Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/18204
DOI URL: http://dx.doi.org/10.21474/IJAR01/18204

RESEARCH ARTICLE

REVIEW OF THE LITERATURE ON THE IMPACT OF THE FUNCTIONAL INSULIN THERAPY

Mohammed-Amine Essafi[1], Hayat Aynaou[1,2] and Houda Salhi[1,2]

1. Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition. Hassan II University Hospital Center. Fez. Morocco.
2. Laboratory of Epidemiology, Research in Health Sciences, Faculty of Medicine and Pharmacy, USMBA, Fez, Morocco.

Manuscript Info

Manuscript History
Received: 17 November 2023
Final Accepted: 23 December 2023
Published: January 2024

Key words:-
Functional Insulin Therapy, Type 1 Diabetes, Glycaemic Control

Abstract

Aims: Functional insulin therapy is a therapeutic education concept that allows type 1 diabetic patients (T1D) to manage their treatments in a personalized way. Since the discovery of this method, it has been increasingly used for T1D patients. The aim of our study was to evaluate the impact of functional insulin therapy (FIT) on glycaemic control and quality of life in the literature.

Methods: We searched the scientific literature for studies on the impact of functional insulin therapy.

Results: A total of 34 articles were included, 24 of which studied the impact of FIT on glycaemic control and quality of life. Regardless of initial glycaemic control status, improvement in glycaemic control and quality of life were reported in all studies included in this review. In the long term, these effects are debated, in particular the impact on HbA1c could weaken in contrast to the impact on quality of life and hypoglycaemia which persisted. Concerning the impact on the evolution of weight is controversial, some teams have shown an increase in weight, others, a stagnation and a loss of weight has been reported only in a few studies. After the introduction of FIT, these studies showed a decrease in basal insulin dose.

Conclusions: FIT provides better glycaemic control by reducing hypoglycemics episodes, especially severe ones, and improves the quality of life of T1D patients.

Introduction:-

Type 1 diabetes represents about 5% to 10% of diabetes cases; 10,000 in Morocco, and 160,000 in France [1]. The annual incidence of T1D is constantly increasing and varies greatly from one country to another, ranging from 1.7 per 100,000 in Japan to 41 per 100,000 in Finland [2-3]. Therapeutic education has become one of the keys to the management of chronic diseases.Therapeutic education as a concept was published by the World Health Organization (WHO) in 1998 [4]. Functional insulin therapy (FIT) is a therapeutic education program developed in this sense. It is a concept that aims to mimic physiological insulin secretion and consists of teaching the patient to manage his treatment properly. It is widely used in Germany, Switzerland and Austria.

Corresponding Author:- Mohammed-Amine Essafi
Address:- Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition. Hassan II University Hospital Center. Fez. Morocco.

The aim of this study is to evaluate in the literature the different practices of FIT training canters and the impact of FIT on glycaemic control, frequency and severity of hypoglycaemia, weight loss and quality of life of patients.

History of functional insulin therapy:

In 1969, an article was published in the journal Lab Word about the discovery of a device that measures blood glucose levels within minutes [5]. Richard K. Bernstein (b. 1934), an engineer by profession, diagnosed with type 1 diabetes in 1946, ordered the device on behalf of his doctor-wife, as patients were not allowed to have it [6]. He invented the basal-bolus method by increasing the number of insulin injections per day [6]. Then he discovered that the evolution of vascular complications stabilized after intensification of treatment, and in 1977 he decided to change his profession and become a physician [6]. Functional insulin therapy came into being at the end of the 1970s, when Dr. Bernstein published a method of insulin therapy, adapted to meals, and he also experimented with insulin injections according to blood sugar levels and in case of snacks [7]. In 1980, a German team from Düsseldorf set up a therapeutic education program, Düsseldorf Diabetes Treatment and Teaching Program (DTTP) [8]. In 1983, this method reached other Germanic countries with Howorka [9]. In Austria, Berger in German-speaking Switzerland and Grimm in French-speaking Switzerland [10]. The concept of prandial insulin dose calculation was introduced by Howorka in 1990 [9]. Functional insulin therapy arrived in the British Isles in 2002, through a program called DAFNE (Dose Adjustment For Normal Eating) [11].

