

Low pH Hypromellose (Taffix™) nasal powder spray reduced SARS-CoV-2 infection rate post mass-gathering event at a highly endemic community: An observational prospective open label user survey

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Short Report

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Abstract

The city of Bney Brak, Israel, (population 210,000 mostly ultra-orthodox Jews) tops Israel list of COVID-19 infection rate and mortality. In mid-September before the Jewish New Year (an intensive two day gathering for prayers) PCR positivity rates were 17.6% and those climbed to 28.1% two weeks later.

Taffix - is an innovative nasal powder inhaler that creates a protective gel layer over the nasal mucosa and effectively blocks viruses from infecting the nasal cells. Taffix is approved for use in Europe and Israel. In vitro studies demonstrated that Taffix blocks viruses (including SARS- CoV-2) from infecting human cells (<99%). It is well established that the nose is the main gateway of SARS- CoV-2 to the body. Taffix™ was developed as an additional virus protective tool beyond the currently recommended preventive measures.

In a prospective users survey, 243 members of a Jewish ultra-orthodox synagogue community in Bney Brak that participated in the two days holidays prayers (7 hours spent daily in the synagogue) were followed up for the following 14 days to measure the effect of Taffix in this potentially “super spread” (post mass gathering) event . 83 collected and used Taffix throughout Rosh Hashana prayers and for the following two weeks (intention to treat group, ITT) . 81 of them used it regularly as instructed (per protocol, PP) while two used it rarely if at all. The remaining 160 did not use Taffix .

At the end of the two weeks follow up - in the ITT population, 2/83 (2.4%) of the Taffix users and 16/160 (10%) of the Taffix non users were infected. The odds ratio for SARS-CoV-2 infection in Taffix users were 0.22 (0.05-0.99, Mid P exact =0.028), a reduction of 78% (95%CI 1%-95%) in odds of infection. No side effects were reported.

We suggest that Taffix can be an additional powerful tool against COVID19 spread. To our knowledge this is the first time that any measure to prevent infection in SARS-CoV-2 virus, beyond the use of masks. was proven effective.

Introduction

Following a sharp decline in SARS-CoV-2 incidence during May 2020, Israel suffered a gradual increase in the number of cases on June-July and a sharp increase in August[1]. On September 18 2020, Israel was a world leader in the number of new COVID-19 cases per million citizens. The infection rate among its ultra-orthodox communities was double that of the general population. On September 30th there were 23.6 confirmed COVID-19 patients per 1000 citizens in Bney Brak, and a total of 4741 active confirmed cases.

Since the beginning of the pandemic in Israel 18,743 Bney Brak citizens contracted the disease that cost the lives of 80 individuals. (as of September 29 2020)^{Error! Bookmark not defined.}. Of note the mortality rate in Israel is 182 per million citizens while the calculated mortality in Bney Brak is more than double that: 380 per million.

During September, Jewish high holydays are characterized by mass gatherings and prayers. Of special concern as a source of additional spread of the disease were Rosh Hashana (the Jewish New Year) prayers: a two- days holiday that is spent mostly in synagogues and in large family gatherings. In 2020 Rosh Hashana began on the evening of September 18 and lasted for two days ending in large celebrations involving big crowds. This event raised concern as a potential post-mass gathering outbreak.

Indeed, in mid- September just before Rosh Hashana (Jewish New Year) there were about 17.6% positivity rates in the city of Bney Brak, and those actually climbed to 28.1% two weeks later[2]. A similar trend was identified in other ultra-orthodox communities both in Israel and in greater NYC[3].

Viral entry through the nasal mucosa is considered a main mechanism in SARS-CoV-2 infection [4]. Taffix's main ingredient- Hydroxypropyl methyl cellulose, (Hypromellose or HPMC) is a muco-adhesive gel-forming cellulose derivative. Upon reaching the nasal mucosa HPMC is known to absorb fluids and create a micron-sized gel that covers the nasal cells and prevents viruses from engaging with the receptors that are necessary for the viral penetration into the cells [5]. Additionally, Taffix creates a local acidic microenvironment of pH 3.5 on mucosal surfaces, which remains stable for up to 5 hours. An acidic microenvironment in the nose was shown to prevent multiple respiratory viruses such as N1H1 influenza and Rhinoviruses[6] and recently SARS-COV-2[7] from infecting cells.

Taffix™ - is an acidified Hypromellose nasal powder spray inhaler approved for sale and used for prevention of respiratory viral infections. Taffix™ received CE marketing approval (DE/CA09/0760/N18/001) and the Israeli Ministry of Health marketing authorization (Amar- 33010001) and other countries. Taffix is sold in Israel since early July 2020 reaching tens of thousands of users. No reports of adverse events were registered in the post marketing database kept in compliance with regulatory requirement.

