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Review Article

NANO-BIO-GENETIC PRECISION TREATMENTS FOR MUTATING VIRAL DISORDERS

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ABSTRACT

SARS-CoV-2 has conked the lives of around 3.4 million till date, where diseased cases have shown a scale of intense seriousness from subclinical to censorious levels. It has been manifested that various genetic and ecological components have shown disease progeniture and reaction to treatments, where viral load, chronicity, age, gender, blood group are associated with genetic variant host genomes. Vigorous approach and imitate tract have triggered many immune response systems but these findings are not yet deduced in precise medicine in defiance mutating covid-19 virus. Various drugs and treatments currently been used for critical cases of SARS-CoV-2 are chemical and experimental with numeral side effects in patients. So, by understanding about "precise medicinal treatment" we can substantially work on nanobiological treatment which will be more efficacious against SARS-CoV-2. When infection starts reducing possible resources, an innovative plan of action will be developed of necessity, so this review article will delineate with numerous options of treatment that mainly includes precision medicine and non-pharmacological approach.

Keywords: SARS-CoV-2, Precision Medicine, Nanobiological Treatment, Non-Pharmacological approach.

1. INTRODUCTION

With current development in the finding of nanobio-molecular source of disorder, experimental treatments are going to be supplanted by precision treatment to decrease the after effect and to elevate long term efficacy of treatments. It has been manifested that due to genetic variegation, the expression of diseases, concatenation and reaction to drugs defer from person to person. The idiom "precision medicine" was first applied for the drug remedy of genetic diseases, nothingness, after invention the part of genetic milieu in non-genetic disorder for example viral infections, extensive benefit has been certainly awaited. This new modernized field of medicine is categorized into various different areas which involves precise and independent druggability of molecular targets, montage of agile and targeted drug molecules, and the excerpt of experimental drug pipelines. Precision medicine is not restricted only to drug related treatments in genetic and non-genetic disorders, but also includes precise non-pharmacological therapies like surgeries, nutrition treatment, immunotherapy. So, recognizing the complicated molecular track and mechanism which is associated with pathogenesis of SARS-CoV-2 in the evolution of basal disorders which can guide in advancing therapeutic approaches to prognosticate and stave off the trait, metabolic and autoimmune disease in SARS-CoV-2 recuperated patients in coming time.

2. NEWS APPROACH TO TREAT SARS-COV-2 SEVERITY IN INFECTED CASES AND ETHNIC GROUP

If the ongoing prevalence rate are to be managed effectively, and fourth coming waves of infection kept at cover, it is totally necessary that the circumstances and the systems of exposure to SARS-CoV-2 should be under continuous monitoring, also distal severe or lethal clinical complexity [1, 2] should be observed. While recognition of significant chronicity has now assisted to elucidate extensive risk groups, distinguishing retaliation of every single patient will help to evoke unpredicted clinical depreciation that is becoming complicated to prognosticate from initial clinical attributes [3]. Medical practitioners who are treating patients with SARS-CoV-2 are continuously facing clinical predicament on every day basis. The potentiality to interpret an individual's tendency to SARS-CoV-2 infection or critical illness, considering different variations in the host immuno-logical and erythrogenic retaliation, is becoming distinct as a consequence of genetic variation which would be substantial if there is proper infection management [4].

As a result, we can say that the host/genetic components which are interconnected to SARS-CoV-2 now require precision medicine included in treatment. The pursuit of precision SARS-CoV-2 ministrations is now in progress but the way to precision medicine in SARS-CoV-2 needs conspicuously expeditious pace. So now it is necessary to make use of precision medicine as it would be a now distinct approach for SARS-CoV-2 that will definitely help in translation science subunit invention, and modernized taxonomy for carrying further clinical trials [5, 6].