Main principles of functional insulin therapy FIT:

The principle of functional insulin therapy (FIT), is based on three acts: "living, eating and healing". Insulin for "living" or basal insulin calculated during carbohydrate fasting. Insulin for "eating" or prandial insulin calculated according to the carbohydrates of the meal. Insulin for "treatment" or correction to bring the blood sugar level back into the target range, determined according to insulin sensitivity (the evaluation of the effectiveness of a unit of fasting on blood sugar), and correction of hypoglycaemia by determining the amount of carbohydrates needed. The majority of these parameters are initially calculated theoretically using algorithms adopted by the different services; they are then checked on each occasion to validate or correct them [12]. Functional insulin therapy has three main objectives: To improve glycaemic control allowing the avoidance of diabetes complications, and to rule out hypoglycaemia. To improve the quality of life through dietary freedom (quantity, quality, schedule) and to empower the patient in the management of his pathology [13]. These objectives require the ability to calculate, a Basal-Bolus type of insulin therapy, and regular self-monitoring of blood glucose (4 to 6 per day).

Literature review of functional insulin therapy practice:

Education programs:

FIT practice is inspired by Several schools. That of German diabetologists in Düsseldorf, with a 5-day inpatient education program consisting of a carbohydrate fasting test to determine baseline needs, theoretical education sessions, and practical workshops.And another based on the Swiss experience (Grimm and Berger) to create an outpatient FIT education program, called "outpatient self-learning in type 1 diabetes management" [14-15]. In Morocco, the endocrinology and diabetology department of the Ibn Rochd University Hospital in Casablanca was the first civilian hospital in Morocco to start the FIT program, in May 2013. For this purpose, the members of the health care team benefited from a training supervised by Dr. Claude Sachon, from the team of the diabetology department of the Pitié-Salpêtrière hospital group (AP-HP, Paris, France) [16]. The Howorka method of determining personalized algorithms was used [17].

Role of FIT on glycaemic control:

Short-term effects:

Few teams have studied the impact of the FIT program at 3 months [16-18-19-20]. An improvement in mean HbA1c at 3 months of the initial assessment, and at 6 months. within the literature [15-16-18-20-21-22-23-24-25-26-27-28]. Data from the literature are consistent on the value of FIT for glycaemic control (Table I), The Dose adjustment for normal eating (DAFNE) study is one of the largest randomized controlled studies in this area, involving 169 T1D patients, It showed an improvement in HbA1c after FTI, with a -1% decrease at 6 months ($p < 0.05$) [28]. Studies [15-24-29-30] with high baseline HbA1c, had noted that the improvement in glycaemic control is more marked. The decrease in HbA1C can reach 2% at 1 year in the "Bucharest Düsseldorf South" cohort with an initial glycated haemoglobin of 12.3% [30]. The German study by Samann in 2005 [30]involving 9583 patients between 1992 and 2004. After 1 year, HbA1c (decrease from 8.1% to 7.3%) and severe hypoglycaemia decreased significantly. Poorly controlled patients with an HbA1c of 10.8% had improved to 8.4% without an increased risk of hypoglycaemia. Patients with a low HbA1c of 6% and a high rate of severe hypoglycaemia of 0.54, had maintained their HbA1c at

6.3% and decreased hypoglycaemia to 0.16 per patient per year [31]. Other studies have shown similar results at 1 year (Table 1).

Long-term effects:

Most studies assess the effect on HbA1c at 1 year [15-26-29-30-31] or longer [32-33]. The long-term effects on HbA1c may weaken, but the Howorka study showed that HbA1c was improved at 3 years [34]. In an English study in 2010 showed a smaller but significant difference after 44 months [29]. While another study in 2012 showed a decrease in HbA1c at 1 year and an increase at 7 years [35], the same result was observed in an Austrian study in 2004 with an increase in HbA1c at 6 and 12 years, but the decrease in hypoglycaemia was maintained [36].The changes between 6 and 12 months seem to stabilize, and the best impact on HbA1c would be around 3 years after the program [33-36]. In the longer term, glycaemic control deteriorates to a level comparable to that before FIT [36].(Table 1).

