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REVIEW

Pfizer vaccine, questionable efficacy at the expense of safety

LIFE AND BIOETHICS 15_12_2020

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The N. England Journal of Medicine has published the first results of the phase 2/3 trial of Pfizer's Covid-19 Vaccine (called BNT162b2) (https://pubmed.ncbi.nlm.nih.gov/33301246/)

As an advance leak revealed, the new vaccine, which is the first to enter general distribution, boasts excellent efficacy. About 100 days after vaccination, among 18,198 vaccinees there were 8 cases of Covid-19, while among 18,325 subjects who received the 'placebo' (saline solution) there were 162 cases. This breakdown of cases corresponds to 95.0% vaccine efficacy. The cumulative incidence of Covid-19 cases over time between vaccine and placebo recipients began to diverge 12 days after the first dose. The researchers can only be congratulated on this success, which demonstrates if nothing else the great technological capacity achieved in a very short time by biomedical science worldwide and in the USA in particular. Since the end of January, when they became aware of the viral RNA sequence, they have been able to produce the vaccine and test it on thousands of human beings in several stages. The editor writes in a commentary " **This is a triumph**." (https://pubmed.ncbi.nlm.nih.gov/33301245/).

But there are problems, and big ones, that would be dangerous to ignore. To point them out, even in a climate of spasmodic anticipation and at the moment when the inoculations have already started, could be seen as playing the part of the 'perennially disgruntled'. Instead, it is a service to Truth and Science, which develop in the free exchange of ideas and results. It is therefore in everyone's interest, including those who freely choose to be vaccinated. The problems derive essentially from the **haste** with which all the research has been carried out, under enormous commercial and political pressure, and therefore from the fact that we have moved on to the operational phase before the research is completed and we have consistent data on the effectiveness but above all on the safety of the vaccine.

Starting with its efficacy, an initial doubt arises from the fact that there may be a mismatch in the reporting of cases in the two groups (vaccine and saline solution). For practical reasons, the investigators relied on volunteer participants to report symptoms and if necessary present themselves for testing. Subjects who received a saline injection reported significantly fewer symptoms than those who received the vaccine. Considering subjects between 16 and 55 years old, at the first injection pain in the arm occurred in 84% of those injected with the vaccine and in 14% of those who received the saline solution. Other symptoms such as fatigue, headache, joint or muscle ache, and fever appeared more frequently and more severely in those who received the vaccine,

especially after the second dose.

These symptoms are to some extent similar to those of the disease, so it is possible that those vaccinated were less likely to believe that symptoms were due to Covid-19 and therefore less likely to go for tests. Unfortunately, the publication does not state how many swabs were done, nor to whom. It should be remembered that these studies were carried out on several continents, on normal people who were paid to take part, not experts in medicine or clinical trials. In addition, those vaccinated took far more antipyretics than those who received the saline solution (45% versus 13% after the second dose), which may have again distinguished the two groups in the interpretation of symptoms and the use of diagnostic tests. Consequently, it cannot be ruled out that some non-serious cases of Covid-19 in the vaccinees may have been missed because the trialists may have spontaneously resorted to antipyretic treatment, believing the symptoms to be effects of the vaccine. This is not my criticism alone, as it is mentioned in the N. England editorial cited above, and was also raised in a commentary published in the British Medical Journal (https://blogs.bmj.com/bmj/2020/11/27/covid-19-vaccines-where-are-the-data/).

Moreover, important data have not been reported, such as the rate of asymptomatic disease (which could also be assessed in the vaccinated with a quick test for a nucleoprotein other than the spike). Thus, we do not know whether and to what extent the vaccinated have really been 'freed' from the virus, nor whether the vaccine stops contagions.

Let's take a closer look at some aspects, starting with the difference between **relative and absolute** risk. The incidence of Covid-19 among the unvaccinated was 8.84 per 1000. The incidence among the vaccinated was 0.439 per 1000, i.e. 20 times less (which gives an efficacy of 95%), assuming that the results are correct. In other words, a vaccinated person had a 20-fold lower risk of catching the disease during the period in question than a non-vaccinated person. Fine. But how great was the advantage in absolute terms? In absolute terms, for an unvaccinated person, the risk of catching Covid-19 (of any severity) was 162 out of 18,325, which corresponds to less than 1%. In other words: an efficacy of 95% does NOT mean that an unvaccinated person has a 95% chance of getting sick! Looking at the same figure from a public health perspective, according to the numbers presented, it turns out that more than 100 people have to be vaccinated to avoid one case of Covid-19. This is not due to the ineffectiveness of the vaccine, but to the low probability of getting sick. Obviously, if the protection lasted for a long time, e.g. for two or more seasons, the argument would change towards a greater

advantage to vaccinate, but today this cannot be said. Triumphant trumpeting should have been delayed a little longer.

If we then consider the serious cases of Covid-19, they were 1 out of 21,314 vaccinated and 9 out of 21,259 treated with saline solution, with an effectiveness of 88.9%. The difference in incidence is 8 cases per approximately 21,000 vaccinations. Thus, if in relative terms the vaccinated had 9 times less risk than the unvaccinated, in absolute terms the latter had 1 chance in 2,362 (21,259 / 9) of becoming seriously ill. If we want to look at things from another perspective, we can say that **to avoid one severe case of Covid-19 they had to vaccinate more than 2,000 people.** Then, reading the results even more closely, we find a very clear sentence: "No deaths associated with Covid-19 have been observed". Neither among the vaccinated, nor among the unvaccinated. Thank goodness! That's certainly good news. However, the fact is that the vaccine has not saved any lives so far.

