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How can we better prevent polio?

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Abstract

Polio is a potentially deadly and yet preventable disease. A *vaccine* is available but in order to get rid of the disease, this vaccine needs to have larger coverage. Unfortunately, this is not an easy goal in poorer countries. A single shot of polio vaccine is not enough to prevent the disease, and in developing countries, healthcare workers have difficulties reaching their patients more than once. This is why we wanted to develop a vaccine which requires only one injection. We used safe compounds to mimic the current 2-shot schedule and to stabilize the vaccine. Our tests showed promising results, and hopefully, this approach will help with the development of vaccines against other infectious diseases as well.

Introduction

Poliomyelitis, or polio for short, is a potentially deadly disease, caused by poliovirus (Fig. 1). You can get infected with it when you are in contact with another sick person–especially their feces or if you consume contaminated food or water. But what happens when you get the virus? Most of the time people don't have symptoms, but sometimes the virus can infect the nervous system and cause *paralysis*.

Luckily, this disease is preventable – many people all over the world receive a *vaccine* which protects them against the infection. So why is there still polio out there? The polio vaccine is inactivated, and you need more than one injection over a certain period of time to develop immunity and be protected. In some poorer countries, this is not easy to achieve. The healthcare workers often face difficulties reaching their patients more than once.

This is why we wanted to create a polio vaccine which only required one injection. This poses some challenges:

- The vaccine should work just like the 2-injection vaccine
- There are 3 strains of poliovirus (which could mean 3 different vaccines)
- The *stability* of the vaccine can decrease with changes in the body such as temperature or pH.

There are two main types of vaccines – live and inactivated. Usually, with a live vaccine, a single injection is enough. This is because the virus in the vaccine is weakened, but alive. It can propagate (but not harm you), thus causing a strong immune response in the body. The inactivated or "killed" vaccine contains only particles of the virus so it cannot propagate. In order to have a strong immune response our body has to receive two or three injections of inactivated vaccines.

Figure 1:
A little girl with polio
(Photo courtesy of the World Health Organization).

Methods

We encapsulated the viral particles in PLGA – a biodegradable and safe substance, which can release the vaccine in bursts over time. This is key for the single-injection vaccine. The capsule releases the vaccine twice in the body – at the moment of injection and then a month later. To keep the vaccine stable until the second release, we needed to add other compounds to the capsule. We tested three compounds:

- *Eudragit E*
- *PLL*
- *bPEI*

We wanted to see how well these substances protected against different stressors (such as body temperature and pH). Stress factors make the virus proteins *aggregate* (connect together) and then the body doesn't produce effective *antibodies* against them. We put a certain number of killed viruses in different stress conditions and added different concentrations of the three compounds. We then measured how many stable *antigens* remained. This showed us the best candidate vaccines we should test further.

We also wanted to see how these compounds help the body to develop a strong immune response. We used rats to answer this question.

- we injected rats with a usual two-injection vaccine to use as a positive control
- we injected other rats with the best candidate vaccines
- we used rats with no vaccine as a negative control

We then measured the amount of antibody present in the different rats for 24 weeks.

Results

Our tests showed:
For stabilization:

- the vaccine with PLGA only had low efficiency
- Eudragit E and bPEI were great at protecting against lower pH
- Eudragit E and PLL prevented antigen aggregation

This led us to make a vaccine with Eudragit E.

For the release of the antigens:

- PLL helped with the first release of the antigens of poliovirus types 1 and 3
- PLL helped with the second release of the antigens of poliovirus types 2 and 3
- bPEI significantly increased the second release of antigens, especially for poliovirus type 2

This made us formulate an alternative vaccine containing PLL and bPEI in the most suitable concentrations. It stabilized the antigens significantly.

What about the immune response in rats?
When we compared the vaccine with Eudragit E to the control group it was:

- better for poliovirus type 1
- the same for poliovirus type 2
- weaker for poliovirus type 3 (figure 2)

The alternative vaccine induced the strongest response against poliovirus type 3, but was less effective for the other two types.

