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Original Research Article

COMPARATIVE STUDY OF GLYCAEMIC CONTROL AND TREATMENT ADHERENCE IN PATIENTS RECEIVING FIXED-DOSE COMBINATION THERAPY VERSUS SEPARATE ORAL ANTIDIABETIC TABLETS

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) requires sustained glycaemic control and medication adherence to prevent long-term complications. Fixed-dose combination (FDC) therapy may improve treatment adherence by reducing pill burden and simplifying medication administration compared with separate oral antidiabetic tablets. The aim is to compare glycaemic control, medication adherence, treatment satisfaction, and adverse drug effects among patients receiving FDC therapy versus separate oral antidiabetic tablets.

Materials and Methods: This hospital-based, observational comparative study included 98 patients with T2DM at a tertiary care hospital. Patients were divided into two groups: FDC therapy (n=49) and separate oral antidiabetic tablets (n=49). Demographic characteristics, fasting blood glucose, postprandial blood glucose, HbA1c, daily pill burden, medication adherence, treatment satisfaction, and adverse effects were assessed. Medication adherence was evaluated using the Adherence to Refills and Medications Scale (ARMS) and proportion of days covered (PDC). Statistical analysis was performed using SPSS version 28.0, with $p<0.05$ considered statistically significant.

Results: The mean HbA1c was significantly lower in the FDC group compared with the separate-tablet group (7.27 ± 0.68% vs. 7.69 ± 0.57%; p=0.001). Glycaemic targets (HbA1c <7%) were achieved by 32.65% and 10.20% of patients, respectively (p=0.007). Daily pill burden was significantly lower with FDC therapy (1.84 ± 0.66 vs. 3.27 ± 0.73; p<0.001). Medication adherence was better in the FDC group, with lower ARMS scores (16.94 ± 3.28 vs. 20.71 ± 3.48; p<0.001) and higher PDC (88.91% vs. 82.66%; p<0.001). Treatment satisfaction was significantly higher among FDC recipients (79.59% vs. 53.06%; p=0.005). Adverse drug effects showed no statistically significant differences.

Conclusion: FDC therapy was associated with improved glycaemic control, better medication adherence, reduced pill burden, and greater treatment satisfaction compared with separate oral antidiabetic tablets. FDC therapy may represent a convenient treatment option for patients with T2DM.

Keywords: Type 2 diabetes mellitus; Fixed-dose combination therapy; Glycaemic control; Medication adherence; Oral antidiabetic drugs.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterised by persistent hyperglycaemia resulting from insulin resistance, progressive pancreatic beta-cell dysfunction, and impaired insulin secretion. It represents a major public health challenge worldwide because of its increasing prevalence, prolonged disease course, and association with serious microvascular and macrovascular complications. Changes in dietary habits, sedentary lifestyles, obesity, population