Table 1:- HbA1c evolution after FIT education according to the literature.

	n	Initial HbA1c	HbA1c at 3 months	HbA1c at 6 months	HbA1c at 1 year	Long -term HbA1c	p
P Collin, J Louis. [18]	-	8.4	7.5	7.8			<0.0001
M Cordonnier [19]	-	7.57	7	-			<0.0001
Falconnier B [20]	45	7.2	7	7.1	7.1		<0.0001
A Taheri [16]	39	8,9	8.03	7.8	7.4	7.5	0.04
J Belkhair [21]	20	8.9	8.24	7.46	-		<0.0001
S. Genc [22]	93	8		7.6	-		<0.0001
A Astrid [23]	75	9.4		7.2	-		<0.0001
H kandra [24]	50	9.52		8.16	8.34	8.34 (2 years)	<0.0001
Floriot M [25]	56	7.73	-	7.65	7.42		<0.0001
Cooke D [26]	262	8,5	-	8.2	8.3		<0.001
Mathilde J. [27]	124	8.21	-	7.94			<0.0001
DAFNE [28]	169	9.4	-	8.4	9		<0.0001
Benhamou PY [38]	40	8,3	-	-	8,1		0.075
Gunn D [35]	111	8.6	-	-	8.1	8.3 (7 years)	<0.0001
Hopkins D, [37]	639	8,5	-	-	8,2		<0.0001
Speight J [29]	104	9.32	-	-	8.75	8.96 (3 years)	<0.0001
Sämann A [31]	9583	8,1	-	-	7,3		<0.0001
Hartemann H [15]	110	8.5	-	-	7.8		<0.0001
Mühlhauser I [30]	100	12.3	-	-	9.3	9.5	<0.0001
Sachon C. [39]	115	8,4	-	-	7,6		<0.0001
Langewitz W [40]	250	6.6			6.4		-
Bott S [32]	626	8.3	-	-	-	7.6 (6 years)	<0.0001
Pieber T [33]	205	8.7	-	-	-	7.5 (3 years)	<0.0001
Plank J [36]	123	7.9	-	-	-	7.1 (3 years) 7.8 (12 years)	<0.0001

Evolution of hypoglycaemic episodes after FIT:
One of the main objectives of FIT is to reduce the frequency of hypoglycaemia, and especially its severe form. This has been demonstrated in the majority of studies in the literature. According to Hopkins et al [37], FIT reduced the rate of severe hypoglycaemia from 1.93 to 0.61 episodes/person/year (p = 0.001) [37]. Thus, among 125 cases with at least one severe hypoglycaemia in the year prior to the DAFNE study, 62% no longer had an episode of severe hypoglycaemia in the year after FIT [28]. In the Swiss study by Langewitz [40] had objectified a decrease in severe hypoglycaemia.It seems more appropriate to propose the use of a continuous glucose sensor, which is more sensitive to the detection of hypoglycaemia, limits underestimation and at the same time has a very interesting educational role [41].

Weight evolution:
The results of the literature concerning the impact of FIT on weight are controversial (Table 2). Some teams [16-38] emphasize an increase in weight, others [37] a stagnation and, more rarely, a loss of weight [15-39].In the majority of studies [15,20,28,29,37], weight remained relatively stable at 1 year after FIT education. Weight gain after FIT education is a criticism sometimes made by some diabetologists. Hence the interest of dietary education and physical activity which remain essential during the FIT education program to fight against weight gain. Dietary consultations during the follow-up are also very interesting to correct dietary errors and to advise a healthy and balanced diet.

Table 2:- Weight evolution after FIT education according to the literature.

	Weight before FIT	**Weight at 1 year after FIT**	**p**
Sachon C, et al [39]	68	67	NS
Hopkins D, et al [37]	75,1	75,1	NS
Benhamou P, et al [38]	66,9	68,1	0,003
Hartemann-Heurtier A[15]	68,4	67	–
A Taheri [16]	64,8	68,4	0,02

Impact on quality-of-lifeQOL:
The impact of type 1 diabetes affects the patient physically as well as psychologically and emotionally. There are several questionnaires assessing quality of life in diabetic patients. Quality of life assessments after FIT generally show improvement [15,20,26,28,29,42]. Table 3.

