

Complementary antioxidant medicine in COVID-19 management and the place of haematology evaluation: Brief critical and scoping review-based commentary

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Abstract

The purpose of this commentary is to articulate herbal remedies for COVID-19 among geriatric care clients and also the role of haematology evaluation in non-symptomatic individuals. Two review methods were employed to develop this narrative commentary. First, data in social media article and refereed research journals critically reviewed. In particular, knowledge about treatment options are used to substantiate potential implications for geriatric care and haematological tests in asymptomatic patients. This commentary touched on (1) alternatives to vaccination, (2) COVID19 treatment roadmap, (3) difference in response of adults and children, and (4) geriatric and asymptomatic individuals' need for haematology. Second, a brief scoping review was done to discuss the question "if medicines we already have are good enough to buy patients more time". The highlight is antioxidant naturopathy for COVID-19 management. What has yet to be really authenticated, which constitutes the contribution of this article, is that immunocompromised status of geriatric care clients underlies unavoidable burden of frailty. This contraindicates at least 25% of COVID-19 vaccines being researched; and warrants caution in consideration of anti-inflammatories that constitute 52% of drugs currently being developed. The implication is that geriatric care could benefit more for alternative traditional medicine such as herbs based on their antioxidant and immunomodulation properties. Further, routine haematology vis-à-vis full blood count is indicated also in asymptomatic individuals.

Introduction

Alternatives to vaccination

It is a given that vaccination is one of four ways by which individuals get immunized and get their immune system boosted. Development of the vaccines follow conventional process that require time for trials before approval. In the current COVID, all four types of vaccine technology are covered albeit in unequal proportion (Figure 1). Of relevance to geriatric care clients is that their immune system is weak, which contraindicates live vaccine. This implies that geriatric care clients are unlikely to benefit from at least 25% of vaccines being researched.

What is worth bringing to the fore is vaccines are not equally effective across different age and/or genetic populations. Further, there have pandemics in history of humans. Report indicates that apart from the second century when 200 million deaths were recorded during the bubonic plague and 19th century yellow fever pandemic that took 125 million lives, there have been reduction in deaths (Figure 2).

In particular, both acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) coronaviruses have been known for several years, but there has yet to be any licensed vaccine for the two coronavirus [1-3]. Instead, there is indication of possible immunopathology being side-effect of some candidate vaccines [4], which could translate to contraindication among geriatric care clients. Therefore, it is imperative to consider the alternatives to vaccines in terms of what have been done in centuries past, especially as geriatric clients are more likely to benefit from potential alternative therapy relative to apparently health younger adults.

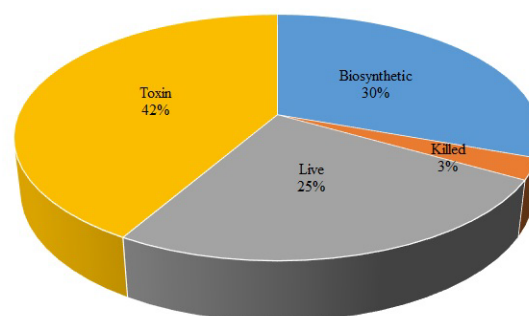


Figure 1. Distribution of vaccines being developed into technology type [1]

Pandemics	Timelines across centuries				
	2 nd	17 – 18 th	19 th	20 th	21 st
Bubonic	200 million				
Smallpox		56 million			
Yellow fever			125 million		
Spanish flu				45 million	
Swine flu					200 thousand
COVID-19					96 thousand

Figure 2. History of pandemics with highest number of deaths [2]

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Currently, management of MERS includes avoidance of raw animal foods [5]. It is known that traditional Chinese medicine effective during SARS revolves around herbs [6-9]. However, one salient missing mechanism of action is the antioxidant potential of the herbs in boosting immune status. For instance:

- » The patented herbal mixture, *Shuang-Huang-Lian* [8,10], is antioxidant but has been reported to possess additional anti-inflammatory effect that could translate to immunosuppression side-effect among immunocompromised geriatric clients.
- » Nitric oxide donors, such as glycyrrhizin compound in licorice root are antioxidants [11], has been speculated to be one of several potentially effective treatment options [6].

Treatment roadmap

Perhaps, it is pertinent to note that there has been fear of coronavirus being deliberately released [4,12]. Also, bioterrorism was queried during Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak with note that it will be difficult to recognize [13]. Therefore, there is need to establish universally available and affordable clinical test method to screen people, especially the asymptomatic individuals.

