

COVID-19 knowledge and therapeutics, past, present and future

Abstract

The outbreak and impacts of coronavirus (COVID-19, SARS-Co-2) is still a mystery. Yet a sign of prospective epidemics cannot be ruled out. The current studies of COVID-19 (public health, medical and pharmaceutical) implied a benefit of diagnostic/therapeutic transition. To heighten global campaign for COVID-19 studies, global public healthcare and pharmaceutical strategies are highlighted herein. In the past, epidemic condition, countrywide stipulation and therapeutic variability worldwide were confronted before us. Different patterns of medical experience and pharmaceutical trends should be enhanced in the future.

Keywords: COVID-19, viral treatment, viral structure, herbal medicine, viral vaccines

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Introduction

Epidemic progress

The outbreak and impacts of coronavirus (COVID-19, SARS-Co-2) is still a mystery.¹⁻³ Yet a sign of prospective epidemics cannot be ruled out. The current studies of COVID-19 (public health, medical and pharmaceutical) implied a benefit of diagnostic/therapeutic transition.⁴⁻⁵ To heighten global campaign for COVID-19 studies, global public healthcare and pharmaceutical strategies are highlighted herein. Previously, epidemic condition, countrywide stipulation and therapeutic variability worldwide were confronted before us.³ Different patterns of medical experience and pharmaceutical trends should be enhanced in the future.

New challenges

The outbreak and impacts of COVID-19 is a global public healthcare catastrophe. Quick reactions and reorganization of global resources were the first reaction and convention in the earliest.⁶⁻⁹ Some lines of clinical evidence and biomedical associations are carefully analysed and undergone trial-and-error therapeutic verification. Epidemic control measures, effective therapeutic evaluation and medical device production worldwide were aimed.¹⁰⁻¹⁴ We eager to facilitate this medical discipline transition in medical and pharmaceutical guidelines in future.

COVID-19 origin, different possibilities

Significance

To avoid repeat outbreak of COVID-19, viral origin discovery is the first priority.³ In the past discovery, wild animals, such as bats, snakes and others are attributed for this virus outbreak (zoonotic arguments) in expert's opinions. However, government in China has shut down most of wild-animal markets for several months in the beginning of viral outbreak. No sign of viral infection halt was found. Other risk factors may also be possible for viral outbreak. Further studies are needed.

Possibilities and hypothesis

Several possibilities are given in the past;⁷ several viral origin possibilities are raised from current science and technology advances.

Wild-animal contacts or eating; Zoonotic hypotheses is the most popular arguments globally. Chemical or biological factors to modify virus from normal to pathogenic ones; viral evolution; gradual drift viral genome and transit it from normal virus to pathogenic sources in nature. These pioneer studies should be focused now.

Vaccine development

Disease prevention

Vaccine development is always the final aids for new virus epidemics for "non-toxic" and "wide spread". It may be effective in the future.¹⁴⁻¹⁸ Apart from economic and ethical consideration, the complexity of COVID-19 (molecular and structural) may make vaccine production perfection for long period of time. The efficacy of viral vaccine needs to be carefully evaluated.

Risk- and efficacy- re-evaluation

At present, nearly 100 different COVID vaccines have been tested worldwide. Owing to this potential risk, gradual comparisons for different vaccines (efficacy and undesired risk factors) should be emphasized. The commercialization of COVID-19 vaccines may need longer procedures.

Currently, many different types of vaccine manufactory techniques are presented. Among these techniques, mRNA vaccines are more favourable because they can combine more viral components in one vaccine product.¹⁷

Early treatment

Therapeutic systems in the past

This world has a shortage of licensed drugs against COVID-19 infection. In global markets, drug licenses need several years. At first, clinicians use anti-viral drugs of other viruses for reducing viral load and proliferation.¹⁹⁻²⁴ Nonetheless, most anti-viral drugs have many undesired side-effects, such as blood, neural and cardiovascular toxicity when over-uses.⁴ Correspondingly, the drug dose selection is paramount. These processes included several approaches like administration route, genetic polymorphism of drug metabolic enzymes, and drug concentration level determination in human blood by modern chromatography or capillary electrophoresis and knowledge for drug combinations.

