World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

Check for updates

Improvement of time in range and glucose management indicator in Type 1 and Type 2 Diabetes Mellitus patients after introduction of continuous Glucose monitoring in internal medicine residency clinic

A.Manov *, J. Nazha, S. Antonio and J. House

Internal Medicine and Transitional Year Residency Programs, Sunrise Health Consortium GME, Mountain view Hospital, Sunrise Health Consortium GME, 2880 North Tenaya Way, Las Vegas, Nevada 89128, USA.

World Journal of Advanced Research and Reviews, 2023, 17(03), 824–830

Publication history: Received on 14 February 2023; revised on 21 March 2023; accepted on 24 March 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.17.3.0478

Abstract

Continuous glucose monitoring (CGM)-derived time in range (TIR) correlates with Glucose management indicator(GMI) which correlates with hemoglobin A1c (HbA1c) among patients with type 1 and type 2 diabetes mellitus. Compare to HbA1c it has better correlation with glucose control, because HbA1c can be influenced by conditions like anemia, Chronic kidney disease, Cirrhosis of the liver etc. With our current project we wanted to introduce CGM not in specialized endocrine clinic, but in Internal medicine Residency clinic. The CGM team had 12 Internal Medicine and Transitional year Residents who were functioning under the supervision of Board Certified Endocrinologist who was a member of the clinic also. Twenty Five patients -85% with type 2 DM and 15% with type 1 DM on multiple injections of Insulin per day-3-4, self-monitored their blood Glucose(SMBG). They were given CGM- Dexcom G6 in the clinic. In the first 2- weeks after the switch the TIR of the blood glucose of the patients-70-180 mg/dl was 18%. Their average blood glucose was 286 mg/dl, GMI was 11.21%. During then first 2- weeks after initiation of CGM the patients were educated in length by our CGM team about their diet, physical activity, how to adjust their Insulin based on their blood glucose levels as well as how to treat the hypoglycemia. Members of the CGM team were contacting the patients twice a week to adjust patients treatment with Insulin and other per oral antidiabetic medications and or injectable – GLP1-RAG if needed after consultation with the Endocrinologist in the clinic based on the shared information between the clinic and the patients. Once a month the patients were seen in the clinic by member of the CGM team as well. The patients were followed for 2- years. After 3- months on CGM and followed for the 2 years thereafter the patients TIR improved from 18 % to 74%, GMI decreased from 11.21% to 7.04% and the average blood glucose decreased from 286 mg/dl to 158 mg/dl. There was also significant reduction of the hypoglycemia. Twenty percent of the patients were able to discontinue their Insulin and be treated only with oral antidiabetic medications plus/minus GLP1-RAG and have GMI less than 7%. We have showed that targeted TIR – above 70% which has been associated recently with diabetic micro and macrovascular complications in diabetic patients can be achieved not only in specialized endocrine clinics , but in Internal Medicine residency clinic and can be adopted by other Internal Medicine Residency programs in USA.

Keywords: Diabetes mellitus Type- I and type- II; Continuous glucose monitoring (CGM); HbA1C; Glucose management indicator (GMI); Time in range(TIR); Self– monitoring blood glucose(SMBG); Transitional year; Internal Medicine Residents

1. Introduction

The introduction of CGM is among the major inventions in Diabetology in the last 20- years. With its implementation we can obtain full picture of glucose control of patients with type- 1 and Type- 2 DM throughout the 24- hour period. With Self-Monitoring Blood Glucose (SMBG) we are obtaining information just 3-4 times a day and we are losing the overall

* Corresponding author: A.Manov

picture of glucose variability. Because the DM is a chronic disease treating it without CGM is like taking the long trip without the benefit of the map. The CGM systems have become much more patient's friendly and preferred compare to SMBG. The CGM has become as per ADA the standard of care of patients with type 1 DM and in majority of patients with type 2 DM on 3-4 injections of Insulin per day.

