Original Article

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Efficacy of Different Drugs Used in COVID Patients in Bangladesh

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ABSTRACT

Background: COVID 19 era is continuing globally even one and half years of turning out and claiming lives and startled with newly emerged variants. Many studies regarding COVID 19 treatment were published but some options were beneficiary in early stage and later were contradictory to apply it, making clinicians to dim. So this study was carried out reveal potential efficacy of commonly prescribed regimen in COVID unit.

Materials and methods: This observational study conducted in three dedicated COVID hospital in Chattogram, Bangladesh. Total 209 cases with RT-PCR positive and symptomatic cases with RT-PCR negative subjects were enrolled in this study.

Results: Half of the patients 53% (n=111) who got antiviral remdisivir, 53.6% n=103 were improved, 46.7% n=7 was died and p value < 0.01,comparing to 28.2% (n=59) got favipiravir in whom, 27.6% n=53 were improved, 40% n=6 was died. 16.3% (n=34) patient got Tocilizumab, in whom 73.52% n=25 were improved, 23.52% n=8 was died. 8.6% (n=18) got convalescent plasma in whom 6.3% n=12 was improved, 40% n=6 was died and p value was significant. Those who were given both Tocilizumab and Remdisivir, 76.9% n=20 were improved and 19.2% n=5 were died in comparison to patient treated with Remdisivir only 97.6% n=83 were improved and 2.3% n-2 were died.

Conclusion: Even after 18 months of starting COVID, only established treatment options are oxygen and dexamethasone. As data about efficacy of antiviral and others are so changing according to COVID variants and different country. So emphasize should be about prevention and avoiding injudicious use of anti COVID medications.

Key words: CDC (Centre for Diseases Control); RT-PCR (Reverse Transcription Polymerase Chain Reaction).

Introduction

The COVID-19 pandemic has challenged the world not just in the global health but also the global psychosocial and economic health. World communities were adapted so rapidly, experimenting and inventing so many drugs, even inventing vaccines and starting and continuing vaccination globally within one year is praiseworthy.

The COVID-19 outbreak and response has been accompanied by an 'infodemic' - an over-abundance of information, some accurate and some not – that makes it hard for people to find trustworthy sources and reliable guidance when they need it.

As of May 26, 2021, the outbreak of the Coronavirus Disease (COVID-19) had been confirmed in over 210 countries and territories. The virus had infected almost 169 million people worldwide and the number of deaths had reached almost 3.5 million. The most severely affected countries include the U.S., Brazil, and India.[1]

Between 8th March 2020 and 09th May 2021, there were seven hundred seventy-three thousand, five hundred thirteen (773 513) COVID-19 cases confirmed by RT-PCR, GeneXpert and Rapid Antigen tests including eleven thousand, nine hundred thirty-four (11 934) related deaths (CFR1.54%). Bangladesh is among the top 33 countries and accounts for 0.49% of the COVID-19 cases of the world.[2]

The initial clinical symptoms of COVID-19 are similar to all types of viral pneumonia, with varying degrees of severity. The incubation period of SARS-CoV-2 is generally between 3 and 7 days [US Center of Disease Control (CDC) estimated a 2–14 day range] with the shortest being 1 day and the vast majority within 2 weeks. A proportion of infected subjects may remain

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asymptomatic. Fever, cough, and shortness of breath were the first typical symptoms of COVID-19 pneumonia initially and chills, muscle pain, sore throat, and new loss of taste and smell were later added by CDC to the list.[3]

Remdisivir is a potent RNA-dependent RNA polymerase inhibitor initially developed for the Ebola and Marburg viruses, which was found to have a good effect against respiratory syncytial virus, Junin virus, Lassa Fever virus and coronaviruses, including SARS and MERS and has recently also been shown to have good inhibitory activity against SARS-CoV-2.

Materials and methods

In this observational study, it was included 209 cases of Reverse Transcription Polymerase Chain Reaction (RT-PCR) positive COVID-19 patients as confirmed cases and those with RT PCR negative but with suspected clinical history and radiological evidences marked as probable cases were included in this study. Data were collected between June to December, 2020 from three COVID dedicated hospitals in Chattogram, Bangladesh. A structured questionnaire was used to collect the data and all patients were observed till discharge irrespective of outcome. Written informed consent was obtained from every patient or from legal guardian according to the revised Declaration of Helsinki. The protocol was approved by the Ethical and Scientific Committee of the Chattogram Maa-O-Shishu Hospital Medical College (CMOSHMC). Data were collected regarding commonly prescribed drugs such as favipiravir, Remdisivir, Dexamethasone, methyl-prednisolone and tocilizumab. Regarding using different drugs followed local guideline that was updated regularly. In hospital setting, used antiviral drugs Remdisivir matching with local guideline. But being private COVID hospital, some mild COVID patients were admitted due to panic conditions. If patient is on antiviral favipiravir, was continued the drug and changed if required. Analysis of outcome and duration of hospital stay were assessed. The statistical analysis was carried out using the Statistical Package for Social Sciences version 20.0 for Windows (IBM SPSS Armonk, NY, USA).

