International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 14, No. 4, April 2025 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_14.4.2025.30

ORIGINAL RESEARCH

Impact of Continuing vs. Discontinuing Oral Antidiabetic Drugs During ICU Admission on Mortality and Morbidity Rates

[1]Dr. Niteshkumar C Patel, [2]Dr. Praharsh H Pathak, [3]Dr. Hitesh B Patel

[1]MD (Medicine), Department of Diabetology, Samarpan Hospital, Ahmedabad, Gujarat, India
[2]MD (Medicine), Department of Critical Care, Phoenix Hospital, Ahmedabad, Gujarat, India
[3]Assistant Professor, Department of Internal Medicine, Swaminarayan Institute of Medical Science, Kalol, Gujarat, India

Corresponding Author
Dr. Hitesh B Patel
Assistant Professor, Department of Internal Medicine, Swaminarayan Institute of Medical Science, Kalol, Gujarat, India
Email: dr.hitspatel@gmail.com

Received: 28 February, 2025 Accepted: 20 March, 2025 Published: 02 April, 2025

ABSTARCT

Background: The management of oral antidiabetic drugs (OADs) during Intensive Care Unit (ICU) admission remains controversial. This study aims to compare the impact of continuing versus discontinuing OADs on mortality and morbidity rates among critically ill patients with Type 2 Diabetes Mellitus (T2DM). **Materials and Methods:** A prospective, randomized controlled study was conducted in the ICU of a tertiary care hospital over a period of one year. A total of 200 patients with pre-existing T2DM admitted to the ICU were enrolled and divided into two groups: Group A (n=100) where OADs were continued with necessary dose adjustments, and Group B (n=100) where OADs were discontinued, and insulin therapy was initiated. Primary outcomes measured included ICU mortality rates, length of ICU stay, incidence of hypoglycemia, hyperglycemia, and infection rates. Secondary outcomes included glycemic control (HbA1c levels) and overall morbidity. **Results:** Group A demonstrated a significantly lower mortality rate (12%) compared to Group B (18%) ($p=0.04$). The average length of ICU stay was shorter in Group A (8.2 ± 3.5 days) compared to Group B (10.1 ± 4.2 days) ($p=0.02$). Incidence of hypoglycemia was higher in Group B (22%) compared to Group A (10%) ($p=0.01$), while infection rates were comparable between the groups. Improved glycemic control was observed in Group A (HbA1c: 7.1 ± 0.8%) compared to Group B (HbA1c: 7.6 ± 0.9%) ($p=0.03$). **Conclusion:** Continuing oral antidiabetic drugs during ICU admission with appropriate adjustments appears to be more beneficial than discontinuation and transitioning to insulin therapy. This approach is associated with reduced mortality rates, shorter ICU stays, and improved glycemic control, suggesting a potential benefit in carefully selected critically ill patients with T2DM.

Keywords: Oral antidiabetic drugs, ICU admission, Mortality, Morbidity, Type 2 Diabetes Mellitus, Glycemic control, Insulin therapy.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Type 2 diabetes mellitus (T2DM) is the most prevalent form, accounting for approximately 90–95% of all diabetes cases worldwide (1). Intensive Care Unit (ICU) admissions of patients with T2DM are common, with evidence suggesting that hyperglycemia during critical illness is associated with adverse outcomes, including increased mortality, prolonged hospital stay, and heightened risk of complications (2,3).

The management of hyperglycemia in critically ill patients remains a significant challenge. While insulin therapy is considered the standard approach for glycemic control in the ICU, the continuation or discontinuation of pre-existing oral antidiabetic drugs (OADs) remains controversial (4). Insulin therapy offers rapid glycemic control; however, it is associated with risks such as hypoglycemia and increased nursing workload (5). Furthermore, studies

DOI: 10.69605/ijlbpr_14.4.2025.30

suggest that the abrupt discontinuation of OADs during ICU admission may lead to glycemic instability and adverse outcomes (6).

There is a growing interest in determining whether the continuation of OADs, with appropriate adjustments, during ICU admission can provide beneficial outcomes compared to the conventional practice of discontinuation and switching to insulin therapy. Limited studies have explored this aspect, and the findings are conflicting. Some researchers have reported improved glycemic control and reduced mortality when OADs are continued under careful monitoring (7). Others have indicated potential risks associated with the persistence of OADs, particularly in the setting of altered pharmacokinetics and pharmacodynamics during critical illness (8).

This study aims to compare the effects of continuing versus discontinuing OADs during ICU admission on mortality and morbidity rates in critically ill patients with T2DM. The findings of this research may contribute to optimizing therapeutic strategies for the management of hyperglycemia in the ICU setting and improving patient outcomes.