ageing, and urbanisation have contributed to the growing burden of diabetes. Inadequate glycaemic control increases the risk of diabetic nephropathy, retinopathy, neuropathy, cardiovascular disease, and premature mortality. Therefore, effective long-term management requires appropriate pharmacological treatment, lifestyle modification, regular monitoring, and sustained patient participation in disease management.[1] Achieving optimal glycaemic control is a fundamental objective in managing patients with T2DM. Glycated haemoglobin (HbA1c), fasting blood glucose, and postprandial blood glucose are commonly used parameters for evaluating therapeutic effectiveness. HbA1c reflects average glycaemic exposure over approximately three months and serves as an important indicator of long-term glucose control. An HbA1c target below 7% is generally appropriate for many nonpregnant adults, although individualised targets may be required depending on age, comorbidities, hypoglycaemia risk, and overall health status. Maintaining adequate glycaemic control requires continuous therapeutic assessment, appropriate medication adjustments, and adherence to prescribed treatment. Failure to achieve glycaemic targets may necessitate additional antidiabetic agents and more complex therapeutic regimens.[2] Oral antidiabetic medications remain an important component of T2DM management, particularly among patients who do not require insulin therapy. Commonly prescribed medications include biguanides, sulfonylureas, dipeptidyl peptidase-4 inhibitors, sodium-glucose cotransporter-2 inhibitors, and thiazolidinediones. These agents act through different mechanisms to reduce hyperglycaemia and address underlying metabolic abnormalities. Because T2DM is progressive, monotherapy may eventually become insufficient to maintain adequate glucose control, making combination pharmacotherapy necessary. Combining medications with complementary mechanisms of action can provide broader glycaemic management. However, prescribing multiple drugs separately may increase daily pill burden, dosing frequency, treatment complexity, and medication-related inconvenience. Consequently, treatment selection should consider not only pharmacological effectiveness but also patient preferences, safety, affordability, and ease of administration.[3] Medication adherence is a critical determinant of successful diabetes management and represents a major challenge in routine clinical practice. Adherence refers to the extent to which patients take medications according to agreed therapeutic recommendations. Poor adherence may result from forgetfulness, inadequate disease awareness, financial difficulties, adverse drug reactions, psychological factors, and complicated dosing schedules. Patients with T2DM frequently have coexisting hypertension, dyslipidaemia, and cardiovascular disorders, requiring additional medications and increasing the overall treatment burden. Persistent non-adherence can contribute to uncontrolled hyperglycaemia, therapeutic failure, disease progression, and increased healthcare utilisation. Improving medication adherence therefore requires patient-centred approaches involving appropriate counselling, medication review, shared decision-making, and simplification of treatment regimens whenever clinically suitable.[4] Fixed-dose combination (FDC) therapy has emerged as an alternative strategy for simplifying oral antidiabetic treatment. An FDC contains two or more pharmacologically active agents in a single pharmaceutical formulation, allowing patients to receive combination treatment with fewer tablets. Potential advantages include reduced pill burden, simplified dosing schedules, improved convenience, and better medication adherence. By reducing the number of separate tablets required, FDC therapy may minimise unintentional missed doses and difficulties associated with complex regimens. Nevertheless, fixed-dose formulations may offer limited flexibility for individual dose adjustments and may not be suitable for every patient. Therefore, their clinical usefulness depends on appropriate drug selection, compatible dosage requirements, tolerability, and individual therapeutic needs.[5] The relationship between medication adherence and glycaemic control is particularly important when comparing fixed-dose combinations with separate oral antidiabetic tablets. Although both approaches may contain equivalent pharmacologically active agents, differences in administration convenience, tablet burden, and treatment satisfaction may influence medication-taking behaviour. Adherence can be assessed using validated questionnaires, patient-reported missed doses, prescription refill records, and the proportion of days covered. Treatment satisfaction, perceived regimen complexity, medication affordability, and adverse effects are additional factors influencing treatment continuation. Evaluating these parameters alongside biochemical indicators provides a more comprehensive understanding of the practical effectiveness of oral antidiabetic regimens. Such assessment is particularly relevant in clinical settings where long-term treatment compliance remains challenging.[6]

MATERIALS AND METHODS

The present study was designed as a hospital-based, observational comparative study to evaluate glycaemic control and treatment adherence among patients with type 2 diabetes mellitus (T2DM) receiving fixed-dose combination (FDC) therapy versus separate oral antidiabetic tablets. The study aimed to compare glycaemic parameters, medication adherence, daily pill burden, treatment satisfaction, adverse drug reactions, and factors influencing therapeutic compliance between the two treatment groups. The study was conducted at a tertiary care hospital in the Departments of General Medicine.

Patients attending the outpatient department for routine diabetes management were assessed for eligibility. Clinical evaluation, medication history, biochemical investigations, and treatment adherence assessments were performed using a structured data collection proforma. A total of 98 patients diagnosed with type 2 diabetes mellitus were included using a consecutive sampling technique. Participants were divided into two groups according to their prescribed oral antidiabetic treatment. Group A comprised 49 patients receiving fixed-dose combination therapy, whereas Group B comprised 49 patients receiving separate oral antidiabetic tablets. Patients in both groups were selected based on predefined eligibility criteria, and comparable therapeutic combinations were considered wherever feasible to minimise differences attributable to drug selection.

Inclusion Criteria

Patients aged 18 years and above with established type 2 diabetes mellitus who had been receiving combination oral antidiabetic therapy for at least three months were eligible for inclusion. Patients receiving either fixed-dose combinations or separate tablets containing comparable oral antidiabetic agents, attending regular follow-up visits, and willing to provide informed consent were included. Availability of recent glycaemic investigations and reliable medication history was required.

