A Survey on Side Effects of COVID Vaccine on Human Body

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Abstract: The COVID-19 Vaccine when injected in our body produces Antibody (due to reaction between L-Histidine and DNA molecule of our Body) has side-effects like, fever, body pain, etc. It's due to Bond formation (Temporary) between COVID Vaccine and Blood Component (Iron). This forms a Temporary Complex Compound which results in side effects. But as this bond is temporary it's eventually broken down by Body's Immune System or Medicines taken for Relief and in course of time due to this function our body builds resistance to the virus.

Keywords: COVID Vaccine, Immune System, Iron, L-Histidine

1. Introduction

To understand the nature of side-effects caused due to COVID vaccine we shall need to understand the types of vaccines available, nature of vaccines, action of vaccines on human body. There are 6 types of vaccines available namely:

a) m-RNA:

Many approved vaccine’s in the world are based on m-RNA as it has limited side-effects, faster action (usually starts producing antibody in 1-2 weeks whereas others i.e., DNA, viral vector, etc. can take up to 3-4 weeks). Its action is directed and precise to location (i.e., immunity). Its action is based on action on human brain to stimulate and produce antibody to fight against the virus so some side effects would be felt. Inflammation (fever, headache, body pain or all of the above) would be caused due to the reactions between the stabilizing elements present in Vaccine which would react with the blood while the main reaction (L Histidine and DNA) is occurring. Some stabilizing agents are used like Polysorbate, EDTA, Ethanol, etc. to control the reaction between the main reactions otherwise the reaction cannot be controlled and products of the biochemical reaction would be different and not useful for human body and would not produce antibodies. Another reason for controlling the bio chemical reaction is the control the production of antibodies otherwise the number of antibodies would be more in number and it will also cause problems (duration of side effects will increase, purpose of Vaccine will not be valued and to control the excess number of antibodies we would need to take some other medications, steroids (maybe) to control it).

b)DNA:

In DNA type of vaccine’s it directly transfects a specific antigen-coding DNA sequence into the cells and inducing immunity responses. This are one of the synthetic vaccine’s where we use many stabilizers to stabilize the Vaccine as we artificially involve L Histidine to induce the immunity against the virus. It produces antibodies in 1-2 weeks but the efficacy is not that great but the Vaccine is temperature stable and cold - chain free (i.e., it does not form any side reactions and hence side products are avoided but as it is also not 100 percent so some amount of side reactions occur hence side products are formed and due to that side effects). But DNA type vaccine’s elicite are cytotoxic and humoral immunity (artificially immunity) the titers (efficacy, effectiveness) remains low again and the virus.

c)Live Attenuated Vaccine (LAV):

In LAV (Live attended Vaccine) is based in giving a mild (very small) dose of virus in order to study the reaction between the response of human body against the virus. These is one of the least preferred type of Vaccine but used during medical emergency (it's being used now at the time of corona pandemic, it was a bit used during the 2009 H1N1 pandemic). In this side effects are caused but it tough to say that it caused due to the virus or it's due to Vaccine as the composition of this Vaccine is only the mild dose of virus(COVID virus) and L-Histidine (as this is a DNA component). We don't use any biochemical or biomedical stabilizers in order to stabilize the Vaccine. It's usually inoculated to people who have at least once infected with the virus as their body is a bit known to the virus composition and its characteristics. After its approval its component (i.e., small doses) are administered and used in making viral vector vaccines. But using LAV type of Vaccine is the person who has been inoculated would have side-effects but he would be safe from virus but he can spread the virus most actively than compared to any of the type of Vaccines.

d)Inactivated Virus Vaccine:

In inactivated virus vaccine is based on inactivation of the virus and administrating to the people. It is bit similar to LAV but here the virus is dead and by using in activators we inoculate it but due to the virus is dead there are no such
side effects but people have an average efficacy. But this Vaccine is stable compared to all the types of Vaccine. But as the virus is not alive and not actively participating in producing antibodies or reacting with human body to form the virus transmitted diseases which causes pathogens and causes abnormal behavior which needs treatment. Hence, this Vaccine dies of its effect after nearly 6 months of inoculation we need a booster dose to protect human body from the virus which is widely exposed to the virus.

e) Sub-unit Vaccine:

