

### **The Recovery Trial**

The Randomized evaluation of COVID-19 therapy, the RECOVERY trial, has reiterated what many frontline workers had been experiencing. Steroids work! This was a 176 center, randomized control pragmatic trial comparing the effect of 6 mg dexamethasone for 10 days along with usual care to usual care alone in patients with COVID-19 infections.

There were 2104 patients who received dexamethasone and 4321 got only usual care. Primary outcome measured was mortality at 28 days and secondary outcomes were need for oxygen or ventilation. Overall, the dexamethasone group had a significantly lower mortality of 21.6% compared to the non-dexamethasone group (24.6%).

What was more striking was the reduction in mortality in those requiring oxygen or mechanical ventilation. Dexamethasone reduced deaths by one-third in patients receiving invasive mechanical ventilation (29.0% vs. 40.7%;  $P < 0.001$ ) and by one-fifth in patients receiving oxygen without invasive mechanical ventilation (21.5% vs. 25.0%;  $P = 0.002$ ). Patients who were not on oxygen did not benefit from dexamethasone, and, in fact there was a trend for increased mortality in those who received dexamethasone (not statistically significant). Patients who received dexamethasone after 7 days of onset of symptoms showed more benefit than those who received it early in the course of the disease.

Benefits accrued by patients on oxygen or mechanical ventilation and after 7 days of illness suggest that dexamethasone makes a difference at a stage when immune-mediated injury predominates over the initial viral replication. The low cost and wide availability of the drug make it an attractive option in serious COVID-19 infections.

*(MedRxiv 22 June 2020)*

### **Utility of Antibody Tests in COVID-19 Infections**

Two recent meta-analyses have evaluated the utility of serological tests for SARS-CoV-2 infections. One included 40 studies and the other 54. Three types of antibody tests were used - Enzyme linked immunosorbent assays (ELISA), chemiluminescent immunoassays (CLIA) and lateral flow immunoassays (LFIA). The LFIA is typically used for point of care testing with either a dipstick format or cassette such as used in the common pregnancy test.

The sensitivities and specificities depended on the type of test done, the timing of the test after onset of illness, the

type of antibody looked for (e.g. IgA, IgM or IgG) and the population characteristics. If the test was done between day 1-7, the sensitivity for a combination of IgG/IgM was 30.1%. It was 72.2% for day 8 to 14 and 91.4% for day 15 to 21. For day 21-35, the sensitivity was 96% but there was inadequate data for tests done beyond day 35. The sensitivity of the LFIA (which is the potential point of care test method) was lowest at 66%. Tests using ELISA had sensitivities of 84.3% and CLIA fared best at 97.8%. Specificities of all tests range from 92-98%.

The performance of the test also depends on the population being tested. For example, in healthcare workers with respiratory symptoms with an expected prevalence of 50%, in 1000 people tested, 43 would be missed and 7 would be falsely positive. In national surveys where one would expect a prevalence of 5%, of every 1000 people tested 4 would be missed and 12 would be falsely positive.

Overall it appears that antibody testing may be useful clinically after 15 days of onset of illness to complement other tests.

*(Cochrane Database Syst Rev 2020; BMJ 1 July 2020)*

### **Lessons from the Spanish Seroprevalence Study**

A nationwide COVID-19 seroprevalence study of more than 60,000 people conducted in two stages in April and May, 2020 in Spain (ENE-COVID) has revealed valuable information. A history of symptoms was collated and point of care testing for antibodies using LFIA was done, with further testing using a chemiluminescent assay in those consenting.

The country-wide seroprevalence was 5% by point of care testing and 4.6% by chemiluminescent assay. Children had lower levels of seroprevalence with 1.1% in infants and 3.1% between 5-9 years. Seroprevalence in health care workers (10%) was higher than any other occupational group. About 32.7% of people with a positive serology were asymptomatic.

The key message from this well-conducted study was that though Spain incurred a huge burden of mortality in the pandemic, the overall seroprevalence was inadequate to provide herd immunity. This means further epidemic control by allowing natural infections will result in large number of deaths. Social distancing, and identifying and isolating new cases will continue to be important till an effective vaccine is available.

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