Time in range (TIR) and other continuous glucose monitoring (CGM)-derived metrics have been standardized in international consensus conferences. TIR correlates closely with GMI. GMI reflects the HbA1c without its limitations. The goal of TIR of 70% or above - blood sugar goal between 70-180 mg/dl per day correlates with GMI/HbA1c of 6.7-7%. Evidence is emerging about the association of TIR with long-term diabetes complications, and each 10% increase in TIR shows a substantial decrease in risk for long-term diabetic complications. Application of TIR into clinical practice can be easily done with a gradual approach to the analysis and interpretation of CGM-derived metrics and the ambulatory glucose profile report. The education of physicians and their partnership with the patients are crucial for successful implementation of TIR and all CGM-derived metrics in clinical practice.

HbA1c traditionally has been considered the gold standard for monitoring the glycemic control in the last 2-3 months and the main tool to assess the risk of diabetes complications [1,2]. However, HbA1c has several limitations. It does not provide information about glycemic variability, hypo- or hyperglycemi and the glucose trends throughout the 24-hour period. In addition, HbA1c is affected by the age, hemoglobinopathies, pregnancy, chronic kidney disease (CKD), cirrhosis of the liver, and ethnic and racial differences in glycation rates [3].

An expert panel published a consensus report in 2017 identifying several metrics with the purpose of establishing recommendations for the interpretation of CGM data [4,5]. These CGM-derived metrics were further defined in 2019, and 10 core metrics were selected as clinical targets for CGM data interpretation and use in clinical care, to help the clinicians and patients with diabetes in assessing their glycemic status [6]. The evidence is building around TIR as a predictor of long-term diabetes microvascular and macrovascular complications.

The CANDY (Continuous Glucose Monitoring to Assess Glycemia in Chronic Kidney Disease [CKD]) trial was a prospective observational study designed to examine hyperglycemia, glycemic variability, and biomarkers of glycemic control in 105 participants with type 2 diabetes, CKD, and diabetic polyneuropathy (DPN). The prevalence of DPN was inversely correlated with TIR independently of HbA1c. With each 10% lower TIR the risk of Diabetic polyneuropathy(DPN) increased by 25%. In addition, the glucose management indicator (GMI), a CGM-derived estimation of HbA1c, was significantly associated with the prevalence of DPN (odds ratio 1.79, 95% CI 1.05–3.04) per every 1% higher GMI (7).

There is a prospective study of 3,262 patients with type 2 diabetes that revealed an association between TIR and Diabetic retinopathy(DR), with increasing prevalence and severity of DR in patients with lower TIR and higher glycemic variability (P <0.001). Furthermore, the association of TIR with the prevalence of all stages of DR was independent of HbA1c [8].

Another study showed the association between urinary albumin-to-creatinine ratio (UACR) and TIR. The mean change in TIR was 13.2% (95% CI 6.2–20.2%), whereas the change in HbA1c was −1.3% (95% CI −1.6 to −1.0%); the change in UACR was −15% (95% CI −38 to 17%) (all P <0.05). In addition, the changes in UACR from baseline to study end were inversely correlated with the changes in TIR (R = −0.03, P = 0.04), and UACR decreased by 19% for each 10% increase in TIR (P = 0.04) [9].

Studies have also focused on TIR as a predictor of risk for macrovascular complications. A cross-sectional analysis of 2,215 patients with type 2 diabetes investigated the relationship of TIR with carotid intima-media thickness (CIMT), a surrogate marker of cardiovascular disease (CVD). Participants with abnormal CIMT had significantly lower TIR (P <0.001) and higher HbA1c.The risk of abnormal CIMT was decreased by 6.4% for each 10% increase in TIR [10].

Evidence is also emerging regarding the role of TIR as a predictor of mortality risk. A very recent prospective analysis of 6,225 patients with type 2 diabetes, followed for a median of 6.9 years, revealed that TIR is inversely correlated with the risk of all-cause mortality, with each 10% decrease in TIR having a hazard ratio of 1.08 (95% CI 1.05–1.12) for all-cause and 1.05 (95% CI 1.00–1.11) for CVD mortality [11].

A cross-sectional, observational study of 336 patients with type 2 diabetes showed an association between TIR and lower extremities arterial disease (LEAD). Lower TIR was seen in patients with type 2 diabetes and LEAD (P <0.01), whereas the prevalence of LEAD by severity decreased with ascending quartiles of TIR (P <0.05) [12].