In sub-unit Vaccine it's composition is based on proteins (DNA molecules (L - Histidine, histamine) it contains purified parts of the pathogen that are antigenic, or necessary to elicit a protective immune response. Due to that it's the safest of all Vaccine and almost it has no side-effects ( if side effects felt also it would be mild fever or headache ) as it's one of the composition is pathogens and as pathogens are present in the Vaccine it does not need any stabilizing agents in vaccine. But as it contains pathogens that are antigenic due to that it's remembrance in human body is doubtful so after the inoculation of Vaccine is done which produces temporary anti bodies and after some months (usually 6 months) it's power would go off and value of vaccines in human body will be of no use. It's one of the best vaccine's developed till date but as its limitations is very lethal so it's not used much but it's components (L Histidine, protein molecules) are used in making the Vaccine (n - RNA based)

f) Viral vector based vaccine:

In viral vector vaccines it uses a viral (COVID -19 virus)(activated form of virus but in very mild quantity and high strong environment) which has Genetic material for coding for desired antigen into receptors host cell as it uses a genetic code for conveying the Vaccine message through receptors hence it’s a specific and target oriented Vaccine hence we don't need any as such stabilizers for controlling the reaction and the side reaction which may cause is highly negligible as it target oriented but it's side reactions is not 100percent not possible as its efficacy us not 100 percentage and it's one of the highly using vaccines as it gives good efficacy with vigorous immune response. But as this is target specific and if a person who had before taking Vaccine was incubated with the virus it may not be valuable or if a person's immunity is quite high then the Vaccine efficacy would come down. But during medical emergency the Vaccine (viral vector) is one of the first to be approved due to the efficacy and it's high specificity and during its 2nd clinical trials it was approved and was using it.

COVID vaccines are a recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike (S) glycoprotein. Following administration, the genetic material of part of corona virus is expressed which stimulates an immune response

The Components of COVID Vaccines are:

- L-Histidine
- L-Histidine hydrochloride monohydrate
- Magnesium chloride hex hydrate
- Polysorbate 80
- Ethanol
- Sucrose
- Sodium chloride
- Ethylene di amine tetra acetic acid (EDTA)

2. Materials and Method

2.1 Fe- EDTA Method:

The chemicals required here are Fe$^{2+}$, Fe$^{3+}$ and Ethylene di amine tetra acetic acid (EDTA).

2.1.1 Analysis

EDTA which bond with Fe$^{3+}$ of Hemoglobin (Blood Component) which is partially Stable at pH 7-7.5 (Our Body’s pH is 7.4) but whereas Fe$^{2+}$ bonds with EDTA which is stable at this ph. As [Fe$^{3+}$-EDTA] is a Stable complex. Due to this bond formation causes side effects i.e., Fever, Headache, etc. As this Bond is not broken down (Fe$^{2+}$ is broken down while Fe$^{3+}$ is not broken) by body and it stays for longer time in body hence it’s Toxic.

2.1.2 Statistical Model

The reaction between Fe$^{3+}$ Fe$^{2+}$ and EDTA is Exothermic and reaction occurs at high temperature (but Fe$^{3+}$ and EDTA is an undesired reaction which forms a Toxic compound). As normal body Temperature at normal condition is 35C which is favorable for this reaction. As with adequate pH and body Temperature suites the formation of the complex [Fe$^{3+}$-EDTA] and the reaction is Exothermic it Increases the body Temperature from Normal to Abnormal (>37.5C). Which is the condition of Fever and if our body's immune system is weak than normal then it causes body pain as rise in Temperature in Organs causes Body pain, joint pain. As Body is in abnormal condition but as our Indian Immune System are generally Strong so it’s usually limited to Fever and sometime body pain and joints pain. The presence of a fever is usually related to stimulation of the body's immune response. Fever can support the immune system's attempt to gain advantage over infectious agents (viruses) which makes the body less favorable as a host for replicating viruses which are temperature sensitive.

