High dose dexamethasone for COVID-19 not common in a large US hospital network

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This project was supported by Task Order 75F40119F19002 under Master Agreement 75F40119D10037 from the US Food and Drug Administration. The views expressed are those of the authors and are not intended to convey official US Food and Drug Administration policy or guidance. This research was supported 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.

Background and Objective

June 2020: UK Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial reported benefit from dexamethasone (6 mg once daily for 10 days) in severely ill hospitalized patients [1, 2].

- Since then, corticosteroids have been widely used as a first line treatment for hospitalized patients requiring oxygen or mechanical ventilation [3].

February 2021: RECOVERY started a higher dose corticosteroid regimen (20 mg daily for 5 days followed by 10 mg daily for 5 days) compared to usual care, which included standard dose dexamethasone [4].

May 2022: Recruitment into the study closed for those requiring either no oxygen supplementation or simple oxygen only, due to an increased 28-day mortality risk for patients randomized to higher dose dexamethasone compared to standard dose [5].

While potential harm from higher doses is an important concern, little is known about real world dexamethasone dosing in patients hospitalized with COVID-19, in the United States, prior to publication of the RECOVERY trial results [6].

Objective: To examine dexamethasone use in hospitalizations for COVID-19, in a large US hospital Network, to identify use of potentially harmful higher doses

Methods

Data source

- Inpatient encounter data from 142 hospitals in the HCA Healthcare network
- HCA Healthcare is a data partner in the US Food and Drug Administration (FDA)'s Sentinel System

Inclusion criteria

- Hospitalization for COVID-19 defined as presence of an ICD-10-CM code U07.1 at any time during the hospital encounter, between April 1, 2020, and October 31, 2022
- Age ≥18 years

Exclusion criteria

- Use of dexamethasone, methylprednisolone, or prednisone >48 hours prior to admission assessed by inpatient administration data and patient self-report

Exposure

- Dexamethasone use during hospitalization or in the 48 hours prior identified via inpatient medication administration data (NDC codes and text searches). Administration date, time, route, and dose was available
- Daily dose of dexamethasone = sum of all doses administered on a treatment day. Median daily dose assessed over all treatment days
- Median daily doses categories:
  - Standard (≤6 mg daily), Moderately high (>6-≤10 mg daily), High (>10-≤20 mg daily), Very high (>20 mg daily)

Respiratory support

- Respiratory support between admission date and inpatient dexamethasone administration date extracted from semi-structured respiratory support-related nursing documentation
- Respiratory support categories:
  - no oxygen
  - simple oxygen (non-rebreather, oxygen conserving device, nasal cannula, or simple mask)
  - non-simple oxygen (BiPAP/CPAP or high-flow nasal cannula)
  - invasive mechanical ventilation (IMV) or extracorporeal membrane oxygenation (ECMO)
- Multiple categories assigned to the highest severity level
- Median daily dose of dexamethasone was examined for each respiratory support category

Analyses

- Analyses were descriptive and performed using SAS ® version 9.4.
- Classified as public health surveillance by the FDA and exempted from IRB review in accordance with the updated Common Rule

Results

Dexamethasone Utilization

- 305,965 hospitalizations with COVID-19 diagnosis
- 188,467 (61.6%) had dexamethasone administered between 48 hours pre-admission to discharge, 91.5% on or after admission
- Median time from admission to dexamethasone 0 days [IQR, 0-1] and median duration of use was 5 days [IQR, 3-9] days.
- Characteristics of hospitalizations that received dexamethasone are in Table 1

Table 1. Characteristics of hospitalizations that received dexamethasone in HCA Healthcare

