Drivers and enablers of therapeutic inertia: is there a hierarchy?

Driver e fattori abilitanti dell'inerzia terapeutica: esiste una gerarchia?

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During my presentation, I will seek to answer two questions:

1. Is there a single driver of therapeutic inertia?
2. If there are multiple causes, is it possible to establish a hierarchy among the different possible drivers of therapeutic inertia?

An answer to the first question is partially answered by reading Bob Eckel, who provides a good definition of therapeutic inertia as the failure to begin treatment or failure to intensify treatment faced with HbA_{1c} values far beyond the established therapeutic target. This dimension of therapeutic inertia, which Dr Eckel showed us in the context of the United States, can be measured effectively in Italy using data from the AMD Annals. The data tell us that 47% of our patients with type 2 diabetes do not have glycated haemoglobin < 7%, and that 16% of patients have HbA_{1c} values > 8%. If we turn to a composite endpoint, shown by the proportion of patients who simultaneously have glycated haemoglobin values < 7%, LDL cholesterol < 100 mg/dL and blood pressure < 140/90 mmHg, only 20% of the population treated in our country's Diabetology Services meet these criteria.

The published data clearly demonstrate the consequences of therapeutic inertia, which is responsible for an increased risk of developing the chronic complications of diabetes. How aware are we, though, of the possible consequences of therapeutic inertia? To answer this question, we used a web survey, which was taken by a fair number of clinical diabetologists (153) who participate in the activities in our AMD assistance network. Each question could be answered on a scale from 0 (no impact) to 10 (maximum impact).

The first question was, 'In your opinion, what is the impact of therapeutic inertia?'

The survey documented substantial agreement among the participants on the impact of inertia on the risk of having cardiovascular events, of not bringing blood glucose control to target, of developing complications associated with diabetes and, finally, the risk of all causes mortality. For each of these items, the score was very high (7.8-7.9), indicating an awareness among physicians of the significance of therapeutic inertia.

At this point, we could already attempt to answer the first question: is there a single cause of therapeutic inertia? The answer is no. We can frame therapeutic inertia as a very complex, multi-factorial element; this phenomenon is becoming increasingly relevant, and obviously does not only involve diabetes but other chronic conditions as well. Considering therapeutic inertia as a multi-factorial condition,

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we must recognize that some of these factors must be ascribed to the patients, and some are due to us, the healthcare professionals (HCPs), but also partially due to the healthcare system we are working in every day.

A review of the previous studies published more than one year ago effectively summarised the portrait of the factors contributing to therapeutic inertia (fig. 1) (Okemah J et al. Diabetes Ther 2018). Therapeutic inertia, which is today's subject, is at the centre, and it is supported by three tiers of factors: related to the patient, related to the HCP and related to the healthcare system. The barriers correlated to the patient include: a denial of the disease, a lack of awareness of the progressive nature of diabetes, a lack of awareness of the implications of suboptimal blood glucose control, the fear of side effects, the anxiety of not being able to handle complicated treatment regimens during everyday life; too many medications, the cost of treatment (which, fortunately, is not significant for the patient in Italy), a lack of communication with clinicians, or the team; a lack of support; and a lack of trust in the clinician.

In the web survey cited above, we attempted to raise questions about this issue with Diabetologists, to find out what they think: 'In your opinion, how much impact do these factors related to the patient have on therapeutic inertia?'

Infirmity, lack of compliance, advanced age, a patient living in poor social conditions, a patient without good cognitive abilities, and others including fear of hypoglycaemia and poor school education were all considered relevant aspects, with high average scores (around 7).

Going back to the review of the published studies mentioned above, an interesting consideration should be made: when we enrol our patients in a randomised clinical study, the problem of therapeutic inertia does not exist or is very much contained. The most important element making the difference between a patient involved in a randomised clinical study and normal clinical practice is that we clinicians and the team supporting us in a trial provide the patient with continued, constant educational inputs that buffer many of the elements listed above that are the cause and reason for therapeutic inertia on the patient's part.

Therefore, the lesson we can learn from the 'artificial' setting of randomised controlled trials is that good education and continuing support can be – and must be – one of the solutions to therapeutic inertia when we see it in our patients.

From this perspective, it is important to understand our patients' perceptions: fear of beginning or intensifying a treatment is indeed often associated with a feeling of failure in the patient's mind, or them seeing the intensification as a sort of threat: 'After all, I can do something. This suggestion of intensification is just a threat, but I can get along in some other way'.

Patient education plays an essential role in confronting and resolving these perceptions, a role clearly demonstrated by scientific evidence. A systematic review of 118 studies of therapeutic education in self-management of people with type 2 diabetes documented a significant reduction in HbA_{1c} levels to 0.57% compared to the usual care (Chrvala CA et al. Patient Education and Counseling 2015). The same systematic review found that the greatest benefits are obtained if the educational measures last 10 hours or more and if they include a combination of individual and group sessions.