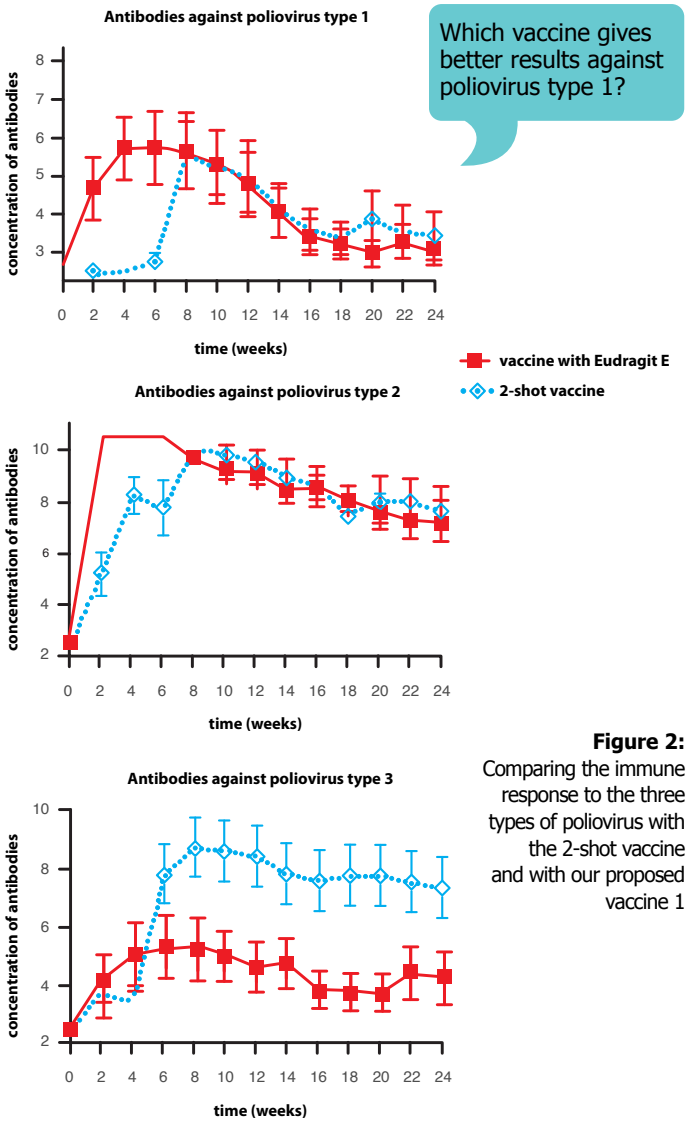

Figure 2: Comparing the immune response to the three types of poliovirus with the 2-shot vaccine and with our proposed vaccine 1

Discussion

We tried different compounds to stabilize the polio vaccine and found out that Eudragit E helped the encapsulating PLGA with the timing of the vaccine release. It was also helpful at preventing antigen aggregation at low pH, which makes it a good stabilizer. While bPEI had similar effects, PLL acted as a physical barrier for antigen aggregation.

The development of a single-administration vaccine would really increase the vaccine coverage – not only for polio but potentially for other diseases as well. Thus our approach may help to control many infectious diseases. Our results are promising and show that the immune response to the different types of poliovirus is different. This further proves how important it is to optimize the vaccine for every antigen.

Conclusion

Have you received a polio vaccine? You can always check your vaccine status by having your blood tested for antibodies against polio. Nevertheless, polio is only one of the diseases that transmit through the so-called *fecal-oral route*. To try and prevent getting any of these diseases in areas where they are present:

- always drink safe water
- always cook your food well
- wash your hands with soap (and clean water) often

Glossary of Key Terms

Aggregation – antigen aggregation - several antigens group together. The body develops antibodies against the aggregate instead of the individual antigen leading to no immunity against the virus.

Antibody – a protein in the blood produced in response to a specific antigen (of a microbe) which protects us from this microbe.

Antigen – a protein or other substance which our immune system perceives as dangerous and produces antibodies against. i.e part of a virus.

bPEI – branched polyethylenimine - a substance used for the delivery of drugs.

Eudragit E – a substance which allows the release of the vaccine in a scheduled manner.

Fecal-oral route of transmission – bacteria or viruses found in the stool of a person (or animal) are swallowed by another person - directly or in contaminated water for instance.

Immunity and immune respons – the ability of the body to recognize and fight a disease so that you don't get sick from it. The immune response is the response of the body against antigen.

Paralysis – the loss of the ability to move some muscles; sometimes even the ability to breathe by yourself.

pH and pH drop – a scale used to specify how acidic (or basic) is a solution. The neutral pH is 7, lower pH means acidic and it's a stress factor for polio vaccine antigens.

PLGA – poly(lactic-co-glycolic acid), a safe biodegradable substance we used as a capsule for our vaccine.

PLL – poly(L-lysine), a substance which helps with the delivery of drugs and vaccines, it's also used as a food preservative.

Poliomyelitis – polio, a dangerous disease which can infect the nervous system and cause paralysis. Man is the only host for this disease. Polio is caused by poliovirus which has three types.

Stability of the vaccine – some stressors, such as body temperature and lower pH, can make the antigens aggregate. Aggregation leads to the production (in the body) of inefficient antibodies as they are directed against the group of antigens, not the individual antigen.

Vaccine – an injection of a killed or weakened pathogen, in order to stimulate the immune system against that pathogen (a pathogen is something that makes you sick). This means that the immune system can recognize those pathogens if they ever come back, and destroy or disable them, preventing disease.

Check your understanding

1. Why does the current inactivated polio vaccine need more than one shot?

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2. Why does the one-shot vaccine need stabilizers?

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3. Is our vaccine able to induce an immune response?

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4. Why is antigen aggregation a bad thing for the vaccine?

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5. (Additional) There is a live polio vaccine which needs only one application. What do you think the possible problem with it is?

REFERENCES

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