Results

Among 209 patients, 59(28.2%) got favipiravir of which 53 patients improved and 6 died (Table I). Among all patients, 111(53.1%) got Remdisivir and among them 103 patients improved and 7 died (Table II). Among all patients, 34(16.3%) got Tocilizumab of which 25 improved and 8 died (Table III). Among all patients 18(8.6%) got plasma of which 12 patients improved and 6 patients died (Table IV). Patients who got Remdisivir had more hospital stay then group who was not given (Table VI). Because Remdisivir were given in critical and severe patients and once started dose the Patients who got Favipiravir had less hospital stay then who was not given (Table VII).

Table I Relation of outcome with Favipiravir

			Outcome			Total	p value
			Improved	Died	Improved with disabilities		
Favipiravir	Yes	Count	53	6	0	59	
		% within Favipiravir	89.8%	10.2%	0.0%	100.0%	0.397
	No	Count	139	9	2	150	
		% within Favipiravir	92.7%	6.0%	1.3%	100.0%	
Total		Count	192	15	2	209	
		% within Favipiravir	91.9%	7.2%	1.0%	100.0%	

Table II Relation of outcome with Remdisivir

			Outcome			Total	p value
			Improved	Died	Improved with disabilities		
Remdisivir	Yes	Count	103	7	1	111	
		% within Remdisivir	92.8%	6.3%	0.9%	100.0%	0.869
	No	Count	89	8	1	98	
		% within Remdisivir	90.8%	8.2%	1.0%	100.0%	
Total		Count	192	15	2	209	
		% within Remdisivir	91.9%	7.2%	1.0%	100.0%	

Table III Relation of outcome with Tocilizumab

			Outcome			Total	p value
			Improved	Died	Improved with disabilities		
Toscilizumab	Yes	Count	25	8	1	34	
		% within Toscilizumab	73.5%	23.5%	2.9%	100.0%	
	No	Count	167	7	1	175	
		% within Toscilizumab	95.4%	4.0%	0.6%	100.0%	0.00
Total		Count	192	15	2	209	
		% within Toscilizumab	91.9%	7.2%	1.0%	100.0%	

Table IV Relation of outcome with Plasma therapy

			Outcome			Total	p value
			Improved	Died	Improved with disabilities		
Plasma	Yes	Count	12	6	0	18	
		% within Plasma	66.7%	33.3%	0.0%	100.0%	0.00
	No	Count	180	9	2	191	
		% within Plasma	94.2%	4.7%	1.0%	100.0%	
Total		Count	192	15	2	209	
		% within Plasma	91.9%	7.2%	1.0%	100.0%	

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Table V Relation of outcome with Toscilizumab and different modalities of drugs

				Outcome		
				Improved	Died	Improved with disabilities
				Count	Count	Count
Toscilizumab	Yes	Favipiravir	Yes	4	3	0
			No	21	5	1
		Remdisivir	Yes	20	5	1
			No	5	3	0
		Methylprednisolone	Yes	14	5	1
			No	11	3	0
		Dexamethasone	Yes	10	4	0
			No	15	4	1
		Heparin	Yes	24	7	1
			No	1	1	0
	No	Favipiravir	Yes	49	3	0
			No	118	4	1
		Remdisivir	Yes	83	2	0
			No	84	5	1
		Methylprednisolone	Yes	62	4	1
			No	105	3	0
		Dexamethasone	Yes	76	3	0
			No	91	4	1
		Heparin	Yes	161	6	1
			No	6	1	0

Table VI Duration of hospital stay in Remdisivir group

Remdisivir	Mean	N	Std. Deviation	Median	p value
Yes	14.6937	111	3.10950	14.0000	0.00
No	7.5306	98	2.64849	7.0000	
Total	11.3349	209	4.60693	12.0000	

Table VII Duration of hospital stay in Favipiravir group

favipiravir	Mean	N	Std. Deviation	Median	p value
Yes	8.3559	59	3.52216	8.0000	0.00
No	12.5067	150	4.46124	14.0000	
Total	11.3349	209	4.60693	12.0000	

Discussion

As COVID had shown variable symptoms so prognosis and drug efficacy varies with newly emerged different variants and different protocol adopted by individual country. So results and efficacy of different drugs is found divergent in various countries.