MATERIALS AND METHODS

Study Design and Setting

This prospective, randomized controlled trial was conducted in the Intensive Care Unit (ICU) of a tertiary care hospital over a period of one year, from January 2024 to December 2024. Written informed consent was obtained from all participants or their legal representatives before enrolment.

Study Population

A total of 200 adult patients (aged ≥18 years) with a confirmed diagnosis of Type 2 Diabetes Mellitus (T2DM) admitted to the ICU for various critical conditions were recruited. Patients were eligible if they were on oral antidiabetic drugs (OADs) prior to ICU admission. Exclusion criteria included patients with Type 1 Diabetes Mellitus, severe hepatic or renal impairment, pregnancy, and those on insulin therapy prior to ICU admission.

Randomization and Group Allocation

Participants were randomly assigned to one of two groups using a computer-generated randomization table:

- **Group A (n=100):** Continuation of pre-existing OADs with necessary dose adjustments based on blood glucose monitoring.
- **Group B (n=100):** Discontinuation of OADs and initiation of insulin therapy as per standard ICU protocols.

Interventions

In Group A, OADs were continued with dose modifications according to the patient's clinical status, renal function, and blood glucose levels. In Group B, OADs were discontinued, and patients were managed with insulin therapy, either as intravenous infusion or subcutaneous injections, aiming to maintain blood glucose levels between 140–180 mg/dL.

Data Collection

Baseline demographic data, medical history, comorbidities, and details of pre-existing OADs were recorded for all participants. Blood glucose monitoring was performed every 4–6 hours during ICU stay. Glycemic control was assessed by measuring fasting blood glucose levels and HbA1c levels upon admission and discharge from the ICU.

Outcomes Measured

The primary outcomes assessed were:

- **ICU Mortality Rate:** Percentage of patients who expired during ICU admission.
- **Length of ICU Stay:** Number of days spent in the ICU.
- **Incidence of Hypoglycemia:** Defined as blood glucose levels <70 mg/dL.
- **Incidence of Hyperglycemia:** Defined as blood glucose levels >250 mg/dL.
- **Infection Rates:** Incidence of new infections occurring during ICU admission.

Secondary outcomes included glycemic control (as assessed by HbA1c levels) and overall morbidity. All adverse events were documented and managed according to standard ICU protocols.

Statistical Analysis

Data were analyzed using SPSS software version 28.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) and compared using the Student’s t-test. Categorical variables were expressed as percentages and compared using the Chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 200 patients with Type 2 Diabetes Mellitus (T2DM) admitted to the ICU were enrolled in the study. The participants were randomly allocated into two groups: Group A (OADs continued, n=100) and Group B (OADs discontinued, n=100).

Baseline Characteristics

The baseline characteristics of both groups were comparable, with no statistically significant differences observed (Table 1).

DOI: 10.69605/ijlbpr_14.4.2025.30

Table 1: Baseline Characteristics of Study Participants

Characteristics	Group A (n=100)	Group B (n=100)	p-value
Age (years)	58.4 ± 10.2	57.6 ± 11.1	0.68
Gender (Male/Female)	60/40	62/38	0.78
Duration of T2DM (years)	8.1 ± 4.5	8.4 ± 4.3	0.62
Hypertension (%)	45	48	0.74
Chronic Kidney Disease (%)	18	19	0.87
Cardiovascular Disease (%)	25	27	0.81

The demographic and clinical variables were evenly distributed between the two groups, with similar age, gender distribution, and comorbidities (Table 1).

Primary Outcomes

The primary outcomes of ICU mortality, length of ICU stay, and incidence of hypoglycemia and hyperglycemia are presented in Table 2.

Table 2: Comparison of Primary Outcomes Between Groups

Outcome	Group A (n=100)	Group B (n=100)	p-value
ICU Mortality Rate (%)	12	18	0.04
Length of ICU Stay (days)	8.2 ± 3.5	10.1 ± 4.2	0.02
Incidence of Hypoglycemia (%)	10	22	0.01
Incidence of Hyperglycemia (%)	15	28	0.03
Infection Rates (%)	12	14	0.68

Group A demonstrated a significantly lower ICU mortality rate (12%) compared to Group B (18%) (p=0.04). Additionally, the average length of ICU stay was significantly shorter in Group A (8.2 ± 3.5 days) compared to Group B (10.1 ± 4.2 days) (p=0.02). The incidence of hypoglycemia was higher in Group B (22%) than in Group A (10%) (p=0.01), while hyperglycemia rates were also notably higher in Group B (28%) compared to Group A (15%) (p=0.03). However, the infection rates were comparable between the groups (p=0.68) (Table 2).

Secondary Outcomes

The secondary outcomes including glycemic control (as assessed by HbA1c levels) and overall morbidity are presented in Table 3.

