The management of glycemic control in diabetic patients: the role of glycated albumin

Foglia E.[1], Ferrario L. [1], Schettini F. [1], Avogaro A. [2], Bellia C. [3], Bertuzzi F. [4], Bonetti G. [5], Ceriello A. [6,7], Ciaccio M. [3,8], Corsi Romanelli M. [9,10], Dozio E. [10,11], Falqui L.[12], Girelli A. [13], Nicolucci A. [14], Perseghin G. [15,16], Plebani M. [17], Valentini U. [13], Zaninotto M. [17], Croce D.[1,18],

[1] Centre for Health Economics, Social and Health Care Management, Università Carlo Cattaneo - LIUC, Castellanza, Italy , [2] Department of Medicine, University-Hospital, Padova, [3] Section of Clinical Biochemistry and Clinical Molecular Medicine, Department of Biopathology and Medical Biotechnologies, University of Palermo, Italy, [4] Diabetology Unit, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy,, [5] Central Clinical Chemistry Laboratory, ASST Spedali Civili, Brescia, Italy, [6] Institut d'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS) and Centro de Investigación Biomedica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Barcelona, Spain, [7] Department of Cardiovascular and Metabolic Diseases, IRCCS Multimedica, Sesto San Giovanni, Milan, Italy, [8] Department of Laboratory Medicine, University-Hospital, Palermo, Italy, [9] Service of Laboratory Medicine 1-Clinical Pathology, I.R.C.C.S. Policlinico San Donato, Milan, Italy, [10] Department of Biomedical Sciences for Health, Università degli Studi di Milano, Milan, Italy, [11] Laboratory of Molecular Pathology, I.R.C.C.S. Policlinico San Donato, San Donato Milanese, Milan, Italy., [12] Department of Medicine, Diabetes and Endocrinology, IRCCS Multimedica, Sesto San Giovanni, Milan, Italy, [13] Diabetes Care Unit, ASST Spedali Civili, Brescia, Italy, [14] Center for Outcomes Research and Clinical Epidemiology, Pescara, Italy, [15] Department of Medicine and Surgery, Università degli Studi di Milano Bicocca, Milan, Italy, [16] Department of Medicine and Rehabilitation, Unit of Metabolic Medicine, Policlinico di Monza, Monza, Italy, [17] Department of Laboratory Medicine, University-Hospital, Padova, [18] School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa.

Background

The main aim of the taking in charge of type 2 (T2) diabetic patients and consequently of antyglicemic oral therapy, is the achievement and the maintenance of a good glycemic control

Glycated hemoglobin (HbA1C) is the reference test for long-term glucose monitoring (Goldstein *et al*., 2003), to be done together with oral glucose tolerance test (OGTT) and fasting plasma glucose (FPG), thus representing the standard panel of test for this specific setting

Over the last few years, an innovative glycemic marker emerged in the clinical practice useful for monitoring the glycemic control in T2 patients, assuming oral antiglycemic treatment (insulin-naïve): glycated albumin (GA), to be implemented in addition to the above mentioned traditional monitoring test (HbA1c/FPG/OGTT)

Objective

The study aimed at investigating the clinical, safety, economic, organizational and social implications related to the introduction, in the Italian clinical practice, of glycated albumin (GA), as an add-on technology to the traditional glycemic monitoring systems (Hb1Ac and FPG), for insuline-naïve patients affected by type 2 diabetes, assuming oral therapy, thus supporting the Italian evidence-based decision-making process

Methods

A Health Technology Assessment was conducted, considering the Italian NHS perspective. The dimensions derived from EUnetHTA Core Model (EUnetHTA, 2016), were deployed considering:
i) a systemic literature review, in order to retrieve the safety and the efficacy profiles;
ii) administration of a qualitative questionnaire filled in by 15 healthcare T2 diabetes experts (considering a 7-item Likert scale, ranging from -3 to +3), to retrieve information with regard to the perceived safety, equity, the social, legal and the organizational aspect;
iii) quantitative approaches, useful for the economic evaluation of the clinical pathway, and for budget impact analysis, comparing the "AS IS" situation (use of only the traditional test) with the "TO BE" scenario (introduction of the GA test in addition to the traditional panel of test)

Conclusions

The study showed the strategic relevance of GA, in the improvement of the diabetic patient clinical pathway, freeing-up NHS resources This is particularly important, because both an early diagnosis of diabetes and a strict glucose control are crucial for preventing or delaying the onset of serious, even life-threatening complications

