



Opinion of Brazilian physicians on the treatment of COVID-19

Opinião de médicos brasileiros sobre o tratamento da COVID-19

Opinión de médicos brasileños sobre el tratamiento de la COVID-19

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ABSTRACT

Objective: To investigate the opinion of Brazilian physicians on the early treatment of COVID-19 with hydroxychloroquine/chloroquine and azithromycin in patients with clinical suspicion and on the treatment with corticosteroid therapy in the inflammatory stage of the disease. **Methods:** This is an opinion survey conducted with a convenient sample of physicians working in Brazil. Data were collected from May 26 to June 8, 2020 (13 days) through Google forms made publicly available on social media and chat applications. Data underwent descriptive analysis, independence test, Student t-test, and a logistic regression model using multivariate analysis. **Results:** The survey included 1020 physicians with a mean of 21.9 years since graduation. 72.4% of the participants were in favor of early treatment with hydroxychloroquine/chloroquine and azithromycin and 89.7% of the physicians were in favor of using corticosteroid therapy to treat the inflammatory stage of COVID-19. We also observed that older participants, those who completed medical residency, and those working in the Northeast and North regions were more likely to be in favor of the treatments. On the other hand, professionals specialized in intensive care medicine, infectious diseases and pneumology and working in intensive care units were more opposed. **Conclusion:** Most physicians in this opinion survey were in favor of the early treatment presented and the use of corticosteroid therapy in the treatment of COVID-19. But specialists in intensive care medicine, infectious diseases and pulmonology, and professionals working in Intensive Care Units were more opposed to them.

Descriptors: Coronavirus Infections; Drug Therapy; Hydroxychloroquine; Adrenal Cortex Hormones.

RESUMO

Objetivo: Investigar a opinião de médicos brasileiros sobre o tratamento precoce da COVID-19 com hidroxicloroquina/cloroquina e azitromicina em pacientes com suspeita clínica e sobre o tratamento com corticoterapia na fase inflamatória da doença. **Métodos:** Trata-se de uma pesquisa de opinião, com amostragem por conveniência, com médicos atuantes no Brasil. A coleta dos dados ocorreu no período de 26 de maio a 8 de junho de 2020 (13 dias), por meio de um formulário Google, disponibilizado publicamente nas redes sociais e aplicativos de comunicação. Realizou-se uma análise descritiva dos dados, teste de independência, teste T Student e modelo de regressão logística com análise multivariada. **Resultados:** A pesquisa contou com 1.020 médicos participantes, com média de 21,9 anos de formado. 72,4% dos participantes apresentaram-se a favor do tratamento precoce com hidroxicloroquina/cloroquina e azitromicina e 89,7% dos médicos apresentaram-se favoráveis ao uso da corticoterapia para o tratamento da fase inflamatória da COVID-19. Constatou-se também que participantes com maior idade, com residência médica, atuantes nas regiões Nordeste e Norte possuíam mais chances de serem favoráveis aos tratamentos. Por outro lado, profissionais especialistas em medicina intensiva, infectologia e pneumologia, além de atuantes nas unidades de terapia intensiva, mostraram-se mais desfavoráveis. **Conclusão:** A maioria dos médicos investigados nesta pesquisa de opinião mostrou-se a favor do tratamento precoce apresentado e do uso da corticoterapia no tratamento da COVID-19. Já os especialistas em medicina intensiva, infectologia e pneumologia e profissionais atuantes nas Unidades de Terapia Intensiva mostraram-se mais desfavoráveis.

Descritores: Infecções por Coronavirus; Tratamento Farmacológico; Hidroxicloroquina; Corticosteroides.