Table 3:- Impact of FIT on HRQOL according to the literature:

	Result
DAFNE [28]	Improvement of the overall score
Langewitz W [40]	82% of patients consider the main benefit is dietary freedom, 52% able to fast, 52% autonomy. Anxiety and depression decreased significantly. The relationship between the doctor and the patient was significantly improved
M Cordonnier [19]	All items are improved: (barriers to activity: Δ = -p3.59, (p= 0.0053); psychological distress Δ = -p4.20 (p < 0.0002) eating disorders: Δ = -p8.62 (p= 0.00014)
P Collin, J Louis. [18]	The satisfaction score with diabetes management was improvedfrom 4.2 before to 8.1 after
J Manel [43]	75% fasted in Ramadan. QOL was improved in all patients
J Belkhair [21]	The QOL score was improved in all patients, with the score decreasing from 41.2 to 20.5 after FTI
A Taheri [16]	All patients were highly satisfied with the program, with a score of 5.18 ± 0.94 on the treatment change satisfaction questionnaire

Evolution of basal insulin doses:
The most widely used method for calculating personalized insulin doses is based on research by Howorka [9-44-45]. The application of this method was validated in a study by Sylvia Franc and Guillaume Charpentier [45]. However,

it is not used by all teams. After the introduction of FIT, there is usually a decrease in the basal insulin dose [10]. The study by A Taheri [16] confirms the reduction in basal insulin doses; on average, it was 0.35 U/kg/d initially, compared with 0.31 U/kg/d after FIT. According to the study by Benhamou et al [38] this basal dose remains stable after one year of FIT in the majority of cases.

Limitations of FIT:

In a 2005 article, S. Jacqueminet et al [46] mentioned several limitations to FIT: limitations related to diabetes itself or to the therapeutic means used (glycaemic instability, too short action of basal insulin, postprandial insulin resistance). And limitations related to the patient (depression, lack of motivation, phobia of hypoglycaemia or even eating disorders). [46-47]

Conclusion:-

Functional Insulin Therapy (FIT) is a method that has been widely proven for many years. It allows the diabetic patient to acquire autonomy in his treatment. This review of the literature has shown the improvement of glycaemic control (on HbA1c and hypoglycaemia) and quality of life in various and varied populations of diabetics, whatever the initial state of control.Dietary education and physical activity are pillars of the FIT education program to prevent weight gain. The interest of the implementation of a continuous glucose measurement sensor for the detection of hypoglycaemia, and it has a very interesting educational role.

References:-

[1] Fagot-Campagna A, Romon I, et al. Prévalence et Incidence du Diabète , et mortalité liée au diabète en France - Synthèse épidémiologique . Saint-Maurice (Fra) : Institut de Veille Sanitaire, novembre 2010, 12 p. Disponible sur : www.invs.sante.fr

[2] Diabetes-Epidemiology-Research-International-Group.Geographic patterns of childhood insulin-dependent diabetes mellitus. Diabetes 2000 , 37:1113-19;

[3] Green A,Gale EAM,Paterson CC.Incidence of childhood insulin-dependent diabetes mellitus: The EURODIAB ACE stydy; Lancet 1999,339:905-9

[4] Organization WH. Therapeutic patient education. 1998.

[5]Juan Ruiz, Magali Andrey, Domenico Masciotra, Denise Morel Rev Med Suisse 2011; volume 7.1255-1259

[6]Bernstein RK. Dr Bernstein's diabetes solution. New York Boston London : Hachette Book Group USA, 2007.

[7] Bernstein RK. Virtually Continuous Euglycemia for 5 Year in a Labile Juvenile-onset Diabetic Patient Under Noninvasive Closed-Loop Control. Diabetes Care 1980; 3(1): 140- 143.

[8] Mühlhauser I, Jörgens V, et al. Bicentric evaluation of a teaching and treatment programme for Type 1 (insulin-dependent) diabetic patients: improvement of metabolic control and other measures of diabetes care for up to 22 months. Diabetologia 1983; 25(6): 470-476

[9] Howorka K. Functional Insulin Treatment. New York, Springler- Verlag Telos, 1996.

[10] Grimm J , Berger W, et al. Insulinothérapie Fonctionnelle : éducation des patients et algorithmes . Diabetes & Metabolism 2002; 28: 2S15-2S18.