The infectious treatments and selection in eastern countries may also contain traditional medicine (TM). In Eastern countries, especially China, herbal medicine are also practiced for lower toxicity than anti-viral compounds.²⁵⁻²⁹ There are many reports on viral infection in clinical treatment studies.³⁰⁻³⁵ Chinese doctors generally provide many fixed forms of herbal products. It is easy to handle and control of therapeutics. This therapeutic custom is popular in China nowadays. It has deeper knowledge lasting for thousand years. In addition, many pharmacology and drug treatment studies are tabulated (Table 1).³⁶⁻³⁸

Table 1 Mechanisms for therapeutics against COVID-19

Types	Mechanisms and pathways
	Antiviral (Viral proliferation, viral-host-interaction)
Drugs	Symptom alleviation
	Whole body moderation
Vaccines	Prophylactic (emphasized on safety)
	Treatments (emphasized on efficacy)
	Viral (load, sequence, replication, moderation and cell-cycle)
	Antibody and immune response (interleukin)
Diagnostics	Pulmonary damage and overall images
	Blood tests (different components and lymphatic cells)
	Underlying diseases
	Biomarkers (inflammatory, viral cellular entry and replication)
Foods	Nutritional (immune stimulation and normal physiological function)
	Supplementary (vitamin, mineral and trace elements)
	Drug dose optimizing in patients
Drug toxicology & doses	Avoid unnecessary or toxic drug treatments
	Pharmacogenomics
	Preventive commercial products
Herbal medicine	Fixed products (either mild or severe cases)
	Prescript for individual patients

Therapeutic variability

Currently, different therapeutic selections have variable challenge and limitation in the clinic. We conclude them as therapeutic variability in the world. Diagnostic and therapeutic transition is needed.⁴

Plasma therapy: The plasma (containing anti-viral antibodies in rehabilitation patients) is a known therapeutics for critical stage patients. Its utility is evaluated by medical doctors of many counties. From our opinion, this therapeutic paradigms can save the life of many patients. Immune mechanisms of such therapy needs to be discovered.

Retroviral or protease inhibitors; viral infection and spread is used by retroviral or viral-protein inhibitors in the clinic. Currently, Remdesivir, favipiravir and arbidolas are widely used for COVID-19 infection treatments. However, there is no decisive drug for critical conditioned of all. But this condition is kept until now.

Inflammation targets; Inflammation plays important role in disease pathogenesis and should be well targeted. Anti-inflammatory agents are not viral-load inhibition yet symptom alleviation. Carefully evaluating and comparison of their actions and pharmacological characters, especially drug combination against COVID-19 is useful. Further scientific work, technology and pharmaceutical studies is needed for therapeutic broadening and transition. Among different types of viral therapies, effective and toxicity of drugs should be aimed at first. More effective drug evaluative architectures should be used in drug discovery and development.

Traditional medicine

Due to the long process of drug licensing, some traditional medicine can be used at the beginning of viral outbreaks. TM is difficult to practice. 90% global doctors or clinicians do not know it. To solve this issue, some forms of commercial herbal powders and balls have been made for most doctors (most famous powder like 板蓝根冲剂 water dissolving ban-lan-gen powders).

Human infections (fever, nose fluid, cough, headache, respiratory difficult and many other others) can be selected with 牛黄解毒片 (Niu-huang-jie-du-pian), 柴胡冲剂 Chai-hu-chong-ji (radix bupleuri), 上清饮口服液 (Shang-qing-ying fluids) and some others. They are cheaper than licensed drugs in developed countries for symptom management and viral load reduction.

Convention and new initiatives

Drug dose control

Majority antiviral agents or drugs commonly have a high degree of undesired side effects or toxicities in humans.^{37,38} The accurate drug dosing and administrative routes needs to be carefully optimized in clinical treatments. Any kind of drug over-dosing may cause serious symptoms or toxicity to potential patients. This kind of toxicological researches in the clinic needs to be executed by longer terms and vigilant observations in treatments in the future.

Patients with co-morbidity

Patients with underlying diseases, such as obesity, type 2 diabetes and cardiovascular are usually more difficult to recover from acute viral infections, surgery or other emergency treatments.³ There is an urgent requirement for clarifying these differences in experimental and clinical studies. These researches will help our understanding of COVID-19 spread, diagnosis and treatments.

