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The Effect of Stem Cell Therapy Prior to SARS COV-2 Infection: A Retrospective Cohort Study

R. Rabii[1, 2], K. Balar[3], M. Guennouni[1, 2], K. Jemal[1, 2], M. Rachid[1, 2], K. Belhaj[1, 2]

[1]Mohammed VI University of Health Sciences, Faculty of Medicine, Casablanca, Morocco
[2]Cheikh Khalifa International University Hospital, Casablanca, Morocco
[3]Hassan II University, Faculty of Legal, Economic and Social Sciences, Casablanca, Morocco

Abstract: ***The rapid development of regenerative medicine and stem cell therapy (SCT) is emerging as a promising therapeutic option. Indeed, it gives new hope for all diseases considered incurable until now: from diabetes to nephropathies, including degenerative diseases such as Alzheimer's. The year 2020 was marked by the emergence of the SARS-CoV-2 pandemic that seems to have escaped the attention of the most eminent scientist: SARS. The aim of our study is to investigate if SCT could prevent or decrease human infection with SARS-CoV-2. This is a retrospective study involving a total of 93 patients of all ages and genders. Forty-three of them received SCT and the other 50 did not. The survey was carried out using a questionnaire administered during individual interviews. The survey included questions relating to SCT: indications, side effects and its subjective efficacy, as well as questions in regard to their COVID-19 illness including; the severity of the attack and the adoption of barrier gestures. The data was then analyzed through the SPSS and SPHINX software. The most predominant age category was the age group between 45 and 60 years of age representing 52.7% of the patient population. The male gender represented 74.4% of our patient pool. The most common indication of SCT with 44.2% was for the treatment of Type 2 Diabetes Mellitus (DMII). We have identified 52 cases of contamination by COVID-19 out of the 93 patients. Fifty patients who have not benefited from the SCT and 2 of the patients who had SCT were contaminated with SARS-CoV-2. Among the infected patients, 29 were carriers of chronic diseases. The majority of the patients (~82.7%) did not have to resort to outpatient treatment. The calculation of the P-value resulting from the crossing of the variables "patients having benefited from the therapy" and "infection by COVID-19" found a value of <0.0001. SCT, through its ability to prevent, limit or repair tissue damage in the human body, could therefore prove to be a potential candidate in the fight against the COVID-19 virus, which still currently represents a scientific and medical mystery.***

Keywords: Stem Cell Therapy, COVID-19, Prevention, SARS-CoV-2

1. Introduction

Cell therapy is a technique by which human cells are isolated and injected for tissue repair or as a means to prevent, treat or palliate a local or systemic pathology. [1] Embryonic stem cells were first discovered in mice in 1981 and in humans 1998. [2] A stem cell is an undifferentiated cell capable of self-replication, of differentiation into other cell types and proliferation in culture. Stem cells are extracted either from embryonic or fetal, or from adult human tissues with or without transformation, they can also be obtained by nuclear transfer. [3]

Stem cells have different functions in the body. In the early stages of embryonic development or in the fetal stage, they multiply to gradually generate all the different cell types in the body, whether differentiated or undifferentiated. [4] In adult tissues, stem cells are much rarer and clustered in specific regions within organs. They contribute to the natural renewal of tissues (ie. a RBC lives on average 120 days and must be replaced) or to their repair in the event of injury. [5]

In recent years, an increasing number of innovative cell therapies have progressed from clinical trials to large-scale distribution, and some of them represent major breakthroughs where previously research and modern therapy was a dead-end. The tools allowing the implementation of these new therapies are more abundant while their clinical applications are showing promising results. [6]

The challenge regenerative medicine is setting; to contribute in developing therapeutic advances in pathologies considered until now as incurable [7]. We can mention degenerative diseases as an example: namely multiple sclerosis, Alzheimer's disease, and diabetes, but also other chronic osteo-articular pathologies but not limited to osteoarthritis, and rheumatoid arthritis. [8] Also, this study is of more interest in the context of the current pandemic: COVID-19.

The emergence of this novel virus has challenged conventional therapies. Indeed, despite the extensive research undertaken as part of the study of the different strains of the virus, as well as the few therapeutic alternatives offered, still little is known on COVID-19. [9]

This is where regenerative medicine takes charge. Indeed, understanding the role of stem cells would open up new therapeutic possibilities that could help in the fight against COVID-19. Accordingly, stem cell therapy (SCT) would stimulate the immune response and therefore provide better protection, and therefore prevent the spread of infection. [10]

2. Methodology

The objective of this study is to highlight the possible protective effect of SCT against COVID-19 infection. This is a retrospective study, evaluating the records of 93 patients of which 43 benefitted from SCT at Cheikh Khalifa Hospital in Casablanca, Morocco over a period of three years between 2019 and 2021. The 50 remaining patients have been contaminated by COVID-19 without benefiting from SCT. The inclusion criteria for the patients in the intervention arm have benefited from SCT prior to being infected with COVID-19, regardless of age and gender, while the patients

in the control arm were infected with COVID-19 without having benefited from SCT. The patients excluded from this study are those who refused to participate in the study.