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RESUMEN

Objetivo: Investigar la opinión de médicos brasileños sobre el tratamiento precoz de la COVID-19 con la hidroxiclороquina/cloroquina y la azitromicina en pacientes con sospecha clínica y bajo el tratamiento de corticoterapia en la fase inflamatoria de la enfermedad. **Métodos:** Se trata de una investigación de opinión con la muestra de conveniencia realizada con médicos de Brasil. La recogida de datos se dio en el periodo entre 26 de mayo y 8 de junio de 2020 (13 días) a través de un formulario Google que ha estado disponible públicamente en las redes sociales y los aplicativos de comunicación. Se realizó un análisis descriptivo de los datos, la prueba de independencia, la prueba T Student y el modelo de regresión logística con el análisis multivariado. **Resultados:** La investigación tuvo 1.020 médicos participantes, con la media de 21,9 años de término del grado. El 72,4% de los participantes se presentaron a favor del tratamiento precoz con la hidroxiclороquina/cloroquina y la azitromicina y el 89,7% de los médicos se presentaron favorables a la utilización de la corticoterapia para el tratamiento de la fase inflamatoria de la COVID-19. Se constató también que los participantes de más edad, con el curso de residencia medica y que eran de las regiones Noreste y Norte del país eran más favorables a los tratamientos. Los profesionales especialistas de la medicina intensiva, la infectología y la neumología, además de actuar en las unidades de cuidados intensivos parecieron más desfavorables. **Conclusión:** La mayoría de los médicos investigados de esa investigación de opinión se mostró favorable al tratamiento precoz presentado y a la utilización de la corticoterapia para el tratamiento de la COVID-19. Los especialistas de la medicina intensiva, la infectología y la neumología y los profesionales de las Unidades de Cuidados Intensivos se presentaron más desfavorables a los tratamientos.

Descriptor: Infecciones por Coronavirus; Quimioterapia; Hidroxiclороquina; Corticosteroides.

INTRODUCTION

The COVID-19 pandemic has emerged as a serious crisis in the health sector. Worldwide, until the October 24, 2020, figures showed 42,055,863 confirmed cases and 1,141,567 deaths⁽¹⁾. In Brazil until October 23, 2020, there were 5,353,656 confirmed cases, 156,471 deaths, with a lethality rate of 2.9%, 4,797,872 recovered cases and 399,313 cases being followed up⁽²⁾.

COVID-19 evolves in well-defined clinical stages: stage I (infectious); stage II (lung inflammation); and stage III (systemic inflammation). Stage I is the stage of early and mild infection; it is the initial stage that occurs at the time of inoculation and establishment of the disease. In stage II, the disease is considered moderate and lung impairment subdivides this stage into IIA - without hypoxia and IIB - with hypoxia (PaO₂/FiO₂ <300 mmHg). In stage III or severe stage, there is a systemic hyperinflammation. A minority of patients will go through a direct transition to stage III of the disease, which manifests as a systemic extrapulmonary hyperinflammation syndrome⁽³⁾.

Several therapeutic options with chloroquine, hydroxychloroquine, arbidol, remdesivir, favipiravir, tocilizumab, immunoglobulin, corticosteroids, ozone therapy, oseltamivir, lopinavir/ritonavir, IFN-alpha, teicoplanin, ribavirin, among others, are being submitted to clinical studies to test their efficacy and safety in the treatment of COVID-19 in several countries around the world, both in the early and advanced stages, with some promising results achieved so far. The main results, therefore, were presented regarding the early treatment with hydroxychloroquine and the use of corticosteroid therapy, but the treatment of COVID-19 still faces several uncertainties⁽⁴⁻⁶⁾.

According to the Federal Council of Medicine (*Conselho Federal de Medicina – CFM*)⁽⁷⁾, there are dozens of scientific studies in the medical literature showing benefits from early treatment with the drugs mentioned above. Others point out that they have no beneficial effect against COVID-19. In other words, science has not yet definitively concluded whether or not there is any benefit from the use of these drugs. CFM addressed early treatment for COVID-19 in Opinion No. 4/2020. In the document, CFM decided that it is up to the physician responsible for the case to carry out the treatment they deem appropriate, provided that the patient agrees with it after being informed there is no proven benefit from the pharmacological treatment of this disease and providing their informed consent. In this context, in the absence of an efficient therapy and medical autonomy to carry out the treatment deemed appropriate, we wanted to investigate the opinion of Brazilian physicians on the early treatment of COVID-19 with hydroxychloroquine/chloroquine and azithromycin in patients with clinical suspicion and about treatment with corticosteroid therapy in the inflammatory stage of the disease.

METHODS

This is an opinion survey using convenience sampling and carried out in 2020 with physicians working in Brazil. Data were collected online through Google Forms from May 26 to June 8, 2020 (13 days) from 1,023 participants who completed the form.

The link to the form was made available publicly through the researchers' social media (Facebook). There was no invitation to participate in the study for any participant, but all of them declared their opinion spontaneously and fully anonymously. Forms with responses that were inappropriate for the research theme were excluded from the study, thus resulting in a final sample of 1,020 physicians, which represents approximately 0.21% of the 473,875 physicians in Brazil (data obtained up to February 2020)⁽⁸⁾.