Different viral strains

Relation between different strains of coronaviruses and therapeutic selection is basic because of a variety of infectious COVID-19 virus worldwide. Comparison and validity of different viral strains to establish infectious animal models is indispensable. In-depth drug evaluation, knowledge enrichments, clinical assessments and therapeutic strategy utility is underway. The relation study between viral pathology and drug development will embrace new hope for therapeutic breakthroughs in future.

Tracing geographical and epidemics sources

The geographic and epidemic source of COVID-19 is important to reduce costs and mortality worldwide.⁷ Growing pathological and viral lineage (phylogenomic) study of coronaviruses may be cornerstone of medical knowledge and therapeutics. Clinical therapeutic paradigm and strategies is very benefiting to global people. Any new knowledge discovery will be important to patients with COVID-19 infection.

Sourcing of global viruses can help the promotion of better diagnosis and treatments of serious patients. Monitoring globally will guide the viral governance at any location and areas of this world.

Human genomes

Hypothesized before, human genomic study is very useful for viral infection in human bodies and associated with patient’s survivals.^{39,40} Many genomic alterations, especially viral integration to human genome might associate with disease seriousness and human deaths. However, there is little medical knowledge about COVID-19 infection and treatment until now. It suggests that human genomic study may shed new light for conquering COVID-19 and a great reduction of infected patient mortalities.⁴¹

Drug discovery

Currently, effective drugs for COVID-19 is lacking. Evaluative models for anti-COVID-19 agents and drugs, especially artificial intelligence are improving.⁴²⁻⁴⁴ Certainly, it needs to be based on pathological knowledge and pharmacological study. Useful animal and human cell models (in vitro, in vivo and in silico models) are indispensable. Druggable targets and pathways are tabulated (Table 2).

Table 2 Proposed drug mechanisms and categories in future

Drug types	Genes, molecular, pathways and mechanisms
DNA/RNA	Retroviral polymerase inhibitors (competitive or others)
	Si-RNA mediated knock-down
	Genome editing (CRISPR/Cas9)
	P53 (cell function and survival)
	Membrane trafficking & ubiquitin conjugate
Proteins	Bind-proteins (viral-host-interaction)
	Viral enzymes
	Viral-hijacking (host binding and mobilization proteins)
	DNA helicases
Key components & pathways	Protein kinases
	Valosin-containing proteins (VCP)
	Glyco-conjugates (sialic acids)
	NF-kB associated
	Secretary pathways (nsp2, nsp3, nsp5, COPI)
	Oxidative-reductive stress
	Interleukin
Immunity & inflammation	Cytokine
	Interferon
	Antibody (plasma therapy)
	Oxidative-reductive stress (ORS)

Cellular	Endocytosis
	Cytoplasm releasing and viral replica
	Rodent
Modality	Rabbits
	Large animals

Molecular-docking

Computational analysis and design of drugs for COVID-19 is flourishing. A lot of molecules are testified and reporting in the past.⁴⁵⁻⁴⁷ More new genetic or molecular drug molecules and targets should be discovered.

Future direction

Research and therapeutic trends

Entering into 2022, the epidemic condition and global society is eased a great deal. However, the quest for new diagnostic, therapeutic and public health care is continuing and sustainability.⁴⁸⁻⁵¹ In addition, relationship between COVID-19 and other viral infection should be investigated.⁵²⁻⁵⁵ Several approaches are discussed in the following.

Drug combination strategies

Drug combination shows great therapeutic potential such as HIV infection and cancer metastasis.⁵⁶⁻⁶⁰ Apart from steady output of more effective drugs, drug combination studies are indispensable. However, drug combination principle and rules are lag behind.⁶¹ In the normal patient treatment, such rule and principle discoveries will be followed up.

Hypotheses verification

A lot of biomedical hypotheses are associated with COVID-19 treatment-origin, human genome-integration, different lineage and pathogenesis.³⁹⁻⁴⁰ To prove these hypotheses, sustainable governmental funding should be better allocated in this area. Hypotheses provention can lead to high quality viral control and treatment. Great social and healthcare significance is achieved by hypothesis verification.

Conclusion

The outbreak and impacts of COVID-19 is huge now. Thus, new medical knowledge, technology and clinical protocols should be pursuit. This Article states new thoughts for wining this battle forever. Some routine of traditional medicine, diagnostics and nursery are emerged to tackle viral epidemics at any times and locations globally.

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Conflicts of interest

The author declares that there is no conflicts of interest.

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