

A study of intravenous Insulin infusion in hyperglycemic Covid 19 patients

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Abstract :

Background :

Many patients with covid 19 infection have increased blood sugar at the time of admission. Some of them are not a known diabetic patients before. The covid infection and the use of steroids in treatment worsens the glygemic status of the patients. The hyperglycemia has a significant impact on the outcome . This study compares the management of hyperglycemia in covid 19 patients using subcutaneous insulin with the use of continuous insulin infusion.

Methods :

This is a single centered , prospective , case control study conducted in a tertiary care centre for a period of 6 months. Covid 19 patients with moderate and severe symptoms who are admitted with hyperglycemia are recruited for the study. They were randomised into Group A who were treated with continuous intravenous insulin infusion and Group B who were treated with subcutaneous insulin. The mortality , duration of hospital stay and the hypoglycemic events were studied as outcome.

Results :

During the study period 316 patients with admission blood sugar ≥ 200 mg/dl were recruited in the study. Of the 163 patients in group A who were treated with intravenous insulin infusion 12 patient died and of the 153 patients in group B who were treated with subcutaneous insulin 23 died. The mean duration of stay among the group A and and group B was 3.28 and 4.71 days respectively. The number of hypoglycemic events in group A were 24 and in group B were 17 which was not statistically significant.

Conclusion :

The continuous intravenous insulin infusion strategy to treat hyperglycemia in covid 19 patients has a significant reduction in the mortality and duration of hospital stay without significant increase in hypoglycemic events.

Key words :

Covid 19 , intravenous infusion , subcutaneous insulin.

Introduction

The corona virus disease 19 (Covid 19) is caused by severe acute respiratory syndrome corona virus 2 (SARS – CoV 2). Diabetes is one of the most common comorbid associated with covid 19 infection. The presence of diabetes worsen the outcome of covid 19 infection^{1,2} . In many studies it has been found that diabetes is the major risk factor for disease severity and mortality^{3,4}. Uncontrolled hyperglycemia almost doubles the chance of ICU admission and triples the mortality⁵ and good glycemic control improves the outcome in covid 19 patients⁶⁻⁹ . A well controlled blood sugar between 70 – 180 mg/dl significantly reduces the mortality and severity. For every 10 mg/dl drop in the blood sugar there is a 11% relative severe disease risk risk reduction in covid 19 infection^{10,11}. Though various subcutaneous insulin protocols were proposed for the treatment of hyperglycemia in covid patients¹²⁻¹⁴ continuous intravenous infusion have been a better method of insulin delivery for the control of acute severe hyperglycemia¹⁵⁻²⁰. This study compares the covid 19 patients treated with intravenous vs subcutaneous insulin.

Materials and methods:

This study was a single centre, prospective case control study carried out at Government Thiruvannamalai Medical College Hospital, Thiruvannamalai, Tamil Nadu, India.

This study was conducted from January 2021 to June 2021 (6 months).

Inclusion criteria :

- 1) Patients aged above 18 years with covid 19 infected patients as proven by RT-PCR positive nasopharyngeal swab.
- 2) Random admission blood sugar at the time of admission above 200 mg/dL
- 3) Clinical features suggestive of moderate to severe COVID-19.(box 1)

Exclusion criteria :

- 1) Patients with comorbidities like CAD,CKD, Coagulopathies, DCLD, and Seizure disorders.
- 2) Patients on anticoagulants and long term medications except anti-diabetics and anti-hypertensives.

After applying inclusion and exclusion criteria, a total of 316 patients were included in the study.

The total patients are randomized based on Age, Sex and BMI into 2 groups.

Group A had 163 patients who were given IV Regular Insulin infusion which was titrated hourly based on the Capillary Blood Glucose(CBG) levels as per Slidings scale.(Box 2)

Group B had 153 patients who were given a subcutaneous 3 times rapid with bed time basal regimen which was titrated daily based on 4 point blood sugar taken pre-breakfast, post-breakfast, pre-dinner and post-dinner. (Box 3)

Patients were treated with oxygen, antibiotics, steroids, anticoagulants and other supportive measures as per institutional protocols. The outcomes like mortality, duration of hospital stay and number of hypoglycaemia episodes were studied.

Results:

Of the 163 patients of Group A, 151 survived and 12 died and of the 153 patients of Group B, 130 survived and 23 died. The average duration of hospital stay in the group A was 3.28 days and in group B it was 4.2 days. The number of hypoglycaemia episodes in group A was 24 and in group B was 17. (Table 2)

Discussion :

In our study treatment of hyperglycemia with continuous insulin infusion has a significant effect in reducing the mortality (P = 0.0299) . The duration of hospital stay is also reduced significantly in IV

insulin treated group (3.28 days vs 4.71 days ; $P < 0.001$) . the hypoglycemic episodes in iv insulin treated group was 24 and in SC insulin group was 17. This was not statistically significant.

Conclusion :

Treating Covid 19 hyperglycemic patients with continuous IV insulin infusion significantly reduces the mortality and duration of hospital stay without increasing the hypoglycemic episodes when compared with subcutaneous insulin treatment.