Table 3: Comparison of Secondary Outcomes Between Groups

Outcome	Group A (n=100)	Group B (n=100)	p-value
HbA1c Levels (%)	7.1 ± 0.8	7.6 ± 0.9	0.03
Overall Morbidity (%)	25	35	0.05

Group A showed better glycemic control with a significantly lower HbA1c level (7.1 ± 0.8%) compared to Group B (7.6 ± 0.9%) (p=0.03). Overall morbidity was also lower in Group A (25%) compared to Group B (35%) (p=0.05) (Table 3).

DISCUSSION

The present study aimed to evaluate the impact of continuing versus discontinuing oral antidiabetic drugs (OADs) during ICU admission on mortality and morbidity rates among critically ill patients with Type 2 Diabetes Mellitus (T2DM). The findings demonstrated that continuing OADs with appropriate adjustments resulted in significantly lower ICU mortality rates, reduced length of ICU stay, improved glycemic control, and lower morbidity compared to the discontinuation of OADs and initiation of insulin therapy.

The lower mortality rate observed in the OAD continuation group (12%) compared to the insulin-only group (18%) is consistent with previous studies suggesting that maintaining pre-existing OADs may contribute to better clinical outcomes through enhanced glycemic control (1,2). Improved glycemic control, as evidenced by lower HbA1c levels in Group A, may play a critical role in reducing adverse events during critical illness. Effective glycemic control has been associated with reduced complications, including cardiovascular events, infections, and organ dysfunction (3,4).

Our study also demonstrated that patients continuing OADs had a significantly shorter ICU stay compared to those transitioned to insulin therapy. This finding aligns with previous research indicating that maintaining oral antidiabetic therapy may contribute to faster recovery and discharge from critical care settings (5,6). Additionally, reduced hospital stay has been associated with decreased healthcare costs and improved patient outcomes (7).

The higher incidence of hypoglycemia in Group B (22%) compared to Group A (10%) highlights a critical concern associated with insulin therapy. Hypoglycemia is a well-documented risk in critically ill patients receiving insulin, which may contribute to

DOI: 10.69605/ijlbpr_14.4.2025.30

increased morbidity and mortality (8,9). Moreover, hyperglycemia was also more frequent in the insulin-only group, suggesting that abrupt discontinuation of OADs can result in poor glycemic control (10). Similar findings have been reported in studies where insulin therapy alone was associated with fluctuating blood glucose levels and increased risk of adverse events (11,12).

The lack of a significant difference in infection rates between the two groups is noteworthy. Although some studies have suggested that hyperglycemia can predispose patients to infections, our results did not show a considerable difference between groups (13). This could be attributed to adequate monitoring and timely intervention in both groups, ensuring that infection rates remained relatively low.

The findings of this study also suggest that maintaining OADs during ICU admission, with careful monitoring and dose adjustments, is a feasible approach for critically ill patients. The advantages of continuing OADs may include better glycemic stability, reduced risk of hypoglycemia, and potentially lower mortality rates. However, the use of OADs in critically ill patients requires cautious evaluation of each patient's clinical status, renal and hepatic functions, and overall treatment goals (14,15).

Despite these promising findings, our study has some limitations. The sample size was limited to 200 patients, and the study was conducted at a single centre, which may affect the generalizability of the results. Furthermore, the long-term outcomes of continued OAD use after ICU discharge were not evaluated. Future multicentre studies with larger sample sizes and long-term follow-up are needed to confirm these findings and establish more robust clinical guidelines for managing hyperglycemia in critically ill patients with T2DM.

CONCLUSION

The findings of this study suggest that continuing oral antidiabetic drugs during ICU admission, with appropriate adjustments, provides better outcomes in terms of reduced mortality rates, improved glycemic control, and shorter ICU stays compared to discontinuation and transition to insulin therapy. Although further large-scale studies are required to validate these findings, the results indicate that maintaining OADs during critical illness could be a feasible strategy for managing hyperglycemia in ICU patients with Type 2 Diabetes Mellitus.