The survey form addressed the following points: 1) age, time since graduation, 2) completion of medical residency, 3) if so, which medical residency, 4) region of work in Brazil, 5) area of medical practice during the pandemic, 6) routine treatment of patients with flu-like illness and 7) treatment of patients with COVID-19. Questions allowed text-entry responses (age, time since graduation and state of work in Brazil), multiple responses (which residency was undertaken and area of medical practice during the pandemic), and all other questions were presented as dichotomous questions.

Initially, a descriptive analysis of the data was conducted for qualitative variables calculating the distribution of absolute (n) and relative (%) frequencies in addition to the main summary measures, such as position and dispersion measures for quantitative variables. In order to assess a potential association between two qualitative variables, independence tests (chi-squared test or Fisher's exact test) were applied to the data. The comparison between the mean age in relation to a group variable was assessed using the Student's t-test.

In order to investigate the effects of physicians' opinions on treatment conduct (in favor of early treatment and in favor of corticosteroid therapy – study statements), a logistic regression model was built for the data, in which the measure of association of interest was given by the odds ratio (OR). For the construction of the multiple model, significant independent variables were selected from the simple logistic regression model. The final model was obtained using the stepwise variable selection technique (backward) using the freely available software R version 3.5 for all analyses and a significance level of 5%.

RESULTS

The survey included 1,020 physicians, with a mean age of 46.8 years (standard deviation of 11.8) and 21.9 years since graduation (standard deviation of 12.5). The majority had completed medical residency 819 (80.3%), including: clinical residency 282 (27.6%), surgical residency 176 (17.3%), gynecology and obstetrics 147 (14.4%), pediatrics 112 (11.0%), intensive care medicine, infectology, pulmonology 75 (7.4%) and others. The percentage of participants by Brazilian region of work was: Northeast 456 (44.7%), Southeast 262 (26.7%), South 128 (12.5%), Midwest 85 (8.3%) and North 71 (7.0%). The majority saw 644 (63.1%) patients with flu-like illness in their routine in addition to having already treated or were treating patients with suspected/notified or confirmed COVID-19 (699 [68.5%]). As for the area of practice of professionals during the COVID-19 pandemic: outpatient clinics/offices 601 (58.9%), emergency/urgency room and emergency 337(33.0%), telemedicine 207 (20.3%), hospital wards 191 (18.7%), surgeries 166 (16.3%), intensive/semi-intensive care unit 138 (13.5%), none 98 (9.6%).

When asking physicians' opinions regarding early treatment with hydroxychloroquine/chloroquine and azithromycin, 738 (72.4%) responded being in favor. As for the use of corticosteroid therapy for the treatment of the inflammatory stage of COVID-19, 915 (89.7%) reported being in favor of using corticosteroid therapy for the treatment of the inflammatory stage of COVID-19.

The results of the analysis of associations between independent variables and early treatment are presented below (Table I), with only the variables with some association depicted. Thus, there was association between the variables: region of work; completing or not completing a medical residency; residency in surgery, intensive care, infectious diseases and pulmonology, gynecology and obstetrics; area of practice in the intensive care unit (ICU)/ semi-intensive care unit (Semi ICU) and no area of practice; and age. For each independent variable, the measure of association (OR) was presented through the simple logistic regression model. For example, professionals with experience in medical residency and/or without any area of practice during the pandemic were 2-3 times more likely to be more favorable to early treatment.

Table II shows the results of the analysis of associations between the independent variables and use of corticotherapy (only the variables that showed some association with the statement variable are presented). An association was observed between the variables: region of work; completing medical residency; medical residency in intensive care – infectology and pulmonology, gynecology and obstetrics –; practicing in outpatient clinics/offices, intensive/semi-intensive care unit, emergency/urgency room and emergency, no area of practice; and age. For each independent variable, the measure of association (OR) was estimated using the simple logistic regression model. Most participants, specialists in intensive care medicine, infectology and pulmonology, working in an intensive/semi-intensive care unit, were opposed to corticosteroid therapy.

Table I - Brazilian physicians' opinions on early treatment of patients with clinical suspicion of COVID-19, Brazil, 2020.