For data collection, a validated questionnaire in French was used that is broken down into three sections: STEM CELL / COVID-19 / DATA SHEET, can be found in the addendum.

The survey poll was conducted during the patients' follow-up consultations, anonymously. The development of the questionnaire as well as the interpretation of the results was done using the SPHINX software: the variables studied were analyzed by 2 different methods.

In fact, the frequency table method focused on gender, age, SCT, indication, socio-professional category, income as well as contamination by COVID-19, as well as their exposure to the virus, by studying contact tracing, quarantine and their compliance of hygiene and safety measures. Then, we studied the diagnostic and therapeutic modalities as well as the side effects linked to contamination.

As for the cross-tabulation method, the variables used were SCT and COVID-19 / COVID-19 and chronic diseases / COVID-19 and age / COVID-19 and contact cases.

To investigate the link between SCT and contamination by COVID 19, we interpreted the cross analysis by using the SPSS software through p-value and Chi-squared test.

3. Results

3.1 Demographics

Out of the 93 patients, there was a predominant population of men with a percentage of 74.4% compared to 25.6% of which were women.

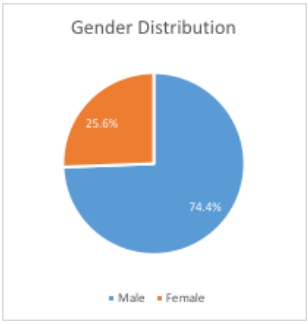

Figure 1: Pie chart showing the gender distribution in the study population

The predominant age category in our study was between 46 and 60 years representing 52.7% of the subjects.

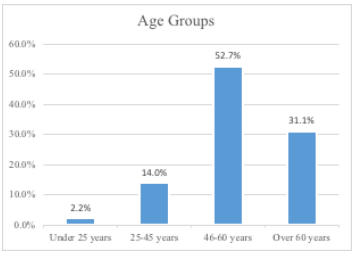

Figure 2: Bar graph representing the prevalence of the different age groups

Among the patients studied, 43 patients in the intervention arm benefited from SCT (46.2%), while 50 patients in the control arm did not (53.8%).

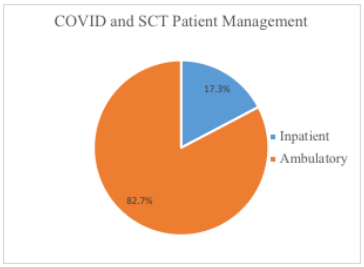

Figure 3: Pie chart demonstrating the types of patient care in patients who previously undergone SCT

3.2 Stem Cell Therapy Recipients' Indications

The indication of SCT in the patient population, who benefitted from it, was predominantly for DMII with a rate of 44.2% compared to degenerative diseases which represented 14% of the indications. Erectile dysfunction accounts for 11.6% of indications, as depicted in the figure below.

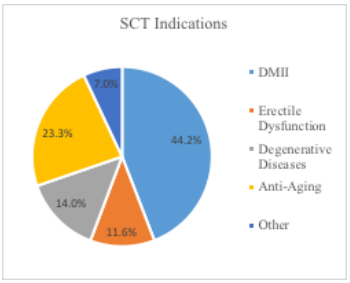

Figure 4: Pie chart illustrating the indications by which SCT was prescribed

3.3 Effect of SCT on patients prior to CoViD Infection

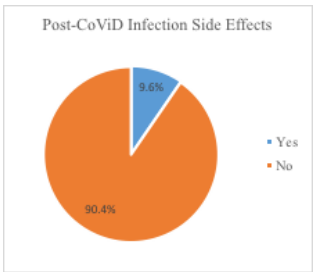

Figure 5: Pie chart illustrating post-infectious side effects with COVID-19

Subsequently, we further analyzed the data by crossing variables to refine our study. We therefore chose to cross the

following variables: COVID infection and SCT and COVID infection and Chronic Disease.

As shown in the table below, two of the 43 patients who received the SCT became infected with COVID-19.

Table 1: Chart crossing two variables: Patients who were infected with COVID19 and patients who were infected with COVID19 and had previously been treated with SCT

SCT \ COViD-19	Yes	No	Total
Yes	2	41	43
No	50	0	50
Total	52	41	93

Table 2:: Chart crossing the two variables: COViD-19 Infection and Chronic Disease

Chronic Disease \ COViD-19	Yes	No	Total
Yes	29	34	63
No	23	7	30
Total	52	41	93

After analyzing the results through SPSS, we calculated a significant P-value of 0.0001 comparing the cross tabulation of patients who received SCT and COVID-19 infection.

4. Discussion

This study explores the possible protective effects of SCT in the prevention of infection by CoViD-19. The majority of patients in this study having benefited from SCT have been less pre-disposed to contracting COVID-19, had less severe CoViD-19 symptoms, lower rates of disease progression and the majority of the SCT patients were treated at an outpatient setting.

We also investigated whether the patients who were previously infected with COVID-19 have had lasting side effects pertaining to their first COVID-19 infection.

From the results obtained, we noticed that only 4% of the population who benefited from the SCT contracted COVID-19 according to the general risk of the population, and that among those exposed: 15 people out of the 17 cases registered contacts were not contaminated.