Regarding adverse reactions, local ones are basically pain, very frequent but in most cases mild or moderate, with some swelling in 6-7% of cases. Systemic adverse reactions, i.e. throughout the body, occurred in more than 50% of the vaccinees (mainly tiredness, headache and muscular pains, see figure below) in the first week and in more than 25% thereafter. The differences compared to saline were very clear. We read that "Systemic reactogenicity was more common and severe after the second dose than after the first dose, although local reactogenicity was similar after the two doses". This means that the vaccine markedly stimulated the immune system already after the first dose and that the risk of an over-response at the second dose is not negligible. The article states that fatigue and headaches affected more than 50% of the subjects after the second dose of vaccine, and that 'severe' fatigue was observed in about 4% of BNT162b2 recipients, a reaction that is higher than that observed in recipients of boosted influenza vaccines for the elderly. Out of 20,000 vaccinees, 4% make up a group of 800 people who experienced severe general fatigue after the vaccine. Should we ask ourselves a few questions, or would that be considered heresy?

Regarding deaths among the volunteer trialists, the article states: "Two BNT162b2 recipients died (one from atherosclerosis, one from cardiac arrest), as did four placebo recipients (two from unknown causes, one from haemorrhagic stroke and one from myocardial infarction). No deaths were considered by the investigators to be related to the vaccine or placebo". This data is important and deserves some comment. First of all, it should be known that a difference between 4 and 2 in such large groups is not statistically significant, so it means nothing about this eventuality, nor was it an aim of

the study. As for deaths in the placebo group, it is reported that 2 out of 4 deaths were from 'unknown' causes. This is puzzling, because it denotes poor precision in a globally important study. A haemorrhagic stroke and myocardial infarction could actually occur in such a large group of people.

The two deaths after the vaccine raise further concerns, not for the number, which as mentioned above cannot in itself represent a danger signal, but for the diagnosis **('atherosclerosis' and 'cardiac arrest')** and the fact that they have not explained in any way how they excluded correlation with the vaccine. It should be pointed out that there are usually many criteria for ruling out vaccine liability, including biological plausibility, time frame, and prior knowledge of what vaccines may or may not do to large groups of people. But if a vaccine is new, how does one rule out in advance that an adverse event may be related?

'Cardiac arrest' is such a general definition as to be unusable, so one can't even comment on it. Everyone dies of cardiac arrest, it seems. As for 'atherosclerosis', it should be noted that it is a chronic inflammatory and degenerative disease of the arteries; it is the most common disease in high-income countries and can last for decades, even asymptomatic. It manifests in old age with complications, due to many triggering factors, which block blood flow in important organs and can lead to death. Therefore, finding 'atherosclerosis' in a person who died after the vaccine does not rule out the possibility that the vaccine may have been a trigger for the terminal event in a person whose vascular system was made fragile by the chronic disease. It does not prove it, but it does not rule it out, and it does not explain how the researchers ruled it out.

It would be wrong to see this issue as an argument 'against' the vaccine. On the contrary, it has a scientific reason in the current issues related to safety and how to assess the **'causal link'** of adverse events observed after vaccination. This issue is explained in detail in a recent paper of mine published in an international peer-reviewed journal: https://f1000research.com/articles/9-170/v2. In short, it argues that when it comes to 'multifactorial' diseases, an adverse event can occur due to the combination of a predisposition (genetic, or other diseases) with one or more triggering factors, including vaccine. Chronic inflammatory diseases are complex diseases by definition. Therefore, it would not be correct, in principle, to exclude vaccine causality by attributing it to another disease present in the subject, which may have been a

predisposing or aggravating cause for the final event.

This issue is more important than one might imagine, because in the coming months the question of 'causation' will arise, i.e. whether to attribute adverse events occurring after vaccination to the treatment itself or to other conditions already present in the subject. If the method of assessing adverse events were to 'absolve' the vaccine in all cases of 'atherosclerosis', there would be a great and widespread risk of underestimating a danger, especially in the elderly. I hope that the responsible authorities will consider this aspect of the problem with sufficient attention, and I am willing to collaborate (free of charge) if deemed useful and requested.

Finally, the issue that I as a scientist consider most serious. In the discussion, the authors literally write: "Although the study was designed to follow participants for safety and efficacy for 2 years after the second dose, given the high efficacy of the vaccine, ethical and practical barriers prevent following placebo recipients for 2 years without offering active immunisation". In practice, this means **that they end the most important and valuable part of the research prematurely**. This sounds logical because they invoke ethics, but it is not at all. In fact, the research targets not only the efficacy, but also the adverse effects of the vaccine. By stopping the planned study now, we will have no answer to the question that was intended to be answered: whether the vaccine does more good than harm. In practice, the possibility that the consequences of the vaccine on the large population are more serious than those from Covid-19 will remain open forever. Contrary to what they would have us believe, this choice is the least ethical one imaginable, because it also nullifies the efforts made so far. Putting efficacy (debatable, as we have seen) before safety is unethical and unscientific. If this were done for commercial reasons, it would be a disgraceful choice.

I conclude by reiterating my hope that the vaccine will give the best of itself and really help to defeat the pandemic. There is still a long way to go before this happens, and it would be dangerous to delude oneself prematurely that there are no problems. Criticism and opposition, if justified, are healthy in science and medicine. They help to test hypotheses better and to uncover possible errors. This is in everyone's interest.

**** Vaccinologist***