Variable	Cat	Statements		p value*	OR	95%CI	p value
		In favor of early treatment					
		No	Yes				
Region of work in Brazil n (%)							
Midwest	Midwest	39 (14.6)	45 (6.1)		Ref	-	-
Northeast	Northeast	115 (43.1)	341 (46.5)		2.6	1.6-4.1	<0.001
North	North	16 (6.0)	55 (7.5)	0.001	3.0	1.5-6.0	0.002
Southeast	Southeast	66 (24.7)	196 (26.7)		2.6	1.5-4.3	<0.001
South	South	31 (11.6)	97 (13.2)		2.7	1.5-4.9	0.001
Completed medical residency n (%)							
	No	73 (27.4)	112 (15.2)		Ref	-	-
	Yes	193 (72.6)	625 (84.8)	<0.001	2.1	1.5-2.9	<0.001
Medical Residency n (%)							
Surgical residency	No	234 (87.6)	595 (80.6)		Ref	-	-
	Yes	33 (12.4)	143 (19.4)	0.013	1.7	1.1-2.6	0.010
Intensive Medicine, Infectology, Pneumology	No	230 (86.1)	700 (94.9)		Ref	-	-
	Yes	37 (13.9)	38 (5.1)	<0.001	0.3	0.2-0.5	<0.001
Gynecology and Obstetrics	No	242 (90.6)	616 (83.5)		Ref	-	-
	Yes	25 (9.4)	122 (16.5)	0.006	1.9	1.2-3.0	0.005
Area of medical practice n (%)							
Intensive/Semi-intensive Care Units	No	205 (76.8)	662 (89.7)		Ref	-	-
	Yes	62 (23.2)	76 (10.3)	<0.001	0.4	0.3-0.5	<0.001
None	No	256 (95.9)	651 (88.2)		Ref	-	-
	Yes	11 (4.1)	87 (11.8)	<0.001	3.1	1.6-5.9	0.001
Age - mean		39.5	49.5	<0.001	1.1	1.1-1.1	<0.001

Cat: Categories; Ref: Reference; *: Fisher's exact test or chi-square test

Table II - Brazilian physicians' opinions on the use of corticoid therapy in the inflammatory stage of COVID-19, Brazil, 2020.

Variable	Cat	Statements		p value*	OR	95%CI	p value
		In favor of corticoid therapy					
		No	Yes				
Region of work in Brazil n (%)							
Midwest		20 (23.3)	64 (7.0)		Ref	-	-
Northeast		33 (38.4)	423 (46.4)		4.0	2.2-7.4	<0.001
North		2 (2.3)	69 (7.6)	<0.001	10.8	2.4-48.0	0.002
Southeast		19 (22.1)	241 (26.5)		4.0	2.0-7.9	<0.001
South		12 (14.0)	114 (12.5)		3.0	1.4-6.5	0.006
Complete Medical Residency n (%)							
	No	26 (30.2)	159 (17.4)		Ref	-	-
	Yes	60 (69.8)	754 (82.6)	0.005	2.0	1.2-3.3	0.004
Medical Residency n (%)							
Intensive Medicine, Infectology, Pneumology	No	67 (77.9)	859 (93.9)		Ref	-	-
	Yes	19 (22.1)	56 (6.1)	<0.001	0.2	0.1-0.4	<0.001
Gynecology and Obstetrics	No	83 (96.5)	772 (84.4)		Ref	-	-
	Yes	3 (3.5)	143 (15.6)	0.004	5.1	1.6-16.4	0.006
Area of medical practice n (%)							
Outpatient clinics/Offices	No	44 (51.2)	359 (39.2)		Ref	-	-
	Yes	42 (48.8)	556 (60.8)	0.041	1.6	1.0-2.5	0.032
Intensive/Semi-intensive Care Units	No	66 (76.7)	798 (87.2)		Ref	-	-
	Yes	20 (23.3)	117 (12.8)	0.011	0.5	0.3-0.8	0.008
Emergency room/Urgency and emergency	No	40 (46.5)	626 (68.4)		Ref	-	-
	Yes	46 (53.5)	289 (31.6)	<0.001	0.4	0.2-0.6	<0.001
None	No	85 (98.8)	819 (89.5)		Ref	-	-
	Yes	1 (1.2)	96 (10.5)	0.009	10.0	1.4-72.4	0.023
Age - mean		39.4	47.4	<0.001	1.065	1.042-1.089	<0.001

Cat: Categories; Ref: Reference; *: Fisher's exact test or chi-square test

After that, a multiple logistic regression model was adjusted to the data in order to assess the independent factors that imply being in favor of early treatment and the use of corticosteroid therapy. The results are shown in Table III.

