal failure, hypertension, hyperuricemia and mixed hyperlipemia, as well as non-autoimmune primary hypothyroidism. He undergoes treatment with metformin (2,550 mg/day) glimepiride (4 mg/day) and insulin glargine in morning doses of 22 IU, atorvastatin (20 mg/day), irbesartan (300 mg/day), hydrochlorothiazide (25 mg/day), levotiroxin (125 µg/day) and acetylsalicylic acid (AAS) (100 mg/day). He never smoked and drank only moderately. He was a professor in his active life. He is very worried because he is losing weight. The fasting glycemia during the last controls was not reduced below 180 mg/dL.

Data corresponding to the last revision
Weight 75 kg, height 169 cm, blood pressure (BP) 138/92 mmHg, abdominal waist 92 cm. The cardiac auscultation reveals pure and rhythmic tones. Abdominal megalies and signs of peripheral vascular failure or edema cannot be observed. There is a reduction of the peripheral vibration and thermal sensitivity, higher in the right foot, as well as of patellar and Achilles reflex. In the differed analytics, the following results appear: creatinine of 1.3 mg/dL, basal glycemia 223 mg/dL, HbA1c 8.6%, uric acid 7.6 mg/dL, total cholesterol 203 mg/dL, triglycerides 148 mg/dL, HDL cholesterol (c-HDL) 47 mg/dL, and microalbuminuria 58 µg/mL. There are no other pathological biochemical determinations, including the thyroid hormones. As regards to the patient’s outpatient control, he undergoes 2 glycemic profiles of 3 preprandial points once a week and BP measurement.

Which modifications would you do to this patient’s hypoglycemic treatment?
Altogether, he is a patient of advanced age, with an apparent good life quality, but with limited life expectation (83 years) and with a treatment based on a long acting insulin analogue in doses that, though they are recommended in elderly persons (0.3 U/kg), they might be possibly insufficient. The glycemic control is not adequate (HbA1c: 8.6%) and he shows an insulin deficiency sign as the loss of weight.

Answer of Dr. Xavier Mundet Tuduri

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List of acronyms quoted in the text:
BHT: blood hypertension; BMI: body mass index; CCT: controlled clinical trials; CVRF: cardiovascular risk factors; DAP: diastolic arterial pressure; NPH: neutral protamine Hagedorn insulin; SAP: systolic arterial pressure.
The glycemic control objectives in an elder patient have to be identical a priori to those of an adult person. However, the balance among the intensification risks of the hypoglycemicant treatment—higher than those of a younger patient—and the benefits—lower than those of the younger persons—should be assessed in detail. The main risks that shall be considered are basically two: the risk of suffering hypoglycemia secondary to the hypoglycemicant drugs and the pharmacological interactions inherent to every patient treated with polypharmacy, as this case. On the contrary, the potential benefits in a person of advanced age are comprised mainly in relation to an adequate metabolic control—and there are evidences in this patient of not having achieved it—and, in a lower extent, though not underestimated, to the prevention of the microvascular complications (retinopathy, nephropathy and neuropathy) or to avoid its progression if they are already present, as it happens in this patient.

In this special case, the hypoglycemia risk is low, as the patient does not refer any previous hypoglycemia events and the baseline glycemias are sufficiently high so as to suppose that he has no risk of suffering them, except if they are due to frequent diet transgressions. As regards to the second risk—the pharmacological interaction—the possibility of this patient is high when receiving treatment with seven drugs besides the insulin. Therefore, to add more medication to what he is already taking should be assessed carefully, especially the balance between the hypothetical benefit, which is supported by the previous evidence, and the possible inherent risk to any treatment.

A relevant datum in this case is the recent loss of weight, which is a concern reason for the patient and for the physician, as this indicates us about the probable insulin deficiency in spite of being already treated with insulin. We have to consider that this is a patient with a body mass index (BMI) value close to the normal weight (26) and without abdominal obesity (abdominal circumference of 92 cm). These two values (BMI and normal waist perimeter) oblige us to think that the main etiopathogenic factor of the inadequate glycemic control is the insulin deficiency, surely much more important than the resistance to the insulin. In view of all this, and considering the lack of data, the optimal alternative for this patient should be to set out an intensification of the insulin therapy (figure 1).¹

In relation to the therapy with oral drugs, we should consider that the patient is already being treated with two of them, metformin and glimepiride, with different action mechanisms. To add another drug taking into account the scarce expected benefits of a third drug, the polypharmacy already received and the expectation of life of this patient, is not an adequate alternative.

As regards to the use of the current hypoglycemicant drugs, metformin might still be used since the glomerular filtration estimated by means of the brief MDRD formula of this patient is of 56 mL/min/1.73 m². With the glomerular filtration is lower than 30 mL/min, the risk of lactic acidosis compels us to withdraw it. As regards to the glimepiride, we should consider that, together with the glicazide, the sulphonylureas are preferable in this elder person because they have a lower risk of hypoglycemia than glibenclamide and are safe in cases of renal failure which is a frequent situation in the patient of advanced age. In spite of the fact that the indicated dose of gliclazide (4 mg) is low, the increase of the dose should not be an effective alternative to reduce the glycosylated hemoglobin, because as it is secretagogue drug it would difficult the improvement the pancreatic reserve. On the contrary, this might worsen mostly due to the exhaustion of the beta cell.