Exclusion Criteria

Patients with type 1 diabetes mellitus, gestational diabetes, or secondary diabetes were excluded. Patients receiving insulin therapy, those with recent diabetic ketoacidosis or hyperosmolar hyperglycaemic state, severe hepatic or renal impairment, active malignancy, acute systemic illness, pregnancy, or significant cognitive impairment affecting medication adherence assessment were excluded. Patients with recent major modifications in antidiabetic treatment or incomplete clinical records were also excluded.

Methodology: Detailed demographic and clinical information was collected, including age, gender, educational status, socioeconomic status, body mass index (BMI), duration of diabetes, family history, smoking status, alcohol consumption, and associated comorbidities. Relevant medical conditions, including hypertension, dyslipidaemia, cardiovascular disease, and diabetic complications, were documented. Anthropometric measurements included weight, height, and BMI calculated as weight in kilograms divided by height in metres squared. Blood pressure was recorded using standard procedures.

Assessment of Antidiabetic Treatment: A detailed medication history was obtained, including the names of oral antidiabetic agents, prescribed doses, frequency of administration, number of tablets consumed daily, and total daily pill burden. Patients receiving FDC therapy were compared with those taking the corresponding antidiabetic agents as separate tablets. Treatment affordability, medication-related inconvenience, frequency of missed doses, and reported adverse effects were assessed. Particular attention was given to gastrointestinal intolerance, symptomatic hypoglycaemia, and difficulties associated with multiple daily tablets.

Assessment of Glycaemic Control: Glycaemic control was evaluated using fasting blood glucose (FBG), postprandial blood glucose (PPBG), and glycated haemoglobin (HbA1c). Blood glucose concentrations were measured using standard laboratory procedures, while HbA1c was estimated using a standardised laboratory method. Mean HbA1c levels were compared between the groups. An HbA1c level below 7% was considered indicative of adequate glycaemic control for the primary comparison, recognising that individualised targets may differ according to patient characteristics. The proportions of patients achieving glycaemic targets were recorded.

Assessment of Medication Adherence: Medication adherence was assessed using the validated 12-item Adherence to Refills and Medications Scale (ARMS), along with patient-reported missed doses and available prescription refill records. ARMS scores ranged from 12 to 48, with lower scores indicating better adherence. Where reliable dispensing records were available, the proportion of days covered (PDC) was calculated, and PDC of at least 80% was considered satisfactory medication availability. For patients taking separate tablets, coverage was assessed for all prescribed oral antidiabetic agents. Common reasons for non-adherence, including forgetfulness, medication cost, polypharmacy, adverse effects, and dosing inconvenience, were documented.

Statistical Analysis: Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics version 28.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, while categorical variables were presented as frequencies and percentages. The Shapiro–Wilk test was used to assess normality. Independent Student's t-test or Mann–Whitney U test was applied for between-group comparisons of continuous variables. Categorical variables were compared using the Chi-square test or Fisher's exact test. Pearson's or Spearman's correlation coefficients were used to assess associations between adherence and glycaemic parameters. Multivariable regression analysis was considered to adjust for relevant confounders. A p-value below 0.05 was considered statistically significant.

RESULTS

[Table 1] Comparison of Baseline Demographic and Clinical Characteristics Between the Two Treatment Groups (N=98)

A total of 98 patients with type 2 diabetes mellitus were included in the study, with 49 patients each receiving fixed-dose combination (FDC) therapy and separate oral antidiabetic tablets. The mean age of

patients was 55.75 ± 7.34 years in the FDC group and 57.88 ± 9.33 years in the separate-tablet group, with no statistically significant difference (p=0.213). Male patients constituted 57.14% and 55.10% of the respective groups (p=0.839). The mean BMI was comparable between the groups (26.67 ± 2.76 vs. 26.82 ± 2.80 kg/m²; p=0.786). The mean duration of diabetes was slightly lower in the FDC group (7.25 ± 3.61 years) than in the separate-tablet group (8.37 ± 3.87 years), although the difference was statistically insignificant (p=0.144). Hypertension was present in 55.10% and 61.22% of patients, while dyslipidaemia was observed in 48.98% and 51.02%, respectively. A family history of diabetes was reported by 42.86% of patients receiving FDC therapy and 44.90% receiving separate tablets.