[11] Howorka K, Thoma H, et al. Phases of functional, near-normoglycaemic insulin substitution: what are computers good for in the rehabilitation process in type I (insulindependent) Diabetes mellitus Computer Methods and Programs in Biomedicine 1990; 32: 3 19-323.

[12]Seray Burcu Genc. Les changements que l'insulinothérapie fonctionnelle apporte dans la vie des patients et dans leur vécu du diabète. Sciences du Vivant [q-bio]. 2013. ffhal-01732292f

[13] Sachon C, Heurtier A, et al. L'insulinothérapie dite "fonctionnelle". Diabetes & Metabolism 1998; 23: 556-559.

[14] Slama G , Elgrably F . L'insulinothérapie fonctionnelle : ses buts , ses moyens , ses résultats . In : Grimaldi A , Charpentier G, Slama G. Insulinothérapie fonctionnelle ou l'insuline à la carte . Elsevier, 2008 : 11 à 14.

[15] Hartemann-Heurtier A, Sachon C, et al. Functional intensified insulin therapy with short acting insulin analog: effects on HbA1c and frequency of severe hypoglycemia: An observational cohort study. Diabetes & Metabolism 2003; 29(1): 53-57.

[16] A. Taheri1, S. El Aziz1,Insulinothérapie fonctionnelle , de la théorie à la pratique . Première expérience du CHU Ibn Rochd de Casablanca, Maroc

[17] Howarka K, Pumpiria J. Algorithm adaptation under functional insulin treatement during transfer from regular to insulin Lispro. Diabetes Nutr Metab 1998,11:266-272

[18] P Collin, J Louis. Impact de l'insulinothérapie fonctionnelle sur l'équilibre glycémique et la qualité de vie du diabétique de type 1. Diab-Endocrino Hôpital Notre Dame et Reine Fabiola . Diabetes Metab 2008.35 : 692-512

[19] M Cordonnier , V Legand . Influence bénéfique de l'insulinothérapie fonctionnelle sur la qualité de vie de diabétique type 1.Endo-Diab-Maladies métaboliques Centre Hospitalier Valencienne .Lille. Diabetes Metab 2009. 36 :662-51

[20] Falconnier Bendik C, Keller U, et al. Training in flexible intensive insulin therapy improves quality of life, decreases the risk of hypoglycaemia and ameliorates poor metabolic control in patients with type 1 diabetes. Diabetes Research and Glinical Practice 2009; 83(3): 327-333.

[21] J. BELKHAIR Les effets de l'insulinothérapie fonctionnelle sur l'équilibre glycémique et sur la qualité de vie chez le diabétique type 1 These 2016

[22] S .Genc LES CHANGEMENTS QUE L'INSULINOTHERAPIE FONCTIONNELLE APPORTE DANS LA VIE DES PATIENTS ET DANS LEUR VECU DU DIABETEThèse 2013

[23] B Astrid Flexible multiple injection therapy education for adults with Type 1 diabetes: experience and innovation in the Australian setting. These 2017

[24] Hajer Kandara Flexible Insulin Therapy: Results of a Tunisian Experience

[25] Floriot M, Halter C. Impact de l'éducation à l'insulinothérapie fonctionnelle sur les apports alimentaires .Diabète-Nutr-H$opital Jeanne d'Arc Nancy. Diabetes metabo 2010. 51 :692-76

[26] Cooke D, Bond R, Lawton J, et al; U.K. NIHR DAFNE Study Group. Structured type 1 diabetes education delivered within routine care: impact on glycemic control and diabetes-specific quality of life. Diabetes Care 2013;36:270-2.

[27] Mathilde J . Education thérapeutique à l'insulinothérapie fonctionnelle ,étude cohorte pour évaluation de l'impact sur les paramètres clinico -biologiques et sur la qualité de vie à 6mois. These 2013

[28] DAFNE Study Group. Training in flexible, intensive insulin management to enable dietary freedom in people with Type 1 diabetes: dose adjustment for normal eating (DAFNE) randomized controlled trial. Diabetic Medicine 2002; 325 :746.

[29] Speight J, Amiel SA, et al. Long-term biomedical and psychosocial outcomes following DAFNE (Dose Adjustment for Normal Eating) structured education to promote intensive insulin therapy in adults with sub-optimally controlled type 1 diabetes. Diabetes Research and Glinical Practice 2010; 89: 22-29.