In view of the above, the most adequate in this patient would be to intensify the insulin therapy and, at the same time, to assess the suspension of the treatment with glimepiride keeping the metformin (with a light reduction of doses) if the glomerular filtration is higher than 30 mL/min.

Would you do any changes in the treatment of the rest of the morbidities?
As regards to the cardiovascular disease, it is evident that this is a patient with two cardiovascular risk factors (CVRF) besides the diabetes, as the dyslipidemia and the blood hypertension (BHT). This is a patient who receives at present a treatment for both factors and with a lipid profile and BP values as minimum acceptable, therefore we should analyze if it is justified to intensify the treatment of one or the other.

Treatment of the dyslipidemia
At present, we do not count with controlled clinical trials (CCT) in primary prevention of cardiovascular disease in diabetic patients older than 75 years of age. Many studies of primary prevention have analyzed sub-
groups of patients with diabetes, but the only trial designed specifically is the study CARDS,\(^2\) that will be useful for us as reference. In this clinical trial the patients with cLDL <160 mg/dL and some CVRF (similar case as the one of our patient, though there is no information of the initial cLDL) have been treated with 10 mg of atorvastatin versus placebo, proving a relative reduction of 37% of cardiovascular events in the patients treated with the drug after 4 years. However, we should do several considerations, as that the scope of the analyzed age was of 60-75 years, therefore any recommendation in older ages shall be an extrapolation of the results in younger ages. In second place, all the patients were treated with 10 mg of atorvastatin and our patient is already receiving the double (20 mg) of the dose used in the trial. Therefore, our recommendation would be conservative. The cHDL and the triglycerides are controlled. The cLDL shows a value lower than 130 mg/dL (estimating the LDL as from the analytical data, this result in 126 mg/dL). Taking into account that: 1) there are no studies with patients of this age; 2) the patient does not have any ischemic cardiopathy history, and 3) is receiving already a stand/high doses of statins (20 mg of atorvastatin) it does not seem adequate to increase the dose that the patient is already receiving or add a fibrate.

**Treatment of the blood hypertension**

As regards to the BHT, we shall take into account that, like we have indicated for the hyperlipidemia, we do not...
count with ECC in advanced ages (the scope of age in the UKPDS was of 40 to 65 years) that have given reply to this matter. Though most of the entities (ADA) recommend values of BP <130/80 mmHg in all the diabetic patients, in those with renal or retinal affection (NICE) this recommendation has an evidence level (recommendation of experts), without ECC that endorse such values. An approach based on the evidence and without taking the age into account (the studies are performed in patients under 65 years of age) supports the systolic arterial pressure (SAP) <140 mmHg (UKPDS) and diastolic (DAP) <80 mmHg (HOT), always taking into account that these values are well tolerated by the patient (absence of dizziness or cephalic instability), especially if the patient is of advanced age. No signs of orthostatic hypotension are evidenced in this specific patient, therefore we could intensify the treatment to achieve a main reduction of the DAP (92 mmHg) and secondarily of the SAP (138 mmHg), as this one could be considered more adequate. Given that the patient is receiving a treatment with angiotensin II receptor inhibitors as the irbesartan at full doses (300 mg) (protector of the nephropathy) together with a diuretic –also at high doses: 25 mg of hydrochlorothiazide– it would be recommendable to add a non-dihydropyridine calcium antagonist, as the amlodipine.

As regards to the use of AAS as primary prevention of the cardiovascular disease, though the clinical guidelines they continue recommending its use, the last EEC are conclusive considering the scarce reduction of the risk in diabetic patients. In spite of the fact that in both studies patients older than 60 years of age are included, in the Ogawa study older patients (up to 85 years of age) have been included. Therefore, and taking into account that we are facing a case of primary prevention, we should withdraw the AAS.

**Which is the number of glycemic and pressure controls you consider appropriate for the patient to undergo?**

Initially, we set out an increase of the dose of basal insulin. Determinations should be done on morning capillary glycaemia while we increase the dose of insulin, until achieving that the basal glycaemia is acceptable and the hemoglobin lower than 7%. If we achieve an acceptable basal glycaemia, but the glycosylated hemoglobin is still >7%, we should set out an intensification of the insulin therapy through the bolus basal method that consists of adding one or several fast insulin supplements to the ba-
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sual insulin (ADA-EASD consensus). This guideline needs the performance of preprandial glycemic profile with 3 determinations (breakfast, lunch and dinner), until achieving preprandial glycemias lower than 130 mg/dL. Once we reached adequate preprandial glycemia profiles (6 per day) in order to detect the moment of the day when the hyperglycemia is produced (figure 2). 9

Would you do any complementary test?
As complementary emergency test, the determination of ketonuria / ketonemia should be done in first place to assess the level of insulin deficiency to explain the recent loss of weight. Finally, and though there are no signs of peripheral arteriopathy, it is indicated to determine the ankle-arm index (AAI) in order to detect the silent peripheral arteriopathy, as this is a patient of advanced age, with CVRF and microvascular complications, all of them risk factors for suffering a silent peripheral arteriopathy.

Declaration of potential conflict of interest
X. Mundet Tuduri stated that there is no conflict of interests as regards to this paper.

References