All this studies confirm the role of TIR in developing the micro and macrovascular complications in patients with DM and the goal of the clinicians is to increase the TIR to the accepted goal of 70%.

Objectives

- To improve time in range (TIR) after switching from SMBG to CGM meaning BS between 70-180 mg/dl to 70% per day or above which approximates 17 – hours a day in patients with DM on multiple dose injections (MDI) of Insulin per day plus/ minus oral antidiabetic medications or and GLP1-RAG.
- To improve the quality of care of Patients with DM type-1 and type - 2 who were out of control on 3- or more injections of Insulin per day in Internal medicine Residency Clinic by switching from Self-monitoring blood glucose/SMBG/ 3-4 times a day to Continuous Glucose Monitoring/CGM/ measured by improving patient's Glucose management indicator/GMI/ which approximates HbA1c, but it is more accurate.

2. Material and methods

Twenty- five Patients with uncontrolled DM were recruited in our Internal Medicine Residency by our CGM team in Mountain View Hospital, Las Vegas, Nevada. The team consisted of 4- Transitional Year Residents 8- Internal Medicine Residents and Board- Certified Endocrinologist.

The patients had Type 1 DM- 15% and Type 2 DM- 85%. Their average hbA1C before the switch to CGM was 11.21%. All of the patients were using 3-4 injections of Insulin per day plus minus antidiabetic oral medications or GLP-RAG and were SMBG four times a day.

The patients were between 42-75 years of old.

After the CGM team member in the clinic was notified by the patients about their interest in having CGM instead of SMBG the consent form was signed by the patients after thorough explaining to them the usage of CGM.

The patients with compatible with the CGM I Phones or Android Phones were given by the CGM team a share code. That way the CGM team was able to monitor 24/7 the blood glucose data of the patients. The patients were seen monthly by the CGM team member.

The patients who did not have compatible with CGM I Phones or Android Phones were given receiver and every month were seen in the clinic. There the patient's data were downloaded and the Insulin adjusted as needed.

Both type of patients were contacted by member of the CGM team twice weekly and their Insulin was adjusted based on their blood glucose readings. They were given pamphlets about the carbohydrate content and the calories of different types of food as well as instructions about the physical activity needed. The patients were educated how to treat their low blood sugar. All activities of the CGM team were supervised by the Endocrinologist who was a member of the CGM team.

3. Results

We had -25- patients in the Project with either DM type 2-85% or DM type 1-15%. They were SMBG - 3-4 times per day before starting the CGM. The patients were between 42-75 years of age. The Mean HbA1c before the switch from SMBG to CGM was 11.21%. One hundred and twenty days after starting the CGM and following the patients up to 2- years the HbA1c measured by GMI decreased from 11.21% to 7.04%.

Time in range of BS between 70-180 mg/dl per day was 74% on CGM and surpassed the goal of 70%. On SMBG the patients had only 18 % of the time blood glucose in range.

The average blood glucose per 24- hours decreased from 286 mg/dl using SMBG to 158 mg/dl by using CGM.

Twenty percent of patients were able to discontinue their Insulin and be compensated with GMI less than 7% only with antidiabetic oral medications and or GLP1-RAG.

The mild and more serious hypoglycemia also decreased significantly by using CGM.

The patient's satisfaction improved measured by CGM Quality of life Questionnaire after the switch. This was due to better control of the patient's Diabetes Mellitus and improved patients' physical activity. Patients also started living healthier lifestyles and eating healthier.

4. Discussion

Over the last two decades the CGM has become an increasingly used for real-time monitoring of blood glucose in a variety of diabetes treatment settings and applications [13,14,15]. The CGM devices have become easier to use and operate and are covered by a wider range of insurance plans.

The clinical improvement of glucose control continue to improve using CGM.

The earliest application of the CGM devices was in patients with type- 1 diabetes on intensive insulin therapy with the goal to reduce hypoglycemia and improve glucose control [16].

Recently, the GOLD Trial and the DIAMOND Trial, two randomized controlled trials, have confirmed the independent value of CGM in guiding intensive insulin therapy for type -1 Diabetic patients treated with MDI 16,17].