To assess real-life effect of Taffix in reducing SARS-CoV-2 infection rates following the mass social gathering in closed environment during the Rosh Hashana holiday, we conducted a prospective user survey at an ultra-orthodox synagogue in Bney Brak, a highly endemic community.

Materials And Methods

Taffix has been tested in two in vitro studies to gauge its effectivity in blocking and disabling respiratory viruses SARS-CoV-2 and H1N1 influenza.

The purpose of the study of the SARS-CoV-2 study was to test whether the Taffix™ can form a protective barrier against this virus. A gel of Taffix™ was formed on a 40 um nylon filter, and then seeded with 10,000 PFUs of virus. An untreated filter, seeded with the same amount of virus, was used as an untreated control. After a 10 minute incubation the bottom of the filters were washed with culture media and then tested for live virus by plaque assay and for viral RNA using qRT- PCR Taffix™ reduced the amount of live viruses by more than 99%, and in most experiments no virus was detected or the amount of virus present

was below the limit of detection of the assay in the undiluted flow through. Using qRT-PCR techniques Taffix™ treatment reduced the amount of viral RNA by more than 4 logs (ref .7) The purpose of the H1N1 study was to test the direct effect of the pH of different Taffix formulations on H1N1 virus' ability to reduce the viability of MDCK cells. MDCK cells were treated with saline, Hypromellose, or Taffix with or without virus. Cell viability was measured using a cell proliferation assay kit (XTT based).

H1N1 virus pretreated with saline for 5 minutes reduced cell viability to 27%. Pretreatment of viruses with Hypromellose alone (pH-6.8) reduced cell viability to 37% while pretreatment of viruses with Taffix for 5 minutes resulted in 88% cell viability, attesting to ability of Taffix to disable aggressive respiratory viruses (ref 7)

We collaborated with a medium sized synagogue community comprising of some 250 members. After a preliminary notification members of the community expressed their interest in using Taffix throughout Rosh Hashana prayers and the following two weeks. Critical to the cooperation of the community members and their individual compliance, was the strong support and encouragement of the spiritual leadership of the community: the Rabbi and the wardens (Gabbaim). Typically, in ultra-orthodox communities – this community is very close knit and its members are well familiar with each other as well as to well known to the leaders of the community. The synagogue serves as the center around which the community day lives revolves. Importantly, it was clarified that Taffix offers an extra layer of protection and does not replace the mandatory use of masks. This was clearly and repeatedly explained to all participants.

Each member was eligible to collect a Taffix bottle at the synagogue the day before Rosh Hashana prayer and received written instruction on the proper usage of the device. Family members residing in the same house hold were also eligible to receive Taffix bottles (one each). Members also committed when they signed up to receive Taffix to use it whenever encountering a large social interaction and reapply it every five hours whenever they were leaving their residence for the following two weeks. Weekly reminders to all participants were sent directly through the community email system and close attention and monitoring was carried out to substantiate the number of confirmed (PCR tests offered freely in the city) new cases in the community.

By the 14 day after the Rosh Hashana holiday the wardens of the synagogue followed up each family with a personal phone interview. Members and their families were asked to report whether they have used Taffix, how often and under what circumstances they used it, and whether there were new cases of COVID-19 infection since Rosh Hashana, Information about the total number of confirmed new COVID-19 cases in the rest of the community was also collected and confirmed. Confirmed case were defined as all SARS-CoV-2 PCR positive cases during days 1-14 of the follow up period PCR testing was offered freely at Bney Brak citizens in that period.

Statistical methods

The analysis of the results was performed first on the ITT (Intent-to-treat) population data (All members who used Taffix) and then on the PP (Per-Protocol) population. (members who used Taffix regularly according to instruction)

The Fisher's exact test for the comparison of two proportions (from independent samples), expressed as a percentage, was applied to compare the contagion rate between Taffix users and none users.

Fisher's exact test is used to calculate an exact P-value for a 2x2 frequency table with small number of expected frequencies.

All tests are two-tailed, and a p-value of 5% or less is considered statistically significant

The data was analyzed using the SAS ® version 9.4 (SAS Institute, Cary North Carolina).

Results

Overall, 243 members of the Synagogue participated in the two days holidays prayers (at least seven hours spent in the synagogue each day in a closed room). The day before Rosh HaShana 113 Taffix bottles were collected. Of the 243 members, 83 (34%), men women and children above the age of 12 years, (as per Taffix indication) reported Taffix use, of which 81 (98%) reported per protocol use instructed before entering a populated area and every 5 hours. Two (2%) members used Taffix “once or twice” throughout the 14 days period. There were no reports of side effects and most users commented on the ease of use and had no problem in adapting the use of Taffix to their daily routine. 160 (66%) members of the community from this population of families, either did not collect the Taffix at all or collected it and did not use it at all, not even once.