[30] Mühlhauser I , Bruckner I, et al. Evaluation of an intensified insulin treatment and teaching programme as routine management of Type 1 (insulin -dependent) diabetes. The BucharestDüsseldorf Study . Diabetologia 1987; 30(9): 68 1-690.

[31] Sämann A , Mühlhauser I , et al. Glycaemic control and severe hypoglycaemia following training in flexible, intensive insulin therapy to enable dietary freedom in people with type 1 diabetes: a prospective implementation study. Diabetologia 2005; 48: 1965-1970.

[32] Bott S, Bott U, et al. Intensified insulin therapy and the risk of severe hypoglycaemia. Diabetologia 1997; 40: 926 - 932.

[33] Pieber T, Brunner A, et al. Evaluation of a structured outpatient group education program for intensive insulin therapy. Diabetes Care 1995; 18(5):625-630.

[34] Howorka K, Pumprla J, Wagner-Nosiska D, Grillmayr H, Schlusche C, SchabmannA. Empowering diabetes out-patients with structures education: short-term and long-term effects of functional insuline treatment on perceived control over diabetes. Journal of Psychosomatica Research 48 (2000) 37-44.

[35] Gunn D and Mansell P. Glycaemic control and weight 7 years after Dose Adjustment For Normal Eating (DAFNE) structured education in Type 1 diabetes. Diabetic Medicine 2011; 29(6): 807-8 12.

[36] Plank J, Kohler G, et al. Long-term evaluation of a structured outpatient education programme for intensified insulin therapy in patients with Type 1 diabetes: a 12-year followup. Diabetologia 2004; 47: 1370-1375.

[37] Hopkins D, Lawrence I, et al. Improved Biomedical and Psychological Outcomes 1 Year After Structured Education in Flexible Insulin Therapy for People With Type 1 Diabetes: The U.K. DAFNE experience. Diabetes Gare 2012; 35(8): 1638-1642.

[38] Benhamou PY, Garnier C, Debaty I, et al. Basal insulin dose in 40 type 1 diabetic patients remains stable 1 year after educational training in flexible insulin therapy. Diabetes Metab 2010; 36:369-74.

[39] Sachon C. Insulinothérapie fonctionnelle . EMC - Endocrinologie-Nutrition (Elsevier Masson SAS) 2014;11(2) [Article 10-366-R-35].

[40] Langewitz W , Wössmer B , et al. Psychological and metabolic improvement after an outpatient teaching program of functional intensified insulin therapy (FIT). Diabetes Research and Clinical Practice 1997; 37: 157-164.

[41] Kim SK, Suh S, et al. Three-day continuous glucose monitoring for rapid assessment of hypoglycemic events and glycemic variability in type 1 diabetic patients. Endocrine Journal 2011; 58(7): 535-41.

[42] M Graune, A Haugstvedt . Diabetes-related emotional distress in adults:reliability and validity of the Problem areas in diabetes. International journal of Nursing studies.Elsevier 2012 .125-009-198

[43] J Manel,S Leila . Etude de l'équilibre glycémique et de la fréquence des hypoglycémies et de la qualité de vie chez le diabétique type 1après l'insulinothérapie fonctionnelle . Diabetes Metab 2011, 37, A36-A108
[44] Howorka K, Thoma H, et al. Phases of functional, near-normoglycaemic insulin substitution: what are computers good for in the rehabilitation process in type I (insulin- dependent) diabetes mellitus? Computer Methods and Programs in Biomedicine 1990; 32: 319-323.
[45] Franc S, Charpentier G, et al. Real-life application and validation of flexible intensive insulin-therapy algorithms in type 1 diabetes patients. Diabetes & Metabolism 2009; 35(6): 463-468.
[46] Jacqueminet S, Masseboeuf N, et al. Limitations of the so-called "intensified" insulin therapy in type 1 diabetes mellitus. Diabetes & Metabolism 2005; 31(4, Part 2): 4S45-4S50.
[47] Slama G , Elgrably F . L'insulinothérapie fonctionnelle : ses buts , ses moyens , ses résultats . In : Grimaldi A , Charpentier G, Slama G. Insulinothérapie fonctionnelle ou l'insuline à la carte . Elsevier, 2008 : 11 à 14.