Referances :

1. Fadini GP, Morieri ML, Longato E, Avogaro A. Prevalence and impact of diabetes among people infected with SARS-CoV-2. *J Endocrinol Invest.* 2020;43(6):867–9.
2. Pugliese G, Vitale M, Resi V, Orsi E. Is diabetes mellitus a risk factor for COronaVirus Disease 19 (COVID-19) *Acta Diabetol.* 2020;57(11):1275–85.
3. Roncon L, Zuin M, Rigatelli G, Zuliani G. Diabetic patients with COVID-19 infection are at higher risk of ICU admission and poor short-term outcome. *J Clin Virol.* 2020;127:104354.
4. Zhang Y, Cui Y, Shen M, et al. Association of diabetes mellitus with disease severity and prognosis in COVID-19: a retrospective cohort study. *Diabetes Res Clin Pract.* 2020;108227.
5. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: prevalence, pathophysiology, prognosis and practical considerations. *Diabetes Metab Syndr.* 2020;14:303–10.
6. Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab.* 2002;87:978–82.
7. Pe´rez A, Ramos A, Carreras G. Insulin therapy in hospitalized patients. *Am J Ther.* 2020;27:e71–8.
8. Umpierrez GE, Smiley D, Jacobs S, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 surgery). *Diabetes Care.* 2011;34:256–61.
9. Yang JK, Feng Y, Yuan MY, et al. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. *Diabet Med.* 2006;23:623–8.
10. Sardu C, D’Onofrio N, Balestrieri ML, et al. Outcomes in patients with hyperglycemia affected by Covid-19: can we do more on glycemic control? *Diabetes Care.* 2020;43(7):1408–15.

11. Zhu L, She Z-G, Cheng X, et al. Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. *Cell Metab.* 2020;31(6):1068–77.e3.
12. Gianchandani R, Esfandiari NH, Ang L, et al. Managing hyperglycemia in the COVID-19 inflammatory storm. *Diabetes.* 2020;69(10):2048–53.
13. Davis GM, Faulds E, Walker T, et al. Remote continuous glucose monitoring with a computerized insulin infusion protocol for critically ill patients in a COVID-19 medical ICU: Proof of concept. *Diabetes Care.* 2021;44(4):1055–8.
14. Faulds ER, Boutsicaris A, Sumner L, et al. Use of continuous glucose monitor in critically ill COVID-19 patients requiring insulin infusion: an observational study. *J Clin Endocrinol Metab.* 2021;106(10):e4007–16.
15. Rea RS, Donihi AC, Bobeck M, et al. Implementing an intravenous insulin infusion protocol in the intensive care unit. *Am J Health Syst Pharm.* 2007;64(4):385–95.
16. Tanenberg RJ, Hardee S, Rothermel C, Drake AJ 3rd. Use of a computerguided glucose management system to improve glycemic control and address national quality measures: a 7-year, retrospective observational study at a tertiary care teaching hospital. *Endocr Pract.* 2017;23(3):331–41.
17. Rabinovich M, Grahl J, Durr E, et al. Risk of hypoglycemia during insulin infusion directed by paper protocol versus electronic glycemic management system in critically ill patients at a large academic medical center. *J Diabetes Sci Technol.* 2018;12(1):47–52.
18. Newton CA, Smiley D, Bode BW, et al. A comparison study of continuous insulin infusion protocols in the medical intensive care unit: computer-guided vs. standard column-based algorithms. *J Hosp Med.* 2010;5(8):432–7.
19. Shetty S, Inzucchi SE, Goldberg PA, Cooper D, Siegel MD, Honiden S. Adapting to the new consensus guidelines for managing hyperglycemia during critical illness: the updated Yale insulin infusion protocol. *Endocr Pract.* 2012;18(3):363–70.
20. Asiri AA, Alguwaihes AM, Jammah AA, Alfadda AA, Al-Sofiani ME. Assessment of the effectiveness of a protocol to manage dexamethasoneinduced

hyperglycemia among hospitalized patients with COVID-19.

Endocr Pract. 2021;27(12):1232–41.

Tables and boxes :

Box 1 : AIIMS/ ICMR-COVID-19 National Task Force CLINICAL GUIDANCE FOR MANAGEMENT OF ADULT COVID-19 PATIENTS	
Mild covid 19 infection	Upper respiratory tract symptoms and/or fever WITHOUT shortness of breath or hypoxia
Moderate covid 19 infection	Anyoneof: 1. Respiratory rate ≥ 24 /min, breathlessness 2.SpO : 90% to $\leq 93\%$ on room air
Severe covid 19 infection	Anyoneof: 1.Respiratory rate >30 /min, breathlessness 2.SpO ₂ $<90\%$ on room air

Table 1 : Demographic data and admission blood sugar			
Variables	IV insulin(N=163)	SC insulin(N=153)	P value
Age (years)	50.39 (13.33)	50.93 (13.28)	0.7180
Sex (M/F)	82/81	80/73	0.7248
Body mass index (Kg/m ²)	25.79 (4.33)	25.94 (4.30)	0.7483
Blood sugar(mg/Dl)	274.94 (49.92)	273.61 (42.44)	0.7993

Table 2 : Outcomes			
	IV insulin(N=163)	SC insulin(N=153)	P value
Survived / died	151/12	130/23	0.0299
Duration of Hospital stay	3.28(1.25)	4.71(1.1)	0.0001
Hypoglycemic episodes	0.15 (0.36)	0.11(0.32)	0.3411

Box 2 : IV insulin infusion – titration scale	
Blood sugar (mg / dl)	Insulin dose (units / hour)

200 - 250	3
250 – 300	4
350– 400	5
>400	6
Titrated to a target blood sugar level between 70 – 180 mg/dl	

Box 3 :

SC insulin – titration scale

Blood sugar (mg / dl)	Insulin dose
150 – 200	+ 2
200 - 250	+4
250– 300	+6
350– 400	+8
>400	+10
Titrated to a target blood sugar level preprandial of < 140 mg/dl and post prandial of < 180 mg/dl	

Images :