3. DRUGGABLE COMPONENTS/PRODUCTS OF SARS-COV-2

Antiviral drugs attacking the SARS-CoV-2 are mainly divided into two important categories in which the first category attacks virus-host interlinkage or impedes viral congregation [7]. Another category would involve drugs that can regulate comprehensive host intuitive immune responses or hinder with signaling pathways which are intricated in viral imitation. So, it can be seen that these drugs are proficient in engaging host receptors or proteases which can be employed for viral ingress or may have influenced endocytosis pathways [8-12]. Generally, there are three categories that can be used for screening drugs which are competent of suppressing SARS-CoV-2 namely first is remodeling of antiviral drugs in which components like interferon, alpha, beta and gamma, ribavirin and chemical moderator of cyclophilin 8 [13,14] can be used for assessing antiviral exertion. Second category involves assessment of chemical atheneum that comprises compounds which attack transcriptional systems of different cell lines. Screening techniques have capability to screen substantial athenaeum of drug-inclined chemical components which are possessing antiviral effects [15, 16]. The third category would mostly include evolution of distinct novel envoys which can result into scientific research which can revolve around the genomic and biophysical knowledge of the SARS-CoV-2 lifecycle. siRNA component has the capacity to hinder particular enzymes included in viral repetition cycle and monoclonal antibodies attacking host receptor ACE-2 [17]. But one of the measured obstacles in this approach is the definite drug delivery of molecules and lack of knowledge of siRNA-based methods [18, 19].

4. NANOTOOLS BASED DRUG DESIGN APPROACH FOR SARS-COV-2

Nearly a period of two years has been passed since beginning of pandemic that is SARS-CoV-2 and Middle east respiratory syndrome coronavirus (MERS-CoV) no efficacious drug against CoV family has been approved, therefore there is urgent requirement for discovering new therapeutic approach for treatment. Currently, research is being carried out for finding efficacious vaccines or drugs involving both categories that are conventional therapies and developing therapy like nanomedicine. Nanomedicine has manifested its use via its application in drug delivery and nanosensors in various other disorders [20]. Nanomedicine and its elements perform crucial roles at different phases of prevention, diagnosis, treatment and the research activity which has been carried out related to covid-19. Nanotechnology has numerous benefits by using nanotools, like liposomes, polymeric and lipid nanomaterial which can be efficient for drug encapsulation and development of pharmacological drug properties. Antiviral systems for nanomaterials can attack the binding ingress, replication and burgeon of SARS-CoV-2 [21]. Numerous research studies have put forward that amalgamation of anti-inflammatory therapeutics and nanoparticles can give rise to their stability and resistance. Also it will help to ameliorate targeted drug delivery. For example, tocilizumab (IL-6) plus nanoparticle hyaluronate-Au has been acted strongly in providing the drugs to lungs [22]. Biogenic nanoparticles are sustainable and can be manufactured expediently in huge quantities in precise size and morphology. The morphological and physio-chemical connection of SARS-CoV-2 with synthetic nanomaterial will also develop nanoparticles as an efficacious intercession technique. To carry out particular ramification, nanomaterial should be substantially derivatized with numerous different kinds of polymer and functional groups.

5. PHARMACOGENETIC APPROACHES FOR GENETIC POLYMORPHISMS IN DIFFERENT GROUPS

Circumscribing systems underlying varying drug concentration and reaction gives a point for recognizing genes for coming Pharmacogenetic research. As a consequence, there are numerous major examples in pharmacogenetics which are related to varying drug uptake, metabolism and elimination. Genetic polymorphism is a particular category of genetic diversification between populace gene pools. Single nucleotide polymorphism (SNPs) is the usual category of genetic variation between people. Different polymer-phism is present in genes encrypting phase 1 of cytochrome p450 and phase 2 of drug metabolizing

enzyme or human leukocyte antigen which becomes helpful for prognosticating drug potency and toxicity [23, 24]. Genetic variation of CYP2C9, CYP2D6, CYP2C19 and CYP3A5 are linked with therapeutic consequence of phenytoin [23], tamoxifen [25], tacrolimus [26] sequentially. The dose ramipril of mercaptopurine and irinotecan should be regulated conferring to the polymorphism of thiopurine methyltransferase [27] and UDP glucuronosyltransferase 1A1 [28] correspondingly. The genetic polymorphism comprises basic pharmacogenetics which means that monogenic variants can change the drug response [29]. On the other side PGx is the genome which is mostly used for the analysis of genetic determinants of the drug metabolism enzymes which impact therapeutic potency and safety [30]. So, the understanding of major varying drug responses which seems to be multifaceted has given rise to take interest in PGx where there is rise imitated by augmentation of genetics into genomics. So, having the knowledge of crucial human genetic variants which are linked with clinical therapeutic consequence has the efficacy not only to accelerate immediate usage and approval but also purvey an auxiliary level of safety and potency to patients.