2.1.3 Reactions

\[
\begin{align*}
\text{Fe}^{2+} + \text{EDTA} & \rightleftharpoons [\text{Fe} - \text{EDTA}]^{2+} \\
\text{Fe}^{3+} + \text{EDTA} & \rightleftharpoons [\text{Fe} - \text{EDTA}]^{3+}
\end{align*}
\]

2.1.4 Conditions

\[T=37.5C \text{and pH is 7.4.}\]
2.2.3 Thermal due body’s abnormal temperature bring temperature reaction variations temperature as favourable form) helps Fe2+ due a Haemoglobin The 2.2.1 Statistical Model: The Vaccine contains L - Histidine and Blood contains Haemoglobin (Fe2+- Fe3+) which bonds together and forms a temporary bond .The reason for the side effects caused due to vaccines is forming a Chelate bond i.e., between Fe2+ - L-Histidine in presence of ethanol. Ethanol's -OH helps in making the 2-imidazol pyruvic acid (Activated form) and then it forms a Chelate with Fe 2+ and Fe3+(less favourable as it's unstable at pH 7-7.5 and normal Body temperature 35C).

2.2.2 Analysis: As our body maintains Thermal Equilibrium (i.e. our body temperature maintains constant temperature with variations of up to 1 degree Celsius). But when this reaction happens in our body Heat is absorbed in this reaction (as it's endothermic) so our body needs external temperature (it tries to bring back from Atmosphere) to bring back to normal condition While bringing back this temperature we feel fever , headache( As our body is in abnormal condition). But when we take medicine or the body's natural immunity for relief this bond is broken and due to that the temperature is returned to the body for Thermal equilibrium hence the fever, headache is gone.

2.2.3 Reactions (Fe2+ - L-Histidine)

2.2.4 Reactions (Fe3+ - L-Histidine)

2.2.5 Reaction Conditions: T=35C and at pH 7-7.5 Fe3+- L-Histidine: Del H= 25.71+-1.73 KJ/mol Del S= -202.58+/-5.64 J/K/mol Del G= 648.66+/-19.1 KJ/mol Fe2+ - L-Histidine: Del H= 76.19 KJ/mol Del S= 78.79 J/K/mol

2.3 Problems Associated with the formation of the compounds:
Post Vaccinations Trails were conducted where People were asked about any side-effects/ Symptoms. Some people complained about side-effects while some no side-effects. The side effects experienced were:

a)Severe Acute Respiratory Syndrome:
It’s also called as SARS. Its causes due to Coronavirus when it reached the lungs and creates a blockage due to infection. In the process people have breathing issues, which simulates to Inflammation/fever. When people were
inoculated the trail persons also complained about shortness of breath and mild fever. It’s because of the Formation of The Fe- EDTA complex in the blood while the Vaccine has been injected. The Fe-EDTA complex is crystalline in Nature and it dissolves in water to have water of Crystalline (70 percent of human body is made up of water). The complex causes blockage in the lungs which is acute in nature and hence it blocks the air circulation in body causing shortness of breath and by biological reasons for fever we know that if there is some blockage in lung (causing dyspnea) it automatically causes fever.

b) Infections:

When Vaccinations were conducted on a scale of 200 people, 99 people complained about infections. It’s due to formation of L-Histidine and Fe compound. As the complex forms a chelate it’s a Crystalline in nature. When vaccinated the compound forms in the body and in that process, it is infectious in the body and due to the infections caused Body temperature rises (inflammations) and due to presence of water it tries to simulate and reduce the body temperature and in that process the infections spread and increases. This is one of the most experienced and most hazardous side-effects caused as the body will experience fever, joint pains, fatigue.

c) No-side effects:

There were some cases when people said no side-effects were experienced that was due to High immunity strength. High tolerance of body, Exposure of body to highly vulnerable environment and developing resistance. Post vaccinations people experienced no side-effects that could be due to formation of Fe-EDTA complex but the extent of the complex formation was low as the immune resistance was quite high of the individual hence the crystal which formed but was broken down in quick time by the body. Hence there was no blockage (negligible amount of blockage was formed) and so no fever, shortness of breath was felt. As the immunity was high so the extent for the formation of L-Histidine and Fe complex was low and normally the people of high immunity people are warm blooded. So the inflammation is low and hence no joint pains, fever, fatigue are negligible (but some amounts of infections are caused but they are negligible).

3. Results and Discussions

The reaction between L-Histidine and Fe and Fe-EDTA is a Strong reaction and it’s not broken down easily which stays in the body for a long time which is toxic. Due to that the immune system produces chemicals called pyrogens, which trick the brain’s hypothalamus (where the body's thermostat resides) into sensing an artificially cool body temperature.