Regarding remdisivir, a study conducted in China did not show any benefit in treating patients with COVID-19. However, the National Institutes of Health reported that in a U.S. clinical trial (ACTT-1) remdesivir helped patients with COVID-19 recover faster when compared with patients who did not receive the drug.[4]

Wang et al. enrolled 237 patients (158 assigned to remdesivir and 79 to placebo) in China early in the pandemic and showed a shorter time to improvement (A two-point improvement) with remdesivir: 21.0 days (95% CI, 13.0 to 28.0) in the remdesivir group and 23.0 days (95% CI, 15.0 to 28.0) in the placebo group (Hazard ratio for clinical improvement, 1.23, 95% CI, 0.87 to 1.75).[5] In this study, mean duration of hospital stay in remdisivir group was 14.69 days.

In one study conducted on 1062 patients, 541 assigned to remdesivir and 521 to placebo. Those who received remdesivir had a median recovery time of 10 days (95% Confidence Interval [CI], 9 to 11), as compared with 15 days (95% CI, 13 to 18) among those who received placebo The Kaplan–Meier estimates of mortality were 6.7% with remdesivir and 11.9% with placebo by day 15 and 11.4% with remdesivir and 15.2% with placebo by day 29 (Hazard ratio, 0.73, 95% CI, 0.52 to 1.03).[4]

In this study those who got only Remdisivir in moderate cases mortality rate was 2.35% compare to those who didn't get mortality rate was more 5.55%. But in severe cases where both remdisivir and tocilizumab were used, mortality rate was 19.2% and situation where tocilizumab were used without remdisivir, mortality was 37.5%.

In one meta analysis, total of 1,895 patients from 9 studies were included in this qualitative synthesis. In patients treated with Remdesivir, the mean recovery time was 15.84 days (95% CI 11.68–20, SE 2.12; I^2 = 97.24) and the pooled mortality rate was 11.3% (95% CI 7.9–16%, I^2 = 74.85).[6]

Results from the RECOVERY clinical trial show that the steroid drug dexamethasone reduces deaths in hospitalized patients who have COVID-19. A total of 2104 patients were assigned to receive dexamethasone and 4321 to receive usual care. Overall, 82 patients (22.9%) in the dexamethasone group and 1110 patients (25.7%) in the usual care group died within 28 days after randomization.[7]

In this study, mortality rate is 3.9% n=3 in patients with dexamethasone receiver n=76 in comparison to 40% mortality rate those who was given tocilizumab and dexamethasone combinely n=10, probably related to attending patient in critical conditions.

The latest analysis from Remac CAP trial found that both Actemra (Tocilizumab) and Kevzara reduced mortality by 8.6%, and also improved recovery times among patients who are critically ill with COVID-19. This reflects a reduction in the relative risk of death by 24% when given to patients within 24 hours of entering intensive care.[8] In this study, 16.3% (n=34) got tocilizumab, 73.52% n=25 were improved, 23.52% n=8 was died and p value was highly significant.

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On average, patients treated with these drugs were able to leave the ICU around a week earlier than those not receiving these treatments.

This includes Roche's own phase 3 COVACTA study, in which Actemra did not meet its primary endpoint of improved clinical status in hospitalised adults patients with severe COVID-19-associated pneumonia.

The US FDA recommends the use of donor convalescent plasma with the 1:160 neutralizing titer and studies have shown that early intervention with higher neutralizing antibody titers show better clinical outcomes in COVID-19 patients.[9]

In this study, 8.6% (n=18) got convalescent plasma, 6.3% n=12 was improved, 40% n=6 was died and p value was significant. But in Recovery, Trial there was no significant difference in 28-day mortality between the two groups: 1399 (24%) of 5795 patients in the convalescent plasma group and 1408 (24%) of 5763 patients in the usual care group died within 28 days (Rate ratio 1·00, 95% CI 0·93–1·07, p=0·95).[10]

Conclusion

As there is no specific drugs regarding COVID management other than proved supportive treatment such as oxygen and dexamethasone. So rational uses of antiviral and monoclonal antibody in situations if indicated, should be warranted, as drug side effects , huge cost and short supply of newly invented drugs creates turmoil in covid management. Different protocol used in different countries that varies with severity and prognosis according to different variants.

Recommendation

As most of the COVID information is inodemic, proper guideline regarding COVID treatment should be regularly updated on the basis of multicentric RCT and local variants.

Disclosure

All the authors declared no competing interest.

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