References

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DIMENSIONS OF THE HTA ASSESSMENT

Safety

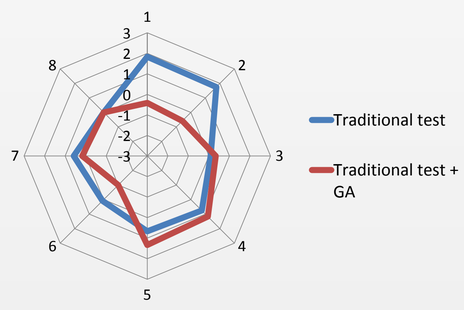
Literature evidence revealed that the introduction of the GA test could be a better predictor of the relative risk, in the development of diabetes complications, if compared with the implementation of HbA1c alone (Nathan *et al*., 2014; Pan *et al*., 2014): a strong association with diabetes complication was thus observed when GA and HbA1c were included together, both effects being nominally significant at the 0.05 level, supporting a potential independent effect of each measurement as a risk factor. Clinicians declared that the introduction of GA test, as an add-on strategy, would be considered the preferable technology (p<0,05), with regard to GA's ability to prevent long-term diabetes complications (1.30 *vs* 2.20, p<0.05), and its sensitivity to sudden oscillations of the average blood glucose level (-0.30 *vs* 1.70, p<0.05)

	Traditional test	Traditional test + GA
Severe adverse events	-0.60	0.10
Mild and moderate adverse events	-0.30	0.10
Invasiveness	-0.50	-0.40
General safety	0.90	1.20
Technology's tolerability	0.60	0.60
Environmental risk	-0.20	-0.30
Ability of the technology to prevent long-term diabetes complications	1.30	2.20
Sensitivity of the technology to sudden oscillations of the average blood glucose level	-0.30	1.70
Average Value	**0.11**	**0.65**

Equity impact

Low-level perceptions resulted with regard to equity aspects (p<0.05)

This consideration may be justified by the low-level perceptions resulting from GA limited accessibility (-0.42 *vs* 1.83), since the innovative technology has not yet been used and implemented in the national laboratories

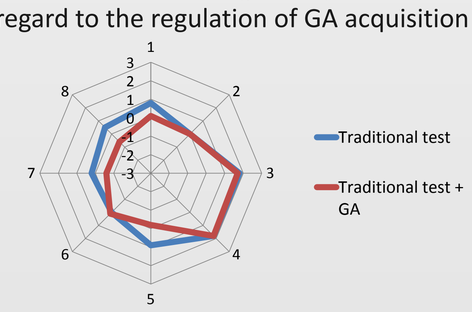


1) Access to care on local level; 2) Access to care for persons of a legally protected status; 3) Impact on the hospital waiting list; 4) Generation of health migrations; 5) Existence of factors limiting the use of the technology for a group of patients; 6) The different willingness to pay of patients could modify the technology accessibility; 7) Level of iniquity of the technology; 8) Patients' Cultural, moral and religious beliefs could modify the technology accessibility

	Traditional test	Traditional test + GA
Average Value	0.72	0.13

Legal impact

An analysis of the legal implications reported that the two technologies under assessment could be considered super-imposable, with regard to their measurement (p<0.05) Additional legal efforts are required with regard to the regulation of GA acquisition



1) Permission level of technology; 2) Need for inclusion of the technology in registry; 3) Fulfillment of the safety requirements; 4) Production warranties; 5) Price control; 6) Infringement of intellectual property rights; 7) The need to regulate the acquisition of technology; 8) The legislation covers the regulation of technology for all categories of patients

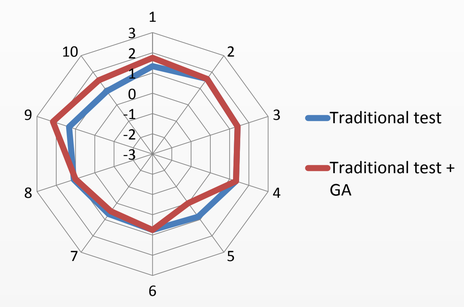
Efficacy

GA reflects shorter-term control of plasma glucose level, thus increasing the number of patients achieving therapeutic success after 3 months of therapy (Shima *et al*., 2014), with a consequent decrease of patients requiring a therapeutic switch

	Traditional test	Traditional test + GA
% of patients achieving a therapeutic success after 3 month of therapy (T3) [difference between marker values (T1-T0 or T3-T0) > 5%]	71.6%	97.0 %