Further, antioxidants constitute a potential mitigation agent coronaviruses [14]; and predominant casualty is the immunocompromised elderly people albeit unavoidable cost of frailty [15]. Hence there is need to give consideration to antioxidant remedies that can be monitored for changes in immune status using routine haematological blood cell counts. This commentary dwells on perspective of two lines of discourse on novel coronavirus (COVID19). First is the treatment roadmap (Figure 3). Second is innate immunity

physiology. It will conclude with harmonization of the two perspectives and comment on quinine's ameliorative hypothesis with recourse to antioxidant potential of herbal remedies and haematological evaluations.

Difference in response between age groups borders routine haematology

Differences have been speculated to occur in COVID19 patients categorized into age or gender subgroups [16,17]. The report on transmission dynamics and clinical characteristics of COVID19 infection among children indicates that white blood cell including absolute lymphocyte counts are virtually normal, which suggests unimpaired immune function, unlike in adult [18]. This can be due to active haematopoiesis in children keeping the white blood profile intact, unlike adults where haematopoiesis is reduced as per aging process.

Another piece of knowledge is that level of temperature increase, as indication of fever during acute phase of infection, declines with age [19]. This is besides baseline body temperature being higher in children relative to adults. During SARS outbreak in 2003 [20], it was speculated that coronaviruses can be destroyed at higher body temperature [21]. The implication is that besides higher fever magnitude during physiological inflammatory response to infection, the relatively higher baseline body temperature and intact white blood profile in children may be additional innate immunological protection. With particular regards to geriatric care clients, fever magnitude and immune response in COVID-19 infection are both likely to be lower compared to children. Yet, the geriatric client has higher tendency to be symptomatic and severe due to the less immune response – the unavoidable burden of frailty [15].

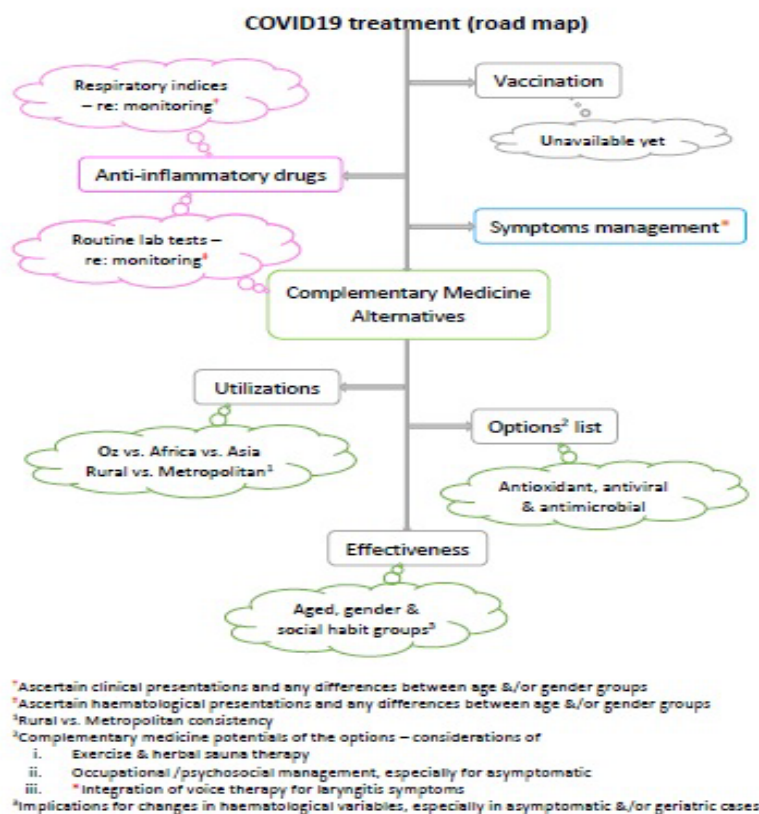


Figure 3. Treatment roadmap of COVID19

In the ongoing COVID19 pandemic, a very recent evaluation has indicated that routinely assessed blood cell counts used in monitoring immune status can be abnormally low among the asymptomatic individuals, and could be more prevalent in the subpopulation that progresses to develop symptoms (Figure 4). What is yet to be reported is how the haematological profiles improve among the subpopulation that do not progress.