[Table 2] Comparison of Oral Antidiabetic Tablet Burden and Dosing Characteristics (N=98)

A significant difference in daily oral antidiabetic tablet burden was observed between the two treatment groups. Patients receiving FDC therapy consumed an average of 1.84 ± 0.66 tablets per day, compared with 3.27 ± 0.73 tablets among patients receiving separate oral antidiabetic medications (p<0.001). Once-daily medication administration was considerably more frequent in the FDC group, accounting for 79.59% of patients, compared with 36.73% in the separate-tablet group (p<0.001). Only 14.29% of patients receiving FDC therapy required three or more tablets daily, whereas this proportion increased significantly to 85.71% among those receiving separate tablets (p<0.001). Furthermore, none of the patients in the FDC group consumed four or more tablets daily, compared with 38.78% of patients in the separate-tablet group (p<0.001).

[Table 3] Comparison of Glycaemic Control Parameters Between the Two Treatment Groups (N=98)

Comparison of glycaemic parameters demonstrated significantly better glycaemic control among patients receiving FDC therapy than among those receiving separate oral antidiabetic tablets. The mean fasting blood glucose level was significantly lower in the FDC group (141.51 ± 27.75 mg/dL) compared with the separate-tablet group (152.96 ± 20.52 mg/dL; p=0.023). Similarly, mean postprandial blood glucose levels were 205.92 ± 30.79 mg/dL and 223.06 ± 28.03 mg/dL, respectively, demonstrating a statistically significant difference (p=0.005). The mean HbA1c level was also significantly lower among patients receiving FDC therapy (7.27 ± 0.68%) compared with those receiving separate tablets (7.69 ± 0.57%; p=0.001). The proportion of patients achieving the glycaemic target of HbA1c below 7.0% was significantly higher in the FDC group (32.65%) than in the separate-tablet group (10.20%; p=0.007). Conversely, HbA1c levels of 8.0% or above were observed in 12.24% of FDC patients compared with 28.57% of separate-tablet patients (p=0.045).

[Table 4] Comparison of Medication Adherence and Treatment Satisfaction (N=98)

Medication adherence and treatment satisfaction differed significantly between the two treatment groups, with more favourable findings among patients receiving FDC therapy. The mean Adherence to Refills and Medications Scale (ARMS) score was significantly lower in the FDC group (16.94 ± 3.28) than in the separate-tablet group (20.71 ± 3.48; p<0.001), indicating better medication adherence among FDC recipients. The mean proportion of days covered (PDC) was also significantly higher in the FDC group (88.91 ± 8.27%) compared with the separate-tablet group (82.66 ± 9.04%; p<0.001). Adequate medication coverage, defined as PDC ≥80%, was observed in 87.76% and 67.35% of patients, respectively (p=0.015). At least one missed medication dose during the previous month was reported by 16.33% of FDC recipients compared with 32.65% of separate-tablet recipients, although this difference did not reach statistical significance (p=0.060). Mean treatment satisfaction scores were significantly higher in the FDC group (4.10 ± 0.71 vs. 3.55 ± 0.89; p=0.002). Additionally, 79.59% of patients receiving FDC therapy were satisfied or very satisfied with their treatment, compared with 53.06% receiving separate tablets (p=0.005).

[Table 5] Comparison of Patient-Reported Barriers and Adverse Drug Effects (N=98)

Comparison of patient-reported barriers to treatment adherence revealed significant differences in forgetfulness and medication regimen complexity between the two groups. Forgetfulness was reported as a barrier by 18.37% of patients receiving FDC therapy compared with 38.78% receiving separate oral antidiabetic tablets (p=0.025). Similarly, regimen complexity was significantly less frequently reported among FDC recipients (16.33%) than among patients taking separate tablets (46.94%; p=0.001). Medication cost was identified as a barrier by 26.53% of patients in the FDC group and 30.61% in the separate-tablet group, without a statistically significant difference (p=0.655). Gastrointestinal adverse effects were reported by 24.49% and 32.65% of patients, respectively (p=0.371). Symptomatic hypoglycaemia occurred in an equal proportion of patients in both groups (14.29%; p=1.000). The overall frequency of any listed adverse effects was 34.69% in the FDC group compared with 44.90% in the separate-tablet group, although this difference was statistically insignificant (p=0.302).