Social and ethical impact

In general, no statistical difference emerged between the two technologies, with regard to the social and ethical impact (1.12 *vs* 1.20, p>0.05). GA test would improve both patients (1.33 *vs* 2.17, p<0.05) and caregivers (0.83 *vs* 1.50 , p<0.05) quality of life, because related to a better glycemic control monitoring and a lower relative risk to develop diabetes' complications and adverse events



1) Ability of the technology to protect the patients' autonomy; 2) Protection of human rights; 3) Ability of the technology to protect the patients' integrity; 4) Ability of the technology to protect the patients' dignity; 5) The use of technology guarantees the social values and the willingness to pay of the patient; 6) Ability of the technology to protect the patients' religion; 7) Impact of the procedure on the social costs; 8) Patients and citizens can have a good level of understanding of technology; 9) Impact of the technology on the patient's perceived quality of life; 10) Impact of the technology on the care giver's life and perception

	Traditional test	Traditional test + GA
Average Value	1.12	1.20

Organizational impact

While GA, in the short time (12 months), requires training courses (-0.80 *vs* 0.10) and equipment update (-0.50 *vs* 0.00), in the long run (36 months), there would be a reduction in the above drawbacks, showing GA organizational benefits (0.01 *vs* 0.30, p<0.05)

	Traditional test	Traditional test + GA
Additional staff	0.00	0.00
Training course for the healthcare professionals taking in charge diabetes type 2 patients	0.00	0.20
Patients' and caregivers' training	-0.20	-0.20
Hospital meetings	0.00	0.00
Learning curve	0.00	-0.10
Additional room space	0.00	0.00
Additional furniture	0.00	0.00
Additional equipment	0.00	0.00
Equipment update	0.00	-0.10
Purchase of equipment	0.00	-0.10
Impact of the technology on the internal processes	0.10	0.90
Impact of the technology on the purchasing processes	0.00	-0.10
Impact of the technology on the hospital processes	0.10	1.40
Impact of the technology on the patient's clinical pathway	0.20	2.30
Average Value	**0.01**	**0.30**

Economic impact

Economic evaluation of the patient's clinical pathway

Traditional test - "AS IS" Scenario

Health expenditure items	Economic evaluation of a patient who has not experienced a therapy switch, within a 12-month time horizon		Economic evaluation of a patient who has experienced a therapy switch, within a 12-month time horizon	
	Economic Value	%	Economic Value	%
Laboratory exams	€ 68.67	31.89%	€ 74.08	26.66%
Specialistic visits	€ 55.99	26.00%	€ 68.59	24.68%
Diagnostic procedures	€ 18.66	8.67%	€ 20.01	7.20%
Self-monitoring of blood glucose	€ 72.00	33.44%	€ 115.20	41.46%
Annual management medical cost	**€ 215.31**	**100.00%**	**€ 277.88**	**100.00%**
Weighted average cost	**€ 233.08**			

Traditional test + GA - "TO BE" Scenario

Health expenditure items	Economic evaluation of a patient who has not experienced a therapy switch, within a 12-month time horizon		Economic evaluation of a patient who has experienced a therapy switch, within a 12-month time horizon	
	Economic Value	%	Economic Value	%
Laboratory exams	€ 79.92	35.27%	€ 96.70	32.18%
Specialistic visits	€ 55.99	24.71%	€ 68.59	22.83%
Diagnostic procedures	€ 18.66	8.24%	€ 20.01	6.66%
Self-monitoring of blood glucose	€ 72.00	31.78%	€ 115.20	38.34%
Annual management medical cost	**€ 226.56**	**100.00%**	**€ 300.50**	**100.00%**
Weighted average cost	**€ 230.61**			

Cost-Effectiveness Analysis

	Traditional test	Traditional test + GA
Weighted average cost	€ 233.08	€ 230.61
Efficacy	71.60%	97.00%
CEV	325.53	**237.74**

Budget Impact Analysis

Traditional test - "AS IS" Scenario	Population	Cost
-no switch	1,028,154	€ 221,373,233.05
- switch	407,815	€ 113,324,686.33
Total Baseline Scenario		**€ 334,697,919.38**
Traditional test + GA ("TO BE" Scenario)	**Population**	**Cost**
-no *switch*	1,392,891	€ 318,201,308.64
- *switch*	43,079	€ 12,945,335.91
Total Innovative Scenario		**€ 331,146,644.54**
Difference (€)	**-364,736**	**€ -3,551,275**
Difference (%)	**-89.44%**	**-1.06%**