As part of AMD's initiatives, a special initiative was promoted aimed at understanding which of the activities a Diabetologist performs in his/her normal daily clinical practice brings about the best results for people with diabetes. In this initiative, called Diabetes Intelligence, we sought to measure the impact on outcomes of all activities performed during our clinical interactions with patients. We asked an especially sophisticated algorithm, driven by Artificial Intelligence (AI), to produce a score; the results show that the highest points in this score can be attributed to educational aspects in our daily interactions with people with diabetes. This gave rise to an experiment aimed at describing what the core curriculum should be for those striving effectively to manage people with diabetes. Consequently we developed an accreditation process for certain clinical skills, most notably one that views the diabetologist as an expert in Diabetes Self-Management Education and that makes a large impact on the resolution of therapeutic inertia.

Turning to another dimension of therapeutic inertia: although patients are part of the system, there are other components that come into play: we as HCPs, and all those elements, not just the organisational ones, that characterise the environment in which we work.

Then there are what we consider to be factors to be attributed to us clinicians that support ther-

apeutic inertia, once again referring to our web survey. Among the causes of therapeutic inertia, we see the practice of defensive medicine, difficulties in managing especially complex therapeutic regimens, the lack of a sufficient and adequate knowledge/understanding of what the new clinical recommendations are, a fear of the side effects of medications we have little familiarity with, or a fear of hypoglycaemia or weight gain. We assigned scores between 5 and 6.5 to these elements.

Regarding clinicians' opinions on the factors to be attributed to the healthcare system, the organisational facility and the world we find ourselves working in, among the elements responsible for therapeutic inertia we find the lack of a team, the lack of time, the need for complex authorisation procedures for prescribing certain drugs, local expenditure ceilings, lack of possibility for General Practitioners (GP) to prescribe certain medications and the financial barriers to their prescription (scores from 6 to 7.5).

When we compare the average scores of the responsibilities we tend to attribute to patients and those attributable to the healthcare system with those we attribute to clinicians, it appears that, while we are aware of having a certain responsibility for part of the problem, we clearly tend to attribute the causes of therapeutic inertia to external factors unassociated with our work.

Now, if we ask the clinician about what can help us resolve this aspect, we find the need for more human resources, for decision-making support to be integrated into our electronic medical records, for more pressure from scientific societies on policy makers to improve treatment plans and prescription limitations, a need for educational campaigns, reducing the cost of treatment, local campaigns to measure therapeutic inertia, regularly performed audits, removing spending ceilings in budgeting discussions, annual, national campaigns to measure therapeutic inertia, with additional educational efforts on this aspect and – why not? – we need the support of new technologies: telemedicine and eHealth.

Something has been done about this: since an experiment started in Italy, in AMD, in the late 1990s, more than 90% of the Italian Diabetes Units now use the same computerised medical records. The record issues an alert when the patient has a fasting blood sugar level and a glycated haemoglobin level that are over the target, with therapy featuring basal insulin, and advises to titre the insulin upwards; or, in another case when the patient has target fasting blood glucose and glycated haemoglobin over the target and only basal insulin as therapy, an approach to postprandial blood glucose control should be introduced, and the system suggests some alternatives. The new version of the software also has a dashboard that proposes treatment goals to the Diabetologist when values are outside the target. We think this would be helpful, but we are already living in the future. A recent systematic review suggests that Artificial Intelligence could change the approach to diabetes treatment (Dankwan-Mullan I et al. Population Health Management 2019). There are many articles emphasizing the possibility of having decision-making support and predictive risk stratification for the patient.

If the future is now, AMD is not simply standing by; we tried proposing a 'white box' AI platform using the Rulex system, a large mass of data to allow evaluation of descriptive and predictive elements with the greatest chances of achieving the therapeutic target, such as with glycated haemoglobin without weight increase.

Diabetologists asked for help in our web survey with regularly measuring therapeutic inertia and implementing educational procedures, and that is what we did. The data from the AMD Annals tell us, when gauging as an indicator the number of people with HbA1c <7%, which we progressively changed from 43% in 2011 to 51% in 2016 and to 53% in 2018. For the proportion of people with HbA1c >8%, we progressively moved from 27% to 18%; those with HbA1c >9% not receiving insulin therapy went from 40% to 28%; then, if we consider the proportion of people with HbA1c >9% although currently using insulin therapy, we dropped from 26% to 16%.

All this did not take place spontaneously: we think that AMD has made a great contribution. For example, our association held many events on therapeutic inertia in 2018 and 2019, and more than 550 diabetologists attended more than 40 meetings. We believe that this initiative, along with others of the same type, if supported by educational campaigns, can make a clear contribution to resolving and improving aspects correlated with therapeutic inertia.