Thus, older professionals were more likely to be in favor of both treatments. When checking the regions of Brazil where they work, participants working in the North and Northeast of the country were two to eight times more likely to be in favor of early treatment and corticotherapy. Physicians who completed medical residencies were also more likely to be in favor of the therapies.

On the other hand, 65.8% of specialists in intensive care medicine, infectology and pulmonology were not in favor of early treatment and 81.3% were opposed to corticotherapy. In addition, 44.0% of professionals working in Intensive Care Units reported being opposed to the early treatment of COVID-19.

Table III - Multiple logistic regression in relation to the early treatment with hydroxychloroquine/chloroquine and azithromycin and the use of corticosteroid therapy in the treatment of COVID-19, Brazil, 2020.

Variable	In favor of the early treatment			In favor of the corticosteroid therapy		
	OR	95%CI	p value	OR	95%CI	p value
Age	1.084	1.067-1.102	<0.001	1.064	1.038-1.091	<0.001
Region of work in Brazil:						
Midwest	Ref	-	-	Ref	-	-
Northeast	2.329	1.347-4.029	0.002	3.598	1.838-7.043	<0.001
North	2.374	1.096-5.143	0.028	8.762	1.907-40.251	0.005
Southeast	1.988	1.111-3.559	0.021	3.235	1.547-6.764	0.002
South	1.972	1.000-3.889	0.050	2.208	0.954-5.109	0.064
Completed medical residency	1.467	0.983-2.191	0.061	1.712	0.955-3.067	0.071
Medical Residency:						
Intensive Medicine, Infectology, Pneumology	0.342	0.197-0.592	<0.001	0.187	0.097-0.359	<0.001
Area of medical practice:						
Intensive/Semi-Intensive Care Units	0.560	0.366-0.856	0.007	-	-	-

Ref: Reference

DISCUSSION

In 2004, an *in vitro* study reported chloroquine as an effective inhibitor of the replication of the Severe Acute Respiratory Syndrome induced by the coronavirus (SARS-CoV)⁽⁹⁾. One year later, another study⁽¹⁰⁾ reported that chloroquine was also effective in preventing the spread of SARS-CoV in primate cell cultures. With the emergence of the new coronavirus (SARS-CoV-2), researchers⁽¹¹⁾ suggest in their studies the use of chloroquine, and preferably hydroxychloroquine, as the initial therapy for patients infected with SARS-CoV-2 *in vitro*⁽¹²⁾ due to better responses of hydroxychloroquine in inhibiting SARS-CoV-2 compared to chloroquine. Other researchers⁽¹³⁾ reiterated that hydroxychloroquine can efficiently inhibit SARS-CoV-2 infection *in vitro* thanks to its direct antiviral activity and its safe anti-inflammatory potential. These studies initially stood out to present the possibility of using medication for the treatment of COVID-19, and most physicians participating in this opinion survey were in favor of the use of these medications.

One of the main clinical studies to demonstrate efficacy with early use of hydroxychloroquine for COVID-19 was a retrospective study⁽¹⁴⁾ with 3,737 patients, including 3,119 (83.5%) treated with hydroxychloroquine and azithromycin for at least three days and 618 (16.5%) patients treated with other methods. Participants in that study had a mean age of 45 years, with 45% being males, and a mortality rate of 0.9%. 2,065 low-dose computed tomography (CT) scans were performed, highlighting lung lesions in 592 of 991 (59.7%) patients with minimal clinical symptoms. There was a discrepancy between spontaneous dyspnea, hypoxemia and lung lesions. Clinical factors (age, comorbidities), biological factors (lymphopenia; eosinopenia; decreased blood zinc; increased D-dimers, lactate dehydrogenase, creatinine phosphokinase and C-reactive protein) and moderate and severe lesions detected on low-dose CT scans were associated with poor clinical outcome. Treatment with hydroxychloroquine and azithromycin was associated with a decreased risk of transfer to the ICU or death (HR 0.18; 0.11-0.27), decreased risk of hospitalization for 10 days or more (OR 95%CI; 0.38; 0.27-0.54) and shorter duration of viral clearance (time to C-reactive protein, PCR, negative:

HR 1.29; 1.17-1.42). Prolonged QT interval (>60 ms) was observed in 25 patients (0.67%), leading to treatment interruption in 12 cases, including 3 cases with a QTc interval > 500 ms. No cases of Torsades de pointes or sudden death have been reported. These results suggest that early diagnosis, early isolation of patients and early treatment of patients with COVID-19, with at least three days of hydroxychloroquine and azithromycin, lead to a significantly better clinical outcome and a faster reduction in viral load. This French study was probably one of the main studies to assure physicians that they were in favor of early treatment with hydroxychloroquine and azithromycin, in agreement with the findings of the current opinion survey.

Studies⁽¹⁵⁻²⁰⁾ that demonstrated the ineffectiveness of hydroxychloroquine or chloroquine did not assess only its efficacy in the early stage of the disease, that is, they present important flaws in the clinical selection of participants, when the medication was used mainly in patients in stages II and III of COVID-19 and not as an early treatment of the disease.

A multicenter, randomized, open-label study⁽²¹⁾, involving hospitalized patients with suspected or confirmed COVID-19 who did not receive supplemental oxygen or received a maximum of 4 liters per minute of supplemental oxygen, randomly assigned patients in a ratio of 1:1:1 to receive standard treatment (symptomatic): 1) standard treatment plus hydroxychloroquine at a dose of 400mg twice daily or 2) standard treatment plus hydroxychloroquine at a dose of 400mg twice daily plus azithromycin at a dose of 500mg once daily, for 7 days. The primary outcome was clinical status within 15 days. A total of 667 patients underwent randomization, with confirmation for COVID-19 in 504 patients. Among patients hospitalized with mild to moderate COVID-19, the use of hydroxychloroquine, alone or combined with azithromycin, did not improve clinical status within 15 days compared with standard care. The fact that patients are hospitalized raises doubts about the classification of the mild condition of the disease, that is, about the real evaluation of hydroxychloroquine in the early treatment of COVID-19.

An open randomized clinical trial⁽²²⁾ in 57 centers in Brazil evaluated whether the addition of azithromycin to standard treatment, which included hydroxychloroquine, would improve the clinical outcomes of patients admitted to the hospital with severe COVID-19. Addition of azithromycin to standard treatment did not improve clinical outcomes, thus not supporting the routine use of azithromycin in combination with hydroxychloroquine in patients with severe COVID-19. Therefore, its use in the early stage of the disease has not been evaluated.

On the other hand, a meta-analysis and systematic review⁽²³⁾ that evaluated the therapeutic options based on publications related to SARS and MERS reported that patients with Acute Respiratory Distress Syndrome (ARDS) (4,282 patients) exhibited a decrease in mortality with the use of corticoids and ribavirin (RR 0.43; 95% CI 0.27-0.68). Thus, there is a possible benefit from the use of corticosteroid therapy for the treatment of COVID-19.

Another study⁽²⁴⁾ evaluated the role of corticosteroids in patients with COVID-19 in the moderate and severe form using 0.5-1mg/kg of methylprednisolone twice daily for 3 days if started early. All patients had at least 14 days of follow-up. The study assessed 81 patients who used corticosteroids without a defined protocol of use and with a median of initiation of therapy of 5 days and 132 who received methylprednisolone (corticosteroid) early with a median of 2 days. The group that received early corticosteroids, and for a short period, had a shorter hospital stay (5 versus 8 days), a lower mortality rate (13.3% versus 26.3%), a lower need for mechanical ventilation (21.7% versus 36.6%), in addition to a lower admission to the ICU (27.3% versus 44.3%). In this context, there is a benefit from the use of corticosteroid therapy, which probably has supported the physicians who responded to this survey in relation to the use of this therapy in the inflammatory stage of COVID-19.