Geriatric and asymptomatic individuals' need for routine haematology

It is common knowledge that virtually every disease condition is associated with some level of inflammation. Hence anti-inflammatory medications as either prophylactic or therapeutic. In the COVID-19 pandemic, it has been accepted that hyper-inflammatory response is one of the major causes of lung damage [23]. This is justification of the anti-inflammatory drugs for COVID-19, which is about 52% of treatment options being development (Figure 5).

One News item and social media circulation is that COVID-19 may be worsened by anti-inflammatory medication. This can be argued as been buoyed by advice from the World Health Organization that such medications “may mask symptoms of infection” [24]. Therefore, it is pertinent to explain that the side-effects of anti-inflammatory drugs in COVID-19 goes beyond masking symptoms and includes immunosuppression. It is known that primary effect of anti-inflammatory drugs is to inhibit normal physiological process of inflammatory response that otherwise fend off sub-virulent infection. Thus, a major mechanism of unwanted effect in COVID-19 is suppression of innate immunity. However, NSAIDs are still used and advise to be with benefit-versus-risk caution, especially among the elderly [25]. This is relevant in geriatric care clients who are immunocompromised. The summarizing questions and answers are:

Question: Can use of NSAIDs increase risks for geriatric care clients?

○ Answer: Yes. NSAID monotherapy would only treat the symptom of inflammation, but this may worsen the immunocompromised status of a geriatric client. Whether this is the case for any patient can be monitored with routing haematology.

Question: Do asymptomatic patients take over-the-counter NSAIDs?

○ Answer: Yes. Though the effects and limitations are not assessed, hence this commentary

At this juncture, it is necessary to emphasize that the anti-inflammatory effect of herbal remedies is different from immune-boosting antioxidant effects. Also, disease conditions are rarely treated with anti-inflammatories alone. Therefore, any of the anti-inflammatory drug options being develop may not be used as monotherapy, but cautiously in combination therapies among geriatric care clients; or consideration of the non-pharmaceutical concepts in age care.

The question “if medicines we already have are good enough to buy patients more time”

Scoping review: For the purpose of this commentary, a very brief scoping review was done. PubMed search engine was discretionally used in a 4-step process, no time limit was applied. Selection criterion for article to be reviewed was report that focused on antioxidant as alternative or complementary medicine we already have. Search terms and relative outcomes are indicated in table 1. Result show that two articles considered diet (Table 1). However, none of the articles

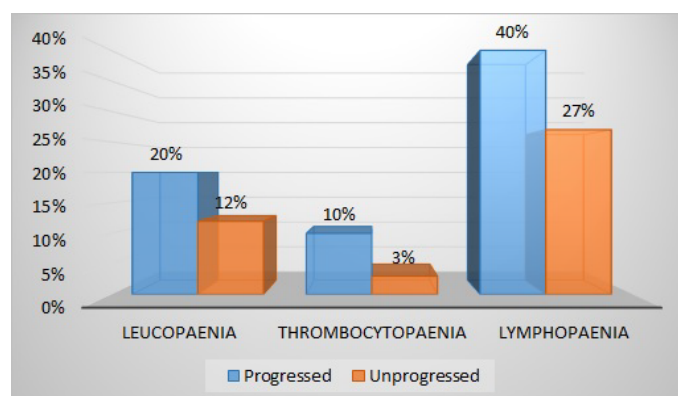


Figure 4. Haematological cell count changes in asymptomatic COVID19 patients [22]

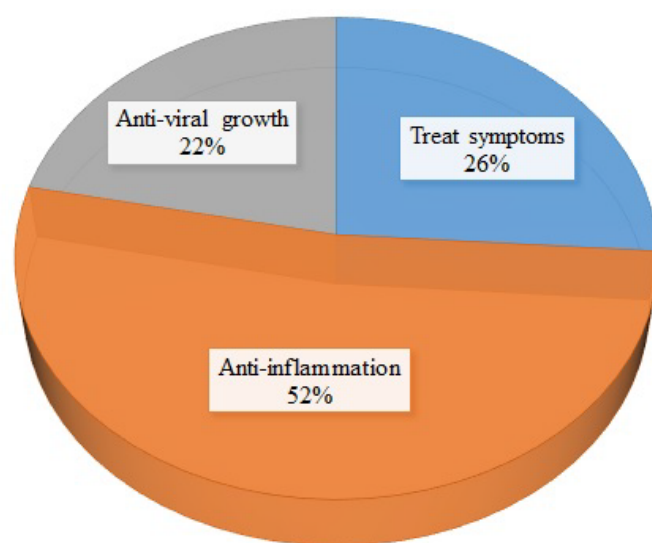


Figure 5. Distribution of drug treatment options being development [1]