Hospitalizations with dexamethasone, n=188,467	
Demographics	**N (%)**
Mean age in years (SD)	62.6 (17)
Sex	
Female	88,326 (46.9)
Male	100,118 (53.1)
Unknown	23 (0.0)
Race	
White	120,122 (63.7)
Black	30,388 (16.1)
AI/AN/H/P*	555 (0.3)
Asian/Asian Indian	4,787 (2.5)
Other	27,656 (14.7)
Unknown	4,959 (2.6)
Ethnicity	
Hispanic or Latino	44,417 (23.6)
Not Hispanic or Latino	135,621 (72.0)
Unknown	8,429 (4.5)
Common conditions present on admission	**N (%)**
Hypertension	115,755 (61.4)
Diabetes	77,547 (41.1)
Hematological disorders	68,604 (36.4)
Liver and renal disorders	69,250 (36.7)
Obesity (diagnosis and procedure codes)	61,972 (32.9)
Ischemic heart disease	44,687 (23.7)
Chronic kidney disease	37,772 (20.0)
COPD	33,007 (17.5)
Heart failure	31,751 (16.8)
Atrial fibrillation	26,386 (14.0)
Smoking	17,390 (9.2)
Asthma	14,300 (7.6)
Acute myocardial infarction	12,384 (6.6)

*American Indian/Alaska Native/Hawaiian /Pacific

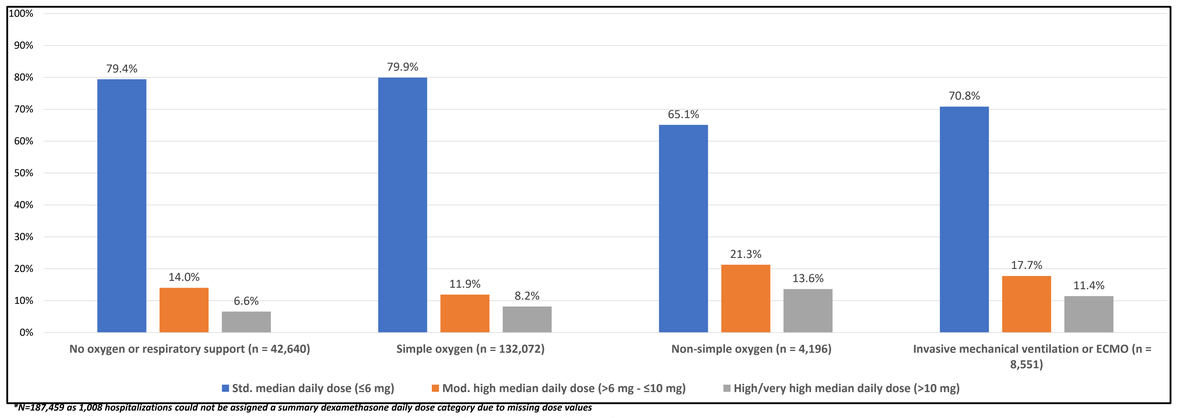
Dexamethasone Dose

Median daily dose 6mg [IQR, 6-7.6]

- Almost 80% of encounters received standard daily doses (≤6 mg)
- 12.9% moderately high daily doses (>6-≤10mg)
- 7.7% high daily doses (>10mg -≤20mg)
- 0.3% very high daily doses (>20 mg)

Dexamethasone Dose and Respiratory Support

- Among encounters requiring no oxygen or simple oxygen only:
  - Standard median daily doses (≤6mg daily) common (Figure 1)
  - Over 20% received higher doses (>6mg)
  - 6.6% and 8.2% received high or very high doses (>10mg), respectively (Figure 1)
- Higher doses slightly more common in hospitalizations requiring non-simple oxygen and IMV/ECMO



**N=187,459 as 1,008 hospitalizations could not be assigned a summary dexamethasone daily dose category due to missing dose values*

Figure 1: Dexamethasone dose by respiratory support categories

Discussion and Conclusions

A high proportion of hospitalizations with a COVID-19 diagnosis, in HCA Healthcare, received dexamethasone (62%) between April 2020 and October 2022.

The majority received standard daily dose dexamethasone (≤ 6mg/day).

However, of concern, over 20% of recipients requiring no oxygen or simple oxygen received daily doses >6mg/day.

In light of recent findings from the RECOVERY trial, suggesting potential harm from higher doses of dexamethasone in those on no oxygen or simple oxygen and the general uncertainty around safety of higher doses in those requiring more intense respiratory support, using standard daily doses of 6 mg or less should be considered.

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