The brain responds like any good warm-blooded animals would, by knocking the thermostat up a few notches. Blood rushes to the body's core, heating the body overall but cooling the surface - hence the chills. The body's metabolic rate goes up and muscles contract. In short, an abnormal condition (Fever). The main component for inflammation (Fever) in human body biologically is:

Bradykinin (L-Histidine): It's a molecule that plays a crucial role in inflammation. It acts as a vasoactive substance when it reacts with L-Histidine it causes inflammation and swelling as its potent vasodilator. Bradykinin plays a prominent role in inflammation. Bradykinin, along with prostaglandins (Present in the human body) and histamine are mediators of vasodilation, in which the arteriolar smooth muscle relaxes, and in turn, increases blood flow. This increased blood flow causes the rubor, or redness, and calor, or warmth, components of the inflammation process. Bradykinin, along with prostaglandin E2 (PGE2), also plays a role in the sensitization of sensory nerve endings, which causes the dolor, or pain, the component of the inflammation process. Thus in the process of inflammation, Bradykinin causes an increase in vasodilation, and an increase in permeability, and an increase in pain.
Cytokines (Fe L-Histidine): The febrile response is thought to be mediated by endogenous mediators, generically called "endogenous pyrogens." (Due to reaction between Fe - L Histidine) In the classical model of pathogenesis, induction of fever is mediated by the release of pyrogenic cytokines (The Reaction Product) such as tumor necrosis factor (TNF), interleukin (IL)-1, IL-6, and interferon into the bloodstream in response to exogenous pyrogens. These mediators act at the level of the organum vasculum of the lamina terminalis in the central nervous system (CNS), inducing synthesis of prostaglandins, which are the central mediators of the coordinated responses leading to fever.

Prostaglandins: It acts as signals to control several different processes depending on the part of the body in which they are made. Prostaglandins are made at sites of tissue damage or infection (damage or infection due to reaction between Fe - EDTA, Fe - L Histidine) where they cause inflammation, pain and fever as part of the healing process.

Eicosanoid (Fe- EDTA): It's biosynthesis is initiated by activation of Fe(3+)/A2 and release of acetic acid(AA) from EDTA from membrane phospholipids(Present in human body). The AA is subsequently transformed by cyclooxygenase (SOX) and lipoxgenase (LO) (Human body's DNA part) pathways to prostaglandins, thromboxane and leukotriene collectively called eicosanoids. Its production is considerably increased during inflammation. The COX pathway is a major target for non-steroidal anti-inflammatory drugs (NSAIDs), the most popular medications used to treat pain, fever and inflammation.

4. Conclusion

This Paper concludes that the Inflammation (fever) caused due to Vaccines when inoculated is due to the side – reactions occurring in human body. The main reactions which occur to produce the antibodies while side by side other reactions also take place to immunize the body from the virus while the antibodies are being formed as it takes some time (the anti-body formation). Different vaccines have different rate at which the antibodies are formed and it depends on nature of human body to form the antibodies. The extent of side – effects depend on Nature of Human Body while inoculation (Acidic or Basic), Normal Body Temperature of the person (as different human body have different body temperature 35 – 37°C) and immunity of the human body. The heat of reactions, Entropy of reactions and Gibbs free energy play a vital role in inflammation as the Human body which feels the side – effects is a warm blooded (37.5 C) he may have less feel of fever while a human body is cold blooded(35C) may feel more side – effect.

When vaccines are inoculated (Infernors are activated) in the human body the IFN-alpha and IFN-Beta cells get Charged up due to infection which also triggers the NK-cells causing a virus load to occur at a peak. When the NK-cells spike the virus-spe CTLs cells get activated which induces immunity against the virus and in-turn increase in PGE2 in the hypothalamus (This causes the Fever, a spike in temperature). NK cells are also involved in protective mechanism the (clearing the opsonized virus) -mechanism is called ADCC. "The typical ADCC involves activation of NK cells by antibodies in a multi-tiered progression of immune control. A NK cell expresses Fcγ receptors. These receptors recognize and bind to the reciprocal portion of an antibody, such as IgG, which binds to the surface of a pathogen-infected target cell."
The whole process takes some time and this mechanism results in activation of immunity and T-cells. The whole mechanism of humoral and cell-mediated immune (Vaccines) responses to viruses: is due to recombinant hIFN currently being used in humans. Because recombinant hIFN is produced in Escherichia coli, in these experiments we considered contaminating endotoxin as the cause of fever. Polymyxin B, which blocks endotoxin, had no effect on the pyrogenicity of hIFN in rabbits. In addition, hIFN injected into an endotoxin-resistant strain of mice produced fever. The Pain Is Summing due to the pathogenesis of the processes are believed to involve the peripheral and central nervous system. Generally, a stimulus to the nociceptors will be transduced into pain impulses and transmitted by nerve fibers C and Aγ which are first-order neurons. A pain stimulus can be in the form of tissue inflammation which will cause the release of inflammatory mediators such as histamine, prostaglandin E2, and leukotriene which will stimulate nociceptors, and can also be in the form of heat, stretching, and others which also stimulate nociceptors (Pain, fever). The Long time Side-effects of COVID: Symptoms are as markedly heterogeneous as seen in acute COVID-19 and may be constant, fluctuate, or appear and be replaced by symptoms relating to other systems with varying frequency.