Table 1: Comparison of Baseline Demographic and Clinical Characteristics Between the Two Treatment Groups (N=98)

Parameter	FDC therapy (n=49)	Separate tablets (n=49)	p-value
Age (years)	55.75 ± 7.34	57.88 ± 9.33	0.213
Male sex	28 (57.14%)	27 (55.10%)	0.839

BMI (kg/m²)	26.67 ± 2.76	26.82 ± 2.80	0.786
Duration of diabetes (years)	7.25 ± 3.61	8.37 ± 3.87	0.144
Hypertension	27 (55.10%)	30 (61.22%)	0.539
Dyslipidaemia	24 (48.98%)	25 (51.02%)	0.840
Family history of diabetes	21 (42.86%)	22 (44.90%)	0.839

Table 2: Comparison of Oral Antidiabetic Tablet Burden and Dosing Characteristics (N=98)

Parameter	FDC therapy (n=49)	Separate tablets (n=49)	p-value
Oral antidiabetic tablets/day	1.84 ± 0.66	3.27 ± 0.73	<0.001
Once-daily medication administration	39 (79.59%)	18 (36.73%)	<0.001
At least 3 tablets/day	7 (14.29%)	42 (85.71%)	<0.001
At least 4 tablets/day	0 (0.00%)	19 (38.78%)	<0.001

Table 3: Comparison of Glycaemic Control Parameters Between the Two Treatment Groups (N=98)

Parameter	FDC therapy (n=49)	Separate tablets (n=49)	p-value
Fasting blood glucose (mg/dL)	141.51 ± 27.75	152.96 ± 20.52	0.023
Postprandial blood glucose (mg/dL)	205.92 ± 30.79	223.06 ± 28.03	0.005
HbA1c (%)	7.27 ± 0.68	7.69 ± 0.57	0.001
HbA1c <7.0% (glycaemic target achieved)	16 (32.65%)	5 (10.20%)	0.007
HbA1c ≥8.0%	6 (12.24%)	14 (28.57%)	0.045

Table 4: Comparison of Medication Adherence and Treatment Satisfaction (N=98)

Parameter	FDC therapy (n=49)	Separate tablets (n=49)	p-value
ARMS adherence score (12–48)	16.94 ± 3.28	20.71 ± 3.48	<0.001
Proportion of days covered (PDC, %)	88.91 ± 8.27	82.66 ± 9.04	<0.001
PDC ≥80%	43 (87.76%)	33 (67.35%)	0.015
At least one missed dose in previous month	8 (16.33%)	16 (32.65%)	0.060
Treatment satisfaction (1–5 score)	4.10 ± 0.71	3.55 ± 0.89	0.002
Satisfied/very satisfied (score ≥4)	39 (79.59%)	26 (53.06%)	0.005

Table 5: Comparison of Patient-Reported Barriers and Adverse Drug Effects (N=98)

Parameter	FDC therapy (n=49)	Separate tablets (n=49)	p-value
Forgetfulness reported as a barrier	9 (18.37%)	19 (38.78%)	0.025
Medication cost reported as a barrier	13 (26.53%)	15 (30.61%)	0.655
Regimen complexity reported as a barrier	8 (16.33%)	23 (46.94%)	0.001
Gastrointestinal adverse effects	12 (24.49%)	16 (32.65%)	0.371
Symptomatic hypoglycaemia	7 (14.29%)	7 (14.29%)	1.000
Any of the listed adverse effects	17 (34.69%)	22 (44.90%)	0.302