Of 243 members of the community, eighteen (7%) were confirmed as new SARS-CoV-2 infections during the 14 days following Rosh Hashana: Among the eighteen new confirmed cases sixteen (89%) of them did not collect or used Taffix, two (11%) collected Taffix but did not adhere to recommended use, that being only once or twice throughout the whole two weeks period. One of them was diagnosed 2 days after Rosh Hashana (possibly exposed prior to the beginning of the survey). All 81 members who used Taffix regularly according to the instruction for use were not infected at all during the study period of 14 days following Rosh Hashana.

In the ITT population, 2/83 (2.4%) of Taffix users and 16/160 (10%) of Taffix non users were infected. The odds ratio for SARS-CoV-2 infection in Taffix users were 0.22 (0.05-0.99, Mid P exact =0.028) and therefore a reduction of 78% (95%CI 1%-95%) in odds of infection.

In the PP population, 0/81 (0%) of the Taffix users and 16/160 (10%) of the Taffix non users were infected. The odds ratio for SARS-CoV-2 infection in Taffix users were 0 (0.00-0.38, Mid P exact <0.001).

Discussion

We conducted a prospective user survey in a densely populated city, during peak epidemic period with high incidence of transmission ahead of what was perceived to be a super-spreading event during the Jewish Rosh Hashana prayers. Users reported no adverse effects and a substantially lower infection rates compared with persons from the same community with similar exposure. This significant reduction despite high risk exposure suggests significant effectiveness of Taffix in prevention of SARS-CoV-2 infection and reduction of above 4 fold in the risk of infection. Of note in this time period the number of new cases in the city of Bney Brak increased by 1.6 folds as positivity rates went from 17.6% to 28.4

Taffix is an acidified Hypromellose powder nasal spray. Upon reaching the nasal mucosa Taffix absorbs water and creates an even micron-sized gel that lasts about 5 hours. This gel creates low pH microenvironment on the nasal mucosa that was proven to prevent viruses from reaching nasal cells and infecting them. In the context of the SARS-CoV-2 epidemic it has been proven that cells of nasal mucosa are the main gateway of viruses into the body and the need to protect the nose is now widely accepted. Taffix is commercially available both in Israel and in Europe as well as other countries in South America and Asia. Based on prior in vitro studies conducted by the developers that showed high viricidal activity of the Taffix we conducted a prospective users survey to gauge the real life effect of Taffix in preventing further outbreak of COVID 19 disease before an event that involved mass gathering of people.

Our results could be influenced by selection bias whereby people who were more concerned about the possibility of infection would choose to use any additional protection offered to them and might be more careful in observing social distancing and use of masks.

While this certainly is a possibility several points should be considered: 1. At this synagogue members could not enter or remain indoors without properly wearing a mask throughout the whole of the services. The prayer room was divided to “capsules” and every effort was made to prevent mingling of people beyond their allocated capsule. 2. Even in countries where the use of masks and social distancing was adhered to and enforced- the infection rate dropped dramatically but did not reach anything near zero infection rate– attesting the relative but not absolute protection of these measures [8]. 3. On a community level even reducing infection rate among people who are more aware of the risks and are not fully protected due to the limitation of the current safety measures and extremely high prevalence in the community- can significantly lower the numbers of patients and the risks associated with contracting the disease. 4. These results suggest further that Taffix provided protection to people who used it as instructed, not only in the community gathering but also at home, where they did not wear a mask, even when they had an infected family member leaving in the same household.

Additional limitation of this user survey might be the relatively small size of the community and lack of information on the different demographics of the ITT and the non-users populations. These are inherent to the use of post marketing survey. Obviously, a prospective clinical study will enrich our understanding of the relative efficacy and the specific circumstances where Taffix will be most efficient in preventing infection. That being said the results of this user survey indicate that among users of Taffix there was a significantly lower infection rate with SARS-CoV-2 infection.

Conclusion

Our prospective user survey showed lower SARS-CoV-2 infection rates in Taffix users during a high risk mass gathering. No adverse events were reported. Further evaluation by controlled clinical trials is warranted to confirm its findings and define ways to encourage better compliance.

To our knowledge this is the first time that any measure to prevent infection in SARS-CoV-2 virus was proven effective beyond the use of masks. Given the excellent safety profile of Taffix and its statistically significant efficacy in preventing infection following what is defined as high risk infection event - it seems that this additional layer of protection can significantly reduce the risks of infection and may enable people to resume some part of their daily routine more safely. While many countries in the world are still struggling to control the epidemic and others are nearing a second wave and additional lockdown- these findings could indeed raise some hope and be added to our meagre arsenal against the SARS-CoV-2.

Declarations

Since Taffix is an approved and commercially available product in Israel- there was no need to get Ethics committee approval for such a survey. That said Nasus made sure that all participants signed a form explaining the correct use of Taffix and their consent to report infection cases.

Conflict and funding:

DM and TL are employees of Nasus Pharma. BM conducted Nasus Pharma funded preclinical research at the University of Virginia.

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Identifying airborne transmission as the dominant route for the spread of COVID-19

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