Muscle fatigue (MF) is usually short-lasting, reversible. MF can be persistent and more serious when associated with pathological states or following chronic exposure to certain medication or toxic composites. In conjunction with chronic fatigue, the muscle feels floppy, and the force generated by muscles is always low, causing the individual to feel frail constantly. The leading cause underpinning the development of chronic fatigue is related to muscle wasting mediated by aging, immobilization, insulin resistance (through high-fat dietary intake or pharmacologically mediated Peroxisome Proliferator-Activated Receptor (PPAR) agonism), diseases associated with systemic inflammation (arthritis, sepsis, infections, trauma, cardiovascular and respiratory disorders (heart failure, chronic obstructive pulmonary disease (COPD)), chronic kidney failure, muscle dystrophies, muscle myopathies, multiple sclerosis, more recently, coronavirus disease 2019 (COVID-19) and COVID Vaccine.

Muscle fatigue can be another strong reason As Due to COVID (Flu type) it stays for long while if we did a workout or stressed our Vascular Muscles it stays for a short period of Time (appp 1 night) whereas Due to COVID Vaccines the Pain stays for at least 2-3 days depends on how severe your side-effects. As the COVID-Vaccine is Vascular based (Means it's inoculated our hand muscle and not directly in Blood) So due to that Shot it reacts with muscle to produce the pain and Vaccine (Being a Steroid Type Medication) Which Induces the Side-effect (Muscle Pain).

Also, Hyperventilation Can be one of the reasons for Muscle fatigue, the persistence of cardiorespiratory symptoms in survivors of severe COVID-19 can be partly explained by the pathophysiology of organ damage during the initial phase of the disease. The SARS-CoV-2 virus predominantly affects the respiratory system, although other organ systems can be compromised as well. The virus uses angiotensin-converting enzyme-2 (ACE2) receptors in pneumocytes of the epithelial alveolar lining to infect the host, thus causing lung injury. So when inoculated with vaccine it causes severe Fatigue and when administered in Hospitalization (to find out the reasons for
severe fatigue). It may be a long-term disease as the lungs have been damaged.

Also, People who have a tendency to do more Work out (Fitness Freak Type of person) may have lots of joint pains as they tend to stress their muscles more (whereas we need to rest to console the Vaccine as it's a foreign body). Due to that it activates more Pain than normal as there is severe fatigue in the body than normally when they do workouts.

Sir I have answered the questions you propagate to the best of my understanding. Please correct me or include anything which I may have missed out.

The research till now has been on COVID-19 Vaccine on how to produce i.e., m-RNA, DNA based, Viral Vector, etc. and analysis based on how many Biotech Companies is there i.e., Bharat Biotech, Pfizer, Moderna, Oxford, etc. My research is based on how the vaccine bond in our body’s immunity (produces antibodies) which has side-effects (due to side undesired reactions) i.e., it bonds and produces new compound (Temporary). I have done based on Covishield Scope for future is to do for other Vaccines i.e., BioNTech, AstraZeneca, etc. and Develop analysis based on other Vaccines.

5. Declarations

a) Ethics approval and consent to participate:

Not applicable

b) Consent for publication:

Not applicable

c) Availability of data and materials:

The datasets generated and/or analyzed during the current study are available in the Google form repository, [https://forms.gle/2Jiar9dixTwxV6q27].

d) Competing interests:

The authors declare that they have no competing interests

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f) Authors' contributions:

RJ Analyses the theory, LM validated the theory.

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I) Code Availability:

Not Applicable

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