DISCUSSION

The present comparative study included 98 patients with type 2 diabetes mellitus, divided equally into fixed-dose combination (FDC) therapy and separate oral antidiabetic tablet groups. The mean age was 55.75 ± 7.34 years in the FDC group and 57.88 ± 9.33 years in the separate-tablet group (p=0.213), indicating comparable age distributions. Male patients constituted 57.14% and 55.10%, respectively, while mean BMI values were 26.67 ± 2.76 and 26.82 ± 2.80 kg/m² (p=0.786). The mean duration of diabetes was 7.25 ± 3.61 years among FDC recipients compared with 8.37 ± 3.87 years among separate-tablet recipients (p=0.144). Hypertension and dyslipidaemia were also similarly distributed between the groups. These findings can be compared with Benford et al. (2012), who evaluated 5,891 patients with type 2 diabetes and reported a mean age of 61.5 years, 57% male patients, and a mean diabetes duration of 5.7 years. Their population was slightly older but had a shorter mean duration of diabetes than the present study population. The comparable baseline characteristics in the present study reduce concerns regarding major demographic imbalance between treatment groups, although unmeasured confounding remains possible.[7] A significant reduction in daily oral antidiabetic tablet burden was observed among patients receiving FDC therapy. The mean number of tablets consumed daily was 1.84 ± 0.66 in the FDC group compared with 3.27 ± 0.73 in the separate-tablet group (p<0.001), representing approximately 1.43 fewer tablets per day. Once-daily medication administration was reported in 79.59% of FDC recipients compared with only 36.73% of separate-tablet recipients (p<0.001). Furthermore, three or more tablets daily were required by 14.29% of patients in the FDC group compared with 85.71% in the separate-tablet group. Similar advantages of simplified dosing were reported by Pan et al. (2008), who compared a fixed-dose combination of metformin and glyburide with the corresponding two-pill regimen and demonstrated an approximately 13% improvement in medication adherence with FDC therapy. Although their study primarily evaluated adherence rather than the exact daily pill counts, its findings support the potential clinical importance of reducing medication complexity.[8] Significant differences in glycaemic control were observed between patients receiving FDC therapy and those receiving separate oral antidiabetic tablets. The mean fasting blood glucose level was 141.51 ± 27.75 mg/dL in the FDC group