6. PRECISE TISSUE ENGINEERING/REGENERATIVE MEDICINE APPROACH FOR SARS-COV2

Present treatment for SARS-CoV-2 is generally used to control rather than curing this extremely infectious disease. So, there is a need for significant medical treatment which would be efficacious against SARS-CoV-2. Inflammation is the prime mover backing coronavirus infection, and the deaths which have occurred due to Covid-19 are resulting due to acute respiratory distress syndrome (ARDS) [31]. It has become vital to restrain the inflammation as soon as possible. Till now, many scientific researches have been carried out for checking the safety and potency of tissue engineering and regenerative medicine (TERM) which includes mesenchymal stem cells (MSCs) and also the derivatives like exosomes for novel coronavirus disease. Latest advancement in the area of tissue engineering which is apropos to coronavirus disease includes a three-dimensional plan of action to evaluate disease progression and to test the potency of antiviral drugs. The TERM is efficient to modernize the entire healthcare system by reinstituting damaged tissues and organs contradictorily to another pharmaceutical and surgical approach that controls rather than curing disorders [32]. ARDS is the major reason behind the deaths due to Covid-19 infection and simultaneously MSCs treatment has been used to treat patients which are suffering from Covid-19. One of the major challenges in the management of MSCs for SARS-CoV-2 is the minimum number of autologous MSCs sources and less timelines to manage increasing case numbers. So, solicitation of a prudent off-the -shelf, allogeneic product with suitable immune response modulation will assist patients for getting finest quality stem cell therapy at the correct movement and efficacious clinical density [33]. Existing clinical trials show the conceivable support of stem cell treatment for Covid-19 patients but due to minimum case concatenation there is lack of precise control arm which makes it difficult for the interpretation to quantify. So, there is need of investigation which would help to understand safety and potency of these treatments and their long-term efficacy.

7. IMMUNOTHERAPY APPROACH FOR THE TREATMENT OF SARS-COV-2

The immunopathogenesis in regards with SARS-CoV-2 has been instituted that surged serum levels of C-reactive protein (CRP), interleukin-6 (IL-6) and contracting CD4+ and the CD8+ T lymphocyte population are the most immunological adjudication in Covid-19 patients. Increasing levels of other inflammatory cytokines and chemokines like IL-2 and IL-8 with growing numbers of neutrophils and eosinophils will persuade immune peculiarity in patients which are suffering from Covid-19. There is increasing corroboration to get a considerable amount of knowledge regarding immune pathogenesis in regards with Covid-19 which will help to build the foundation for the advancement of new potential treatment/therapies [34]. But, distinct and non-distinct immunotherapies like convalescent plasma (CP) are often used for the treatment of the patient with severe Covid-19. The convalescent plasma has vital consequences by its composition firstly in improving the condition of Covid-19 patients and secondly antiviral consequence by counteracting antibody and immunomodulatory consequence by anti-inflammatory cytokines and antibodies [35]. This treatment within two days after admission to the ICU will decrease the use of mechanical ventilation, stay in hospital with recovery to get cogent clinical effectiveness [36]. Also, the therapy called as monoclonal antibodies like 80 R, m396 and S230 which is distinct for S1 domain of SARS-CoV-2 have been seen in counterbalancing Covid-19 infection by hindering binding to the ACE receptors on the host

cell. So convalescent plasma therapy and monoclonal antibody therapy are used and have vital therapeutic paradigms for the superintendence and averting of Covid-19.

8. CONCLUSION

We must not scorn the potentiality that precision medicine holds in advancing treatment. The current review discussed the recent advancement in precision medicine which has included technological progression in delivering old and new drugs with novel diagnostic methodologies. Present clinical acquisitions with nanotools in precision medicine have been largely diagnostic, like the capacity to identify early stages of a disease by a particular ligand-receptor interaction or by using different biomarkers to recognize which therapy or therapeutics would be suitable for the patient suffering from Covid-19. This particular review has given importance on vital therapeutic uses of precision medicine specially their use in immunotherapy, tissue engineering and regenerative medicine all these have colossal capacity in improving potency of precision medicine treatment but still there is a need of clinical progression in this diagnostic application. As there is advancement in precision medicine these could definitely impact the future design of drug carriers for numerous therapeutics in personalized as well as generic by assisting assembly of cargos which involves small molecules, nucleotides and proteins. In precision medicine-pertinent application, the use of nanoparticles will allow to improve cellular targeting and will tailor treatments like multidrug therapy. The insight given by precision medicine like patient heterogeneity and genetic profiling will ultimately help to develop ideal nanoparticle dependent precision treatment.

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