Also recently there are trials confirming the role of CGM in improving the glucose control in patients with type 2 DM as three quarters of the patients on Multiple daily injections of Insulin(MDI) had improvement of HbA1c by 0.5%.

The American Diabetic Association and International Consensus provides recommendations for blood glucose control using CGM as shown in Figure 1[18,19].

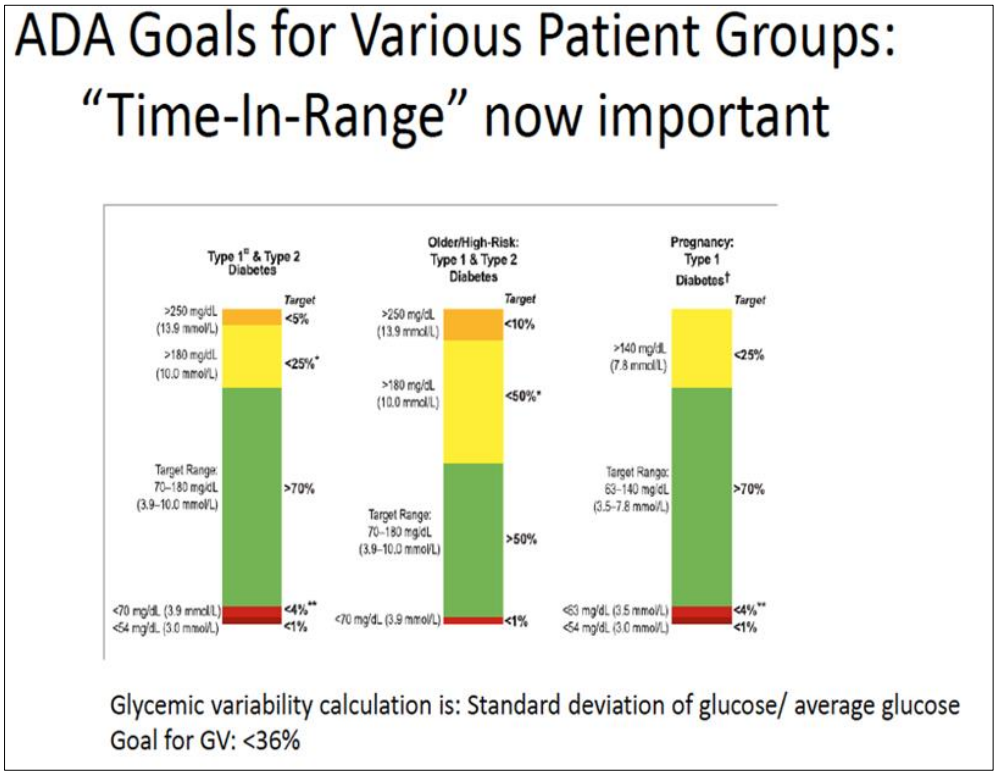

Figure 1 ADA goals using CGM in different type of Patients

The most important goal to be achieved with the usage of CGM is the blood sugar between 70-180 mg/dl. We call this Time in range. The goal is the blood glucose to be in range between 70-180 mg/dl 70% of the time, except in older patients with high risk of hypoglycemia and pregnant patients as you can see from Figure 1.

There is a correlation between time in range and the microvascular complication of patients with type -I and type -II DM as described in figure 2(20).