However, the first study to actually show the benefits of using corticosteroids for treating COVID-19 was the Randomized Evaluation of COVID-19 Therapy (RECOVERY)⁽²⁵⁾ study, which published its preliminary results from 2,104 patients on June 16, 2020. Their results included 6,425 patients randomized to 6mg/d of dexamethasone or usual treatment. Overall, dexamethasone resulted in an absolute reduction in mortality of 2.8% (22.9% vs 25.7% for usual treatment; age-adjusted rate ratio, 0.83 [95% CI; 0.75 -0.93]). The benefit was greatest for patients receiving invasive mechanical ventilation at randomization, with a mortality of 29.3% for dexamethasone vs 41.4% for usual treatment (rate ratio, 0.64 [95% CI; 0.51-0.81])⁽²⁶⁾. This study was presented as a milestone in the advancement of the treatment of COVID-19, being the first to publish a treatment proven to be efficient in the treatment of COVID-19, which would certainly contribute to a greater adherence of physicians in agreeing with the use of this class of drug in the treatment of the disease. However, it should be noted that the RECOVERY study had not yet been published when the current opinion survey was carried out.

In a multicenter, randomized, open clinical trial carried out in 41 intensive care units (ICU) in Brazil⁽²⁷⁾, patients with COVID-19 and moderate to severe acute respiratory distress syndrome (ARDS) were investigated using the Berlin definition. Participants received 20mg of dexamethasone intravenously daily for 5 days; 10mg of dexamethasone per

day, for 5 days, or until discharge from the ICU, plus standard treatment for symptomatic patients (n=151) or standard treatment alone (n=148). Among patients with COVID-19 and moderate or severe ARDS, the use of intravenous dexamethasone plus standard treatment compared to standard treatment alone resulted in a statistically significant increase in the number of days off ventilation (living days and days off mechanical ventilation) for 28 days.

In a meta-analysis⁽²⁸⁾ that pooled data from seven randomized clinical trials that evaluated the efficacy of corticosteroids in 1,703 critically ill patients with COVID-19, the administration of systemic corticosteroids, compared to usual treatment (symptomatic) or placebo, was associated with a lower 28-day mortality. In that regard, an increasing number of new studies corroborate the idea that corticosteroid therapy has been effective in the treatment and reinforces the medical opinion found in the current opinion survey.

According to the Consensus of the Brazilian Association of Intensive Medicine, the Brazilian Society of Infectology and the Brazilian Society of Pulmonology and Phthisiology⁽²⁹⁾, published on May 18, 2020, there were no pharmacological interventions with proven effectiveness and safety to justify their routine use in the treatment of COVID-19. However, after the publication of the RECOVERY⁽²⁰⁾ study on June 16, 2020, the Brazilian Society of Infectious Diseases recommended that all patients with COVID-19 on mechanical ventilation and those requiring oxygen outside the ICU should receive oral dexamethasone or intravenous injection at a dose of 6mg once a day for 10 days⁽³⁰⁾. Thus, such publications are in line with the findings of this research as it is observed that medical professionals specializing in infectious diseases, intensive care medicine and pulmonologists are also in favor of the use of corticoids.

Limitations of the current study include its small sample of physicians in Brazil and the absence of related studies regarding the opinion of physicians to better substantiate the hypothesis. In addition, there is a risk that the survey was sought more often by specific groups of physicians who supported early treatment and/or the use of corticosteroid therapy for COVID-19. Therefore, at no time were participants encouraged to disclose the form to other physicians, with it being freely searchable on social media in order to avoid this bias in this research.

It is understood, however, that larger studies with better design need to be developed to demonstrate the real efficacy of early treatment with hydroxychloroquine, azithromycin and the use of corticosteroid therapy in the inflammatory stage of the disease and to assess the opinion of Brazilian physicians on the therapies for COVID-19.

CONCLUSION

Most physicians who responded to this opinion survey were in favor of early treatment of COVID-19 with hydroxychloroquine/chloroquine and azithromycin and the use of corticosteroid therapy for the treatment of the inflammatory stage of COVID-19.

On the other hand, part of the specialists in intensive care medicine, infectology and pulmonology and professionals working in intensive care units who responded to the opinion survey were more opposed to the therapies assessed.

CONFLICTS OF INTEREST

The authors state that there are no conflicts of interest.

CONTRIBUTIONS

Danilo Rafael da Silva Fontinele and **Sabas Carlos Vieira** contributed to the study conception and design; the acquisition, analysis and interpretation of data and the writing and/or revision of the manuscript. **Tatyanne da Silva Rodrigues** and **Vinicius Fernando Calsavara** contributed to the acquisition, analysis and interpretation of data and the writing and/or revision of the manuscript. All the authors approved the final version of the manuscript for publication and are responsible for its content.

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