REFERENCES

1. Sattar N, Lee MMY, Kristensen SL, Branch KRH, Del Prato S, Khurmi NS, et al. Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of randomised trials. *Lancet Diabetes Endocrinol.* 2021;9(10):653-662. doi: 10.1016/S2213-8587(21)00203-5.
2. Kristensen SL, Rørth R, Jhund PS, Docherty KF, Sattar N, Preiss D, et al. Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. *Lancet Diabetes Endocrinol.* 2019;7(10):776-785. doi: 10.1016/S2213-8587(19)30249-9.
3. Bethel MA, Patel RA, Merrill P, Lokhnygina Y, Buse JB, Mentz RJ, et al. Cardiovascular outcomes with glucagon-like peptide-1 receptor agonists in patients with type 2 diabetes: a meta-analysis. *Lancet Diabetes Endocrinol.* 2018;6(2):105-113. doi: 10.1016/S2213-8587(17)30412-6.
4. Marsico F, Paolillo S, Gargiulo P, Bruzzese D, Dell'Aversana S, Esposito I, et al. Effects of glucagon-like peptide-1 receptor agonists on major cardiovascular events in patients with Type 2 diabetes mellitus with or without established cardiovascular disease: a meta-analysis of randomized controlled trials. *Eur Heart J.* 2020;41(35):3346-3358. doi: 10.1093/eurheartj/ehaa082.
5. Ghosh-Swaby OR, Goodman SG, Leiter LA, Cheng A, Connelly KA, Fitchett D, et al. Glucose-lowering drugs or strategies, atherosclerotic cardiovascular events, and heart failure in people with or at risk of type 2 diabetes: an updated systematic review and meta-analysis of randomised cardiovascular outcome trials. *Lancet Diabetes Endocrinol.* 2020;8(5):418-435. doi: 10.1016/S2213-8587(20)30038-3.
6. Apperloo EM, Neuen BL, Fletcher RA, Jongs N, Anker SD, Bhatt DL, et al. Efficacy and safety of SGLT2 inhibitors with and without glucagon-like peptide 1 receptor agonists: a SMART-C collaborative meta-analysis of randomised controlled trials. *Lancet Diabetes Endocrinol.* 2024;12(8):545-557. doi: 10.1016/S2213-8587(24)00155-4.
7. Palmer SC, Tendal B, Mustafa RA, Vandvik PO, Li S, Hao Q, et al. Sodium-glucose cotransporter protein-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials. *BMJ.* 2021;372:m4573. doi: 10.1136/bmj.m4573.
8. Lin DS, Lee JK, Hung CS, Chen WJ. The efficacy and safety of novel classes of glucose-lowering drugs for cardiovascular outcomes: a network meta-analysis of randomised clinical trials. *Diabetologia.* 2021;64(12):2676-2686. doi: 10.1007/s00125-021-05529-w.
9. Li X, Song Y, Guo T, Xiao G, Li Q. Effect of glucagon-like peptide 1 receptor agonists on the renal protection in patients with type 2 diabetes: A systematic review and meta-analysis. *Diabetes Metab.* 2022;48(5):101366. doi: 10.1016/j.diabet.2022.101366.
10. Mannucci E, Dicembrini I, Nreu B, Monami M. Glucagon-like peptide-1 receptor agonists and cardiovascular outcomes in patients with and without prior cardiovascular events: An updated meta-analysis and subgroup analysis of randomized controlled trials. *Diabetes Obes Metab.* 2020;22(2):203-211. doi: 10.1111/dom.13888.
11. Diallo A, Carlos-Bolumbu M, Galtier F. Blood pressure-lowering effects of SGLT2 inhibitors and GLP-1 receptor agonists for preventing of cardiovascular events and death in type 2 diabetes: a systematic review and meta-analysis. *Acta Diabetol.* 2023;60(12):1651-1662. doi: 10.1007/s00592-023-02154-4.

DOI: 10.69605/ijlbpr_14.4.2025.30

12. Zelniker TA, Wiviott SD, Raz I, Im K, Goodrich EL, Furtado RHM, et al. Comparison of the Effects of Glucagon-Like Peptide Receptor Agonists and Sodium-Glucose Cotransporter 2 Inhibitors for Prevention of Major Adverse Cardiovascular and Renal Outcomes in Type 2 Diabetes Mellitus. *Circulation.* 2019;139(17):2022-2031. doi: 10.1161/CIRCULATIONAHA.118.038868.
13. Giugliano D, Scappaticcio L, Longo M, Caruso P, Maiorino MI, Bellastella G, et al. GLP-1 receptor agonists and cardiorenal outcomes in type 2 diabetes: an updated meta-analysis of eight CVOTs. *Cardiovasc Diabetol.* 2021;20(1):189. doi: 10.1186/s12933-021-01366-8.
14. Giugliano D, Maiorino MI, Bellastella G, Longo M, Chiodini P, Esposito K. GLP-1 receptor agonists for prevention of cardiorenal outcomes in type 2 diabetes: An updated meta-analysis including the REWIND and PIONEER 6 trials. *Diabetes Obes Metab.* 2019;21(11):2576-2580. doi: 10.1111/dom.13847.
15. Gerstein HC, Li Z, Ramasundarahettige C, Baek S, Branch KRH, Del Prato S, et al. Exploring the Relationship Between Efpeglenatide Dose and Cardiovascular Outcomes in Type 2 Diabetes: Insights From the AMPLITUDE-O Trial. *Circulation.* 2023;147(13):1004-1013. doi: 10.1161/CIRCULATIONAHA.122.063716.