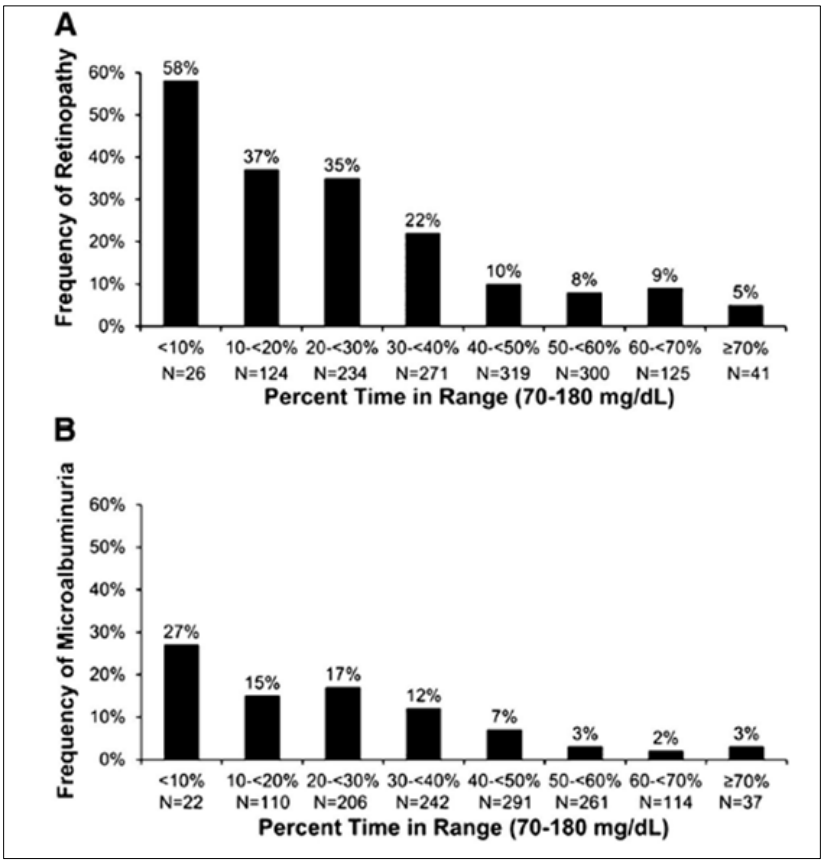

Figure 2 Frequency of development of microvascular complication according to level of TIR (70- 180 mg/dL) computed from quarterly seven-point blood glucose testing

As discussed recently multiple trials showed the correlation between time in range(TIR) and the prevalence of Diabetic Polyneuropathy, Diabetic Retinopathy, Diabetic nephropathy as well as macrovascular complications like lower extremity arterial disease, carotid intima-media thickness as a surrogate marker for atherosclerotic cardiovascular disease and cardiovascular mortality. Usually in majority of these studies 10% change in TIR let to significant change in micro or macrovascular complication rate.

In our study we were able to increase the TIR from 18 % while the patients were SMBG to 74% while using CGM. The average daily blood glucose decreased from 284 mg/dl to 158 mg/dl.

We think that the more significant drop in our population of patients of average blood glucose and increment in TIR compare to other studies was due to the patient's characteristics-more indigent patients in Community settings, with poor understanding of their disease, with poor eating habits and not realizing how to adjust their Insulin dynamically at least twice a week based on the level of their blood sugar, before switching to CGM and counseled by our CGM clinic team.

The reported average improvement of HbA1c in our patient's population was- 4.17%, while on average HbA1c improves based on other studies was between 0.3-0.6%.

We believe that the significant improvement of the TIR after switching to CGM in our patient in long term will decrease the patients diabetic related micro and macrovascular complications.

The biggest obstacle we encountered is educating our patients how to use CGM and interpret the data, to use calorie and carbohydrate counting, to exercise regularly and how to treat their hypoglycemia. Our CGM team did an excellent educational work.

5. Conclusion

According to Prof. I. Tsanov the governing decision plays a key role in the success of medical experiments [21].

This shows that our decision about the utilization of CGM device and proper patients education and follow-up can be done in Internal medicine residency continuity clinic run by Transitional year and Internal Medicine residents. This was done traditionally in the past in specialized endocrine centers.

In our project for the first time as far as we know we have proved that we can improve the TIR and average blood glucose by switching from SMBG to CGM the patients with type 1 and type 2 DM on multiple daily injections of Insulin in Internal Residency Medicine continuity clinic with active participation of Internal medicine and Transitional Year Residents under the supervision of Board Certified Endocrinologist who was a part of the clinic. This can be adopted by other Internal Medicine Residency programs in USA to improve the quality of care of most difficult to treat diabetic patients.

Compliance with ethical standards

Acknowledgments

We want to express our Gratitude to the Research Department, Sunrise Health, GME Consortium, Mountain View Hospital, and Las Vegas, Nevada.

Disclosure of conflict of interest

All authors have declared that no financial support was received from any organization for the submitted work.

Statement of ethical approval

The present research work does not contain any study performed on animals subjects by any of the authors.

Statement of informed consent

Informed Consent was obtained or waived by all participants in this study.