When we shifted the focus from the clinician to the policy-maker or the healthcare system and ask Diabetlogists which parts of the national

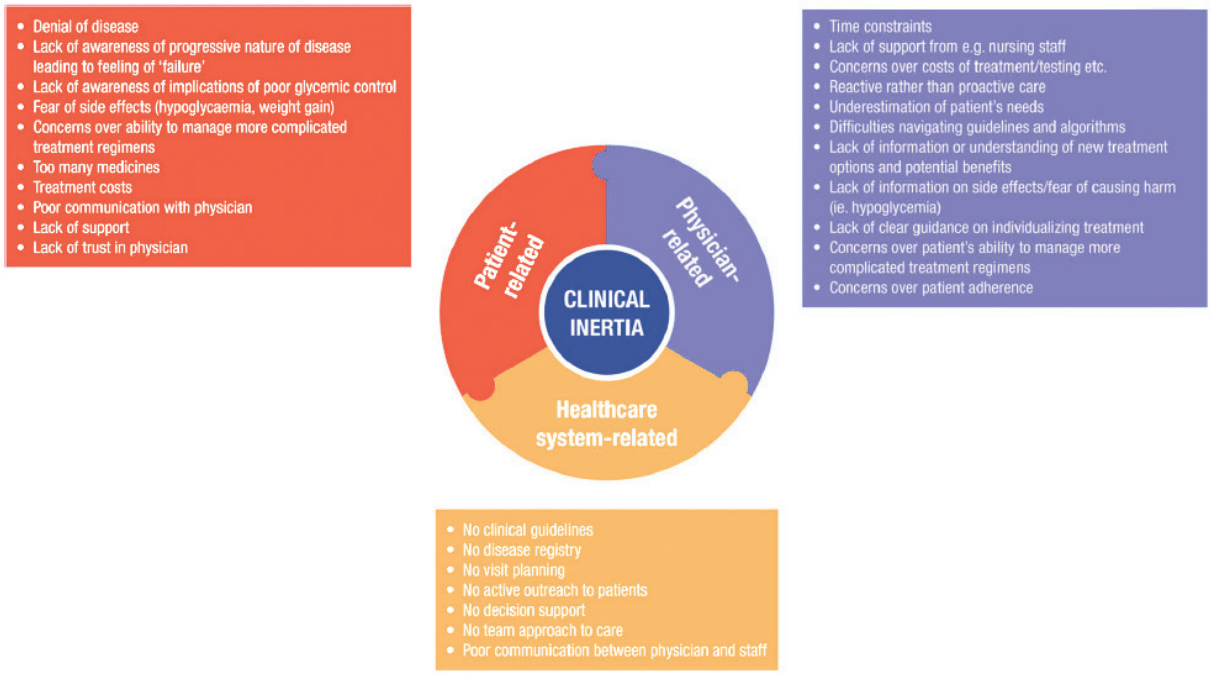

Figura 1 | Factors contributing to therapeutic inertia.

health system contribute to therapeutic inertia, we identified four aspects: the need to get authorisations for some drugs, spending ceilings for local prescriptions, obstacles preventing General Practitioners from writing prescriptions and financial barriers to prescriptions. All these aspects are fundamental to the problems related to costs.

We asked how to resolve these issues. Certainly we need to move away from the mindset of budgeting silos; we must be able to persuade the policy-maker that the level of budget monitoring must shift from simply considering the pharmaceutical therapy as a cost to assess the outcomes, leaving us the freedom (if we truly show that we can be responsible) to allocate resources to what we really think is the right way to invest money to provide positive outcomes for the patient. We think the way to do this is through the development of a virtuous alliance with our General Managers. That is why we designed and created an alliance with the Federazione Italiana Aziende Sanitarie e Ospedaliere [the Italian Federation of Healthcare Organizations] (FIASO), because with them we must describe the educational pathway that allows us clinicians to master the language needed to become credible to the decision-makers; and, most of all, a language allowing us to let the General Managers see that we are now facing solutions that can change the history of diabetes and the history of our patients.

We therefore need a global vision that does not view a single aspect of the problem and allows us to take all the actions we can (and should) do to face and resolve the problem of therapeutic inertia.

In my personal list of the drivers behind therapeutic inertia from the perspective of patients, clinicians and policy-makers, the top item is always the same: a lack of education. Similarly, education is the essential element in helping solve the problem, buffering it and minimising it, for the patients as well as clinicians and decision-makers.

In conclusion, my answer is 'yes' to the question whether there is a hierarchy among the causes of therapeutic inertia. A lack of education for patients, HCPs and decision-makers is at the top of the list of factors fostering therapeutic inertia. I firmly believe that the ADA and AMD have an opportunity to establish a virtuous alliance leading to the sharing of tools and indicators and to the promotion of specific educational projects to help all the stakeholders to overcome their own barriers.