compared with 152.96 ± 20.52 mg/dL in the separate-tablet group (p=0.023). Similarly, mean postprandial blood glucose levels were 205.92 ± 30.79 mg/dL and 223.06 ± 28.03 mg/dL, respectively (p=0.005). The proportion of patients achieving the HbA1c target of less than 7.0% was significantly higher among FDC recipients (32.65%) than among separate-tablet recipients (10.20%; p=0.007). These findings are consistent with Williams et al. (2012), who conducted a retrospective study involving 21,048 patients with type 2 diabetes, including 8,416 receiving FDC therapy and 4,225 receiving loose-dose combinations. Among patients with available HbA1c measurements, glycaemic target achievement was significantly higher in the FDC group (61%) than in the loose-dose combination group (52%; p=0.015). Although the absolute target-achievement rates were lower in the present study, both studies demonstrated a favourable association between FDC therapy and glycaemic control.[9] The mean HbA1c level in the present study was significantly lower among patients receiving FDC therapy (7.27 ± 0.68%) compared with those receiving separate oral antidiabetic tablets (7.69 ± 0.57%; p=0.001), representing an absolute difference of 0.42 percentage points. Furthermore, HbA1c levels of 8.0% or above were observed in only 12.24% of patients receiving FDC therapy compared with 28.57% of patients receiving separate tablets (p=0.045). These findings are supported by Han et al. (2012), who conducted a meta-analysis involving 70,573 patients across 10 studies comparing fixed-dose combinations with coadministered dual antidiabetic therapy. Their analysis demonstrated a significantly greater reduction in HbA1c among FDC recipients, with a pooled mean difference of −0.53 percentage points (95% CI: −0.78 to −0.28; p<0.0001). The difference in HbA1c observed in the present study was comparable in magnitude to the pooled estimate reported by Han et al. Their analysis also demonstrated an 8.6-percentage-point improvement in medication possession ratio among FDC recipients in direct comparisons.[10] Medication adherence was significantly better among patients receiving FDC therapy in the present study. The mean Adherence to Refills and Medications Scale (ARMS) score was 16.94 ± 3.28 in the FDC group compared with 20.71 ± 3.48 in the separate-tablet group (p<0.001), indicating better adherence among FDC recipients. Similarly, the mean proportion of days covered (PDC) was significantly higher with FDC therapy (88.91 ± 8.27%) than with separate tablets (82.66 ± 9.04%; p<0.001). Adequate medication coverage, defined as PDC ≥80%, was achieved by 87.76% and 67.35% of patients, respectively (p=0.015). Comparable findings were reported by Lokhandwala et al. (2016), who evaluated 23,361 patients with type 2 diabetes, including 12,590 receiving FDC therapy and 10,771 receiving loose-dose combinations. Medication adherence, defined by a medication possession ratio of at least 80%, was significantly higher among FDC recipients (57.0%) than among loose-dose combination recipients (50.7%; p<0.0001). The rate of non-persistence was also significantly lower in the FDC group (67.9% vs. 73.4%).[11] The present study also demonstrated a lower frequency of missed medication doses among patients receiving FDC therapy, although the difference did not reach statistical significance. At least one missed dose during the previous month was reported by 16.33% of patients in the FDC group compared with 32.65% in the separate-tablet group (p=0.060). The lower ARMS scores and higher PDC values among FDC recipients nevertheless indicated significantly better overall medication adherence. These observations are comparable with those of Melikian et al. (2002), who evaluated medication adherence among patients receiving oral antidiabetic monotherapy, separate combination therapy, and fixed-dose combination therapy. Among previously treated patients requiring intensification of treatment, adherence was significantly higher among patients switched to FDC therapy (77.0%) than among those receiving separate combination therapy (54.0%). Furthermore, patients who were switched from separate combination therapy to FDC therapy demonstrated an improvement in adherence from 71.0% to 87.0% (p<0.001). However, the investigators did not observe a significant adherence advantage among newly treated patients.[12] Patient-reported treatment satisfaction was significantly higher among individuals receiving FDC therapy in the present study. The mean treatment satisfaction score was 4.10 ± 0.71 in the FDC group compared with 3.55 ± 0.89 in the separate-tablet group (p=0.002). Furthermore, 79.59% of patients receiving FDC therapy reported being satisfied or very satisfied with their treatment compared with 53.06% of patients receiving separate tablets (p=0.005). These findings are consistent with Aoki et al. (2017), who conducted a pilot study involving 38 Japanese patients with type 2 diabetes who were switched from loose-dose combination therapy to equivalent-dose FDC therapy. Their questionnaire assessment demonstrated that 74.2% of respondents considered the reduction in medication numbers to be good or very good. This favourable patient perception was similar to the high treatment satisfaction observed among FDC recipients in the present study, although the questionnaires measured different outcomes. Interestingly, Aoki et al. reported no statistically significant change in HbA1c at two, four, or six months following the switch to FDC therapy.[13] Patient-reported barriers to medication adherence demonstrated significant differences between the treatment groups. Forgetfulness was reported by 18.37% of patients receiving FDC therapy compared with 38.78% receiving separate oral antidiabetic tablets (p=0.025), while regimen complexity was reported by 16.33% and 46.94%, respectively (p=0.001). Medication cost was a barrier among 26.53% of FDC recipients and 30.61% of separate-tablet recipients (p=0.655). Gastrointestinal adverse effects were observed in 24.49% and 32.65%

of patients, respectively (p=0.371), while symptomatic hypoglycaemia occurred in an equal proportion of patients in both groups (14.29%). The overall frequency of any listed adverse effects was also statistically comparable (34.69% vs. 44.90%; p=0.302). These observations can be compared with Böhm et al. (2021), who evaluated 990 patients with type 2 diabetes, including 756 receiving FDC therapy and 234 receiving loose-dose combinations. Their study demonstrated significantly greater improvements in medication adherence with FDC therapy, with adjusted differences of 0.22, 0.25, and 0.29 in the first, second, and third years, respectively (all p<0.001). The investigators also reported no statistically significant between-group differences in changes in adverse drug event occurrence. These findings are consistent with the present study's observations that FDC therapy was associated with fewer adherence-related barriers without a statistically significant difference in reported adverse effects.[14]

CONCLUSION

The present study demonstrated that fixed-dose combination (FDC) therapy was associated with significantly better glycaemic control and medication adherence compared with separate oral antidiabetic tablets among patients with type 2 diabetes mellitus. Patients receiving FDC therapy showed lower HbA1c levels, reduced daily pill burden, improved medication adherence, and greater treatment satisfaction. FDC therapy was also associated with fewer adherence-related barriers, particularly forgetfulness and regimen complexity, without significant differences in adverse drug effects. These findings suggest that FDC therapy may be a convenient and effective therapeutic option for improving diabetes management and supporting long-term treatment adherence.

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