Funding

We did not receive any funding from manufacturer for the publication of these case series.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

References

[1] Nathan DM, Genuth S, Lachin J, et al..; Diabetes Control and Complications Trial Research Group . The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993;329:977–986

[2] UK Prospective Diabetes Study (UKPDS) Group . Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998;352:837–853

[3] Beck RW, Connor CG, Mullen DM, Wesley DM, Bergenstal RM. The fallacy of average: how using HbA1c alone to assess glycemic control can be misleading. Diabetes Care 2017;40:994–999

[4] Galindo RJ, Aleppo G. Continuous glucose monitoring: the achievement of 100 years of innovation in diabetes technology. Diabetes Res Clin Pract 2020;170:108502

[5] Kravarusic J, Aleppo G. Diabetes technology use in adults with type 1 and type 2 diabetes. Endocrinol Metab Clin North Am 2020;49:37–55

[6] Danne T, Nimri R, Battelino T, et al.. International consensus on use of continuous glucose monitoring. Diabetes Care2017;40:1631–1640

[7] Mayeda L, Katz R, Ahmad I, et al.. Glucose time in range and peripheral neuropathy in type 2 diabetes mellitus and chronic kidney disease. BMJ Open Diabetes Res Care 2020;8:e000991

[8] Lu J, Ma X, Zhou J, et al.. Association of time in range, as assessed by continuous glucose monitoring, with diabetic retinopathy in type 2 diabetes. Diabetes Care 2018;41:2370–2376

[9] Ranjan AG, Rosenlund SV, Hansen TW, Rossing P, Andersen S, Nørgaard K. Improved time in range over 1 year is associated with reduced albuminuria in individuals with sensor-augmented insulin pump-treated type 1 diabetes. Diabetes Care 2020;43:2882–2885

[10] Lu J, Ma X, Shen Y, et al.. Time in range is associated with carotid intima-media thickness in type 2 diabetes. Diabetes Technol Ther 2020;22:72–78

[11] Lu J, Wang C, Shen Y, et al.. Time in range in relation to all-cause and cardiovascular mortality in patients with type 2 diabetes: a prospective cohort study. Diabetes Care.

[12] Li J, Li Y, Ma W, et al.. Association of time in range levels with lower extremity arterial disease in patients with type 2 diabetes. *Diabetes Metab Syndr* 2020;14:2081–2085

[13] American Diabetic Association standards of care in Diabetes-2020. Diabetes Care2020,43(Suppl 6)

[14] Poolsup N, Suksomboon N, Kyaw AM: Systematic review and meta-analysis of the effectiveness of continuous glucose monitoring (CGM) on glucose control in diabetes. Diabetol Metab Syndr 2013; 5:39

[15] Janapala RN, Jayaraj JS, Fathima N, et al.: Continuous glucose monitoring versus Self-monitoring of blood glucose in type 2 diabetes mellitus: a systematic review with meta-analysis. Cureus 2019;11:e5634

[16] Lind, M, Polonsky, W, Hirsch, IB, et al. Continuous glucose monitoring vs conventional therapy for glycemic control in adults with type 1 diabetes treated with multiple daily insulin injections: the GOLD randomized clinical trial. JAMA. 2017;317(4):379-387.

[17] Polonsky, WH, Hessler, D, Ruedy, KJ, Beck, RW DIAMOND Study Group. The impact of continuous glucose monitoring on markers of quality of life in adults with type 1 diabetes: further findings from the DIAMOND randomized clinical trial. Diabetes Care. 2017;40(6):736-741.

[18] American Diabetes Association: Glycemic targets: standards of medical care in diabetes-2021. Diabetes Care2021;44:S73–S84

[19] Battelino T, Danne T, Bergenstal RM, et al.: Clinical targets for continuous glucose monitoring data interpretation: recommendations from the International Consensus on Time in Range. Diabetes Care 2019; 42:1593–1603

[20] Roy W. Beck et al. Validation of the time in range measure as outcome for Diabetes Clinical Trials.Diab Care 2019; 42: 400-405

[21] Tsanov,I. The Managerial Decision: Theory and Practice. Monogram. BAC., ISBN978-619-90235-7.