In addition, 100% of the population who did not benefit from SCT contracted the COVID-19.

Therefore, we can assume the protective effect of SCT against COVID-19 infected patients [11]: indeed, these patients only required simple outpatient care and did not seem to present any sequelae following their infection.

The interpretation of the P value by crossing the variables COVID-19 contraction and SCT was 0.0001, which supports our theory regarding the potential protective effect of SCT and the contraction of COVID-19.

After intravenous injection of stem cells, a large population of cells accumulates in the lungs. [12] Their immunomodulation capacity [13, 14] could protect alveolar epithelial cells [15] and restore the pulmonary microenvironment [16]. Thus, preventing pulmonary fibrosis [17], and even regress pulmonary failure [18].

Also, SCT could prevent the cytokine storm seen especially in viral infections associated with COVID-19. " [19, 20]

The literature also reports that numerous studies have shown that SCT is on the way to becoming a go to therapeutic strategy for pathologies refractory to conventional treatment [21, 22] or even those without treatment known to date [23], including viral infections such as COVID-19. " [24] [25]

This therefore supports the results described by our study, which assume the preventive effect of SCT against the emerging virus. [26]

In addition, a study with a similar aim suggests that SCT specifically inhibits pneumonia associated inflammation [27], as well as prevents pulmonary fibrosis [28] while stimulating antibacterial and antiviral immunity [29]. This would significantly reduce the severity of the symptoms of respiratory disease. Recent clinical trials of SCT have shown a significant reduction in morbidity and mortality from COVID-19 infection. [30]

This is in line with the results we have previously found regarding the absence of side effects and the sequelae noted in our patients who were infected.

Thus, our study has shown that SCT has a protective effect in acquiring COVID-19. It also showed that the patients who contracted it presented with a mild form of the disease without having any sequelae.

5. Conclusion

Regenerative Medicine and SCT is an emerging field constantly evolving in recent years. Due to their ability to prevent, limit or repair tissue damage, and more specifically their action against COViD-19.

The advent of these new therapies in the context of the current pandemic, and research in this direction continues to take place. All of which converge on the potential preventive or even curative in COViD-19.

SCT therefore not only seems to provide a great preventive benefit to avoid contracting COViD-19 but may also be curative given the immunomodulation and the protective effect against inflammation and pulmonary fibrosis, evidenced by our study.

SCT is a promising treatment option for patients who are suffering from the novel COViD-19 which currently represents a major scientific and medical challenge.

This therapy is positioning itself as a potential candidate in the fight in what is gradually turning out to be one of the greatest challenges of our time.

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Author Profile

Rabii Redouane, MD, Head of Urology and Sexual Health Department at Cheikh Khalifa Hospital and Professor in Urology at the Mohamed VI University of Health Sciences in Casablanca, Morocco. Professional, self-driven, disciplined, highly organized Professor in Urology with more than 26 years of experience in Urology. More than 160 publications and 80 technical videos. Authored the first book on The Laparoscopic Retroperitoneal Approach in the Treatment of Renal Hydatid Cyst, 2013. Recipient of the Karl Storz Award of Knowledge in Endourology by the Karl Storz Company, 2013.

Balar Khalid, PhD, Professor of Higher Education in Computer Science and Statistical Modeling, Hassan II University Casablanca, Morocco. Coordinator of the IT management module at the Faculty of Legal, Economic and Social Sciences.

Meryem Guennouni, Intern at the Cheikh Khalifa International University Hospital and Medical Student at the Mohamed VI University of Health Sciences in Casablanca, Morocco.

Kawtar Jemmal, Intern at the Cheikh Khalifa International University Hospital and Medical Student at the Mohamed VI University of Health Sciences in Casablanca, Morocco.

Rachid Moussaab, MD, Consultant in Urology at the Department of Urology and Sexual Health at the Cheikh Khalifa International University Hospital and Assistant Professor in Urology at the Mohamed VI University of Health Sciences, Casablanca, Morocco.

Ghassane El Omri, MD Consultant in Urology at the Department of Urology and Sexual Health at the Cheikh Khalifa International University Hospital and Assistant Professor in Urology at the Mohamed VI University of Health Sciences, Casablanca, Morocco.

Younes Houry, MD, Consultant in Urology at the Department of Urology and Sexual Health at the Cheikh Khalifa International University Hospital and Assistant Professor in Urology at the Mohamed VI University of Health Sciences, Casablanca, Morocco.

Abdeljalil Heddat, MD, Consultant in Urology at the Department of Urology and Sexual Health at the Cheikh Khalifa International University Hospital and Associate Professor in Urology at the Mohamed VI University of Health Sciences, Casablanca, Morocco.

Karim Belhaj, MD, MSc, received his MD degree from Alfaisal University; College of Medicine in Riyadh, KSA then pursued his MSc degree in Laparoscopic Surgery at the Queen Mary University of London, Barts and the London School of Medicine and Dentistry in 2019 with Merit. He is currently a Urology Resident at the Mohamed VI and Cheikh Khalifa International University Hospitals.