Table 1. Summary of scoping steps and outcome

Steps	Search term	No. of articles
1	COVID19	12214
2	COVID19//Treatment	3344
3	COVID19//Treatment//Antioxidant	10
4	COVID19//Treatment//Antioxidant//Supplement	1 of 10
	COVID19//Treatment//Antioxidant//Diet	2 of 10*

*Including the singular article on supplement

contextualized antioxidants diet or supplement as complementary medicine we already have. Therefore, this is something worth discussing

Given the general knowledge of Artemisia including antioxidant potentials [26]; and being the purported ingredient in the COVID Organic that is under investigation, ‘COVID19//Artemisia’ was also imputed onto the search engine. Only one article came up [27]. Review of the abstract indicates the authors focused on its anti-inflammatory and antiviral properties without mention of antioxidant potentials. This further justifies the need of conversation to advance the concept of antioxidant potentials visa-a-vis the values of medical nutrition therapy in COVID19.

Discussion

Antioxidants as anticoagulant and immune-modulator: Free radicals cause mitochondrial damage, which can lead to atherogenesis

and coagulopathy. It is known that oxidative stress is involved in atherothrombotic process [28]; and there is implied relevance of copper and zinc as antioxidant micronutrients [29]. Indeed, antioxidants mop up of free radicals, which leads to restoration of calcium homeostasis and reduction is hyper-coagulation process [30]. It is also known that mitochondria damage or mitochondrial ROS production in platelets results in increased risk for thrombovascular events. Hence “preserving platelet mitochondrial function may be an additional means of decreasing the risk of potentially fatal thrombotic events” [31].

With regards to immune functions, antioxidants have been known to be immunomodulatory. For instance, there is report about immunomodulatory activities of glycyrrhizin (liquorice) [11]. In human, the speculated antioxidant activities of serum bilirubin and uric acid have been discussed with regards to autoimmune diseases such as arthritis and Myasthenia gravis [32, 33].

Antioxidants as haematinic: The bioavailability of the iron from vegetables may be lower relative to meat [34], but there is also the antioxidant potentials of vegetables. Indeed, the World Health Organisation recommends with regards to iron deficiency to contextualize and promote iron-rich foods as complementary haematinic [35]. Therefore, in terms of present COVID19 pandemic, what is probably necessary to re-articulate is how of antioxidant naturopathic remedy may be effective and obtained from diet – sequentially highlighted as:

- Oxidative stress reduces (while antioxidants improve) haematocrit [36-38].
- Vegetables reduce oxidative stress, by their antioxidant potentials [38].
- Vegetables indirectly improve haematocrit [35], by their antioxidant potentials

Perhaps, it is pertinent to recognize that red blood cells are suicidal antioxidant cells in erythrocyte oxidative stress phenomenon [39, 40]. A mechanism by which increased death rate of red blood cells lead to anaemia. Therefore, the haematinic function of antioxidants or micronutrients in vegetables is not limited to provision of iron for red blood cell synthesis. Instead, antioxidants’ haematinic effect is primarily by preventing anaemia essentially via offsetting of erythrocyte oxidative stress process.

A question has recently been asked “if medicines we already have are good enough to buy patients more time” [41]. Further, another recent report has highlighted disseminated intravascular coagulation as the haematological complication in COVID19 deaths [42]. This highlights the need for more involvement of haematology department in COVID19 patients’ management. What this discussion draws to the fore is that antioxidants naturopathy (both dietary and supplements) are available and good enough to attenuate pathophysiology, especially the oxidative stress and coagulation processes. This is supported by the ongoing interest on antidiabetes drugs such as metformin that is known to have both antioxidant and immunomodulatory effects [43, 44].

Conclusion

What this commentary advances is that geriatric care clients are more in need of potential antioxidant remedies. In particular, the herbal alternative to vaccination, being sources of antioxidant is noteworthy, especially as there has yet to be any approved vaccine for the coronaviruses that caused pandemic since over 10years. The article emphasizes that the immunocompromised status contraindicates about 25% of COVID-19 vaccines being researched. Low immunity

could be improved by antioxidants, but contrariwise worsened by side-effects of anti-inflammatories that constitute 52% of drugs currently being developed. Further focus is the need for routine monitoring of haematology profiles among both symptomatic and asymptomatic patients.

Acknowledgement

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