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Effects of Antioxidant composition Twendee X on side effects of SARS-CoV-2 mRNA vaccine

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Abstract

To combat the SARS-CoV-2 pandemic, booster doses of the SARS-CoV-2 mRNA vaccine, developed by several pharmaceutical companies, are currently being administered worldwide. However, the emergence of adverse reactions has been a problem associated with this. Lipid nanoparticles (LNPs) are used to protect the mRNA used in the vaccine, but they have strong inflammatory effects, which have been reported to contribute to adverse reactions. As inflammation is a signal of high oxidative stress, it was hypothesized that reducing oxidative stress could lead to symptomatic relief of adverse reactions. TIMA Tokyo Ltd. conducted a web-based survey of people suffering from vaccine adverse reactions, and participants were provided with the antioxidant composition Twendee X (TwX) free of charge. In this survey, participants self-reported the severity of eight major symptoms of adverse reactions (fatigue, breathing difficulty, chest pain, smell and taste disorders, headache, brain fog, joint pain, and dizziness) on a six-point scale at the time of participation and one month after taking TwX. In this interim report, severity scores for all symptoms were significantly reduced. These results suggest that adverse reactions of vaccines are caused by increased systemic oxidative stress and that antioxidants may help alleviate these symptoms.

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Abbreviations: COVID-19, coronavirus disease 2019; LNP, lipid nanoparticle; TwX, Twendee X.
Key words: COVID-19, SARS-Cov-2, vaccine, Twendee X, anti-oxidative effect

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Introduction

During this COVID-19 pandemic, a growing problem worldwide is the increase in severe cases and subsequent deaths due to SARS-CoV-2 infection. To address this issue, several pharmaceutical companies have developed their own SARS-CoV-2 vaccines. However, rapid mutation of SARS-CoV-2 over the past two years, and although the newer strains tend to have milder symptoms and lower mortality rates, the high infection rate has led to the recommendation of not only one or two booster vaccinations, but also a 3rd and possibly a 4th. A corresponding problem is the occurrence of various adverse reactions. Current SARS-CoV-2 vaccine uses mRNA, however, mRNA degrades easily due to enzymes that degrade RNA. Lipid nanoparticle (LNP) is used to protect the breakdown of mRNA, however LNP has strong inflammatory properties, and it has been reported that this may be the source of the adverse side effects of the vaccines[1] . Since inflammation signals high oxidative stress, reducing oxidative stress in patients after they receive SARS-CoV-2 vaccine may help alleviate adverse reactions. In this chapter reports the results and discussion of a questionnaire survey conducted by TIMA Tokyo Inc. on the symptoms of patients suffering from adverse reactions to vaccines before and after taking a one-month dose of Twendee X, an antioxidant blend.

Materials and Methods

Antioxidant Formula

The formula Twendee X (TwX) (manufactured and distributed by TIMA Tokyo Co., Ltd.) was used in this study. TwX is an antioxidant supplement containing eight kinds of active ingredients namely: vitamin C, L-glutamine, cystine, coenzyme Q10, fumaric acid, succinic acid, niacin, and vitamin B2 [2,3]. It has been externally certified that there are no side effects in the safety tests required for pharmaceutical products (preliminary toxicity test (Ina research test number: GL43080), chromosome aberration test (Ina research test number: BV07158), toxicity test (Ina research test number: BV07156), mutation test (Ina research test number: BV07352), and side effects in human clinical trials (Ina research test number: NRP 07-001)). TwX reduces oxidative stress in the cell and mitochondria by 45- 63% and increases superoxide dismutase by 60-147%. Also, it is three times more powerful, than typical antioxidants such as vitamin C, at scavenging hydrogen peroxide, a powerful oxidizing agent. TwX is also 2.5 times more effective than a similar concentration of vitamin E (0.23 mg/ml). Additionally, TwX has been proven to be an effective dietary supplement to aid in the prevention of dementia [4] based on a study conducted by Japan Society for Dementia Prevention.(JSDP). This conclusion is based on the results of a multicenter, double-blinded, placebo-controlled, prospective interventional clinical trial using TwX in a sample of Japanese, aged 65-85 years, with mild cognitive impairment (MCI). The TwX used in this study was kindly donated by TIMA Tokyo Ltd. The patent and trademark for TwX, and the data used in this report are the property of TIMA Group (Liechtenstein). The data in this report was obtained online and is being used with permission from TIMA Tokyo.

Subjects and questionnaire

To date, Pfizer-BioNtech and Moderna SARS-CoV-2 vaccines are the only ones approved to be administered in Japan. Patients in this study were not asked to declare which vaccine they received. At the time of enrollment in this study, participants were asked to visit TIMA Tokyo's website and self-report the time lapse from vaccination to onset of symptoms, the duration of symptoms, and the severity of each major symptom on a six point scale, with zero being no symptoms, and five being severe symptoms (Table 1). After one month of taking TwX, the participants were asked to self-report the severity of each major symptom again on the 6-point scale. To avoid any bias, the pre-treatment data was not shown at the time of the post-treatment reporting. The data was collected by TIMA Tokyo Ltd. with the consent of the participants, and the data was made available online by TIMA establishment (URL:https://www.twendee.com/long-covid-and-twendee-x). TIMA establishment granted permission for secondary use of this data to the authors of this paper only.

Table 1: Questions asked in the questionnaire

Questions	Options
How long did you experience your symptoms?	1-2 weeks, 2-4 weeks, 1-3 months, 3-6 months, over 6 months.
How long did it take for the symptoms to appear?	Immediately, Within 3hrs, Within 6hrs, Within 12hrs, Within 24hrs, Within 48hrs, >48hrs later.
What was the severity of the following symptoms?	
1. Fatigue	0 (None), 1, 2, 3, 4, 5 (Severe)
2. Breathing difficulty	0 (None), 1, 2, 3, 4, 5 (Severe)
3. Chest pain	0 (None), 1, 2, 3, 4, 5 (Severe)
4. Smell & taste disorders	0 (None), 1, 2, 3, 4, 5 (Severe)
5. Headache	0 (None), 1, 2, 3, 4, 5 (Severe)
6. Brain fog	0 (None), 1, 2, 3, 4, 5 (Severe)
7. Joint pain	0 (None), 1, 2, 3, 4, 5 (Severe)
8. Dizziness	0 (None), 1, 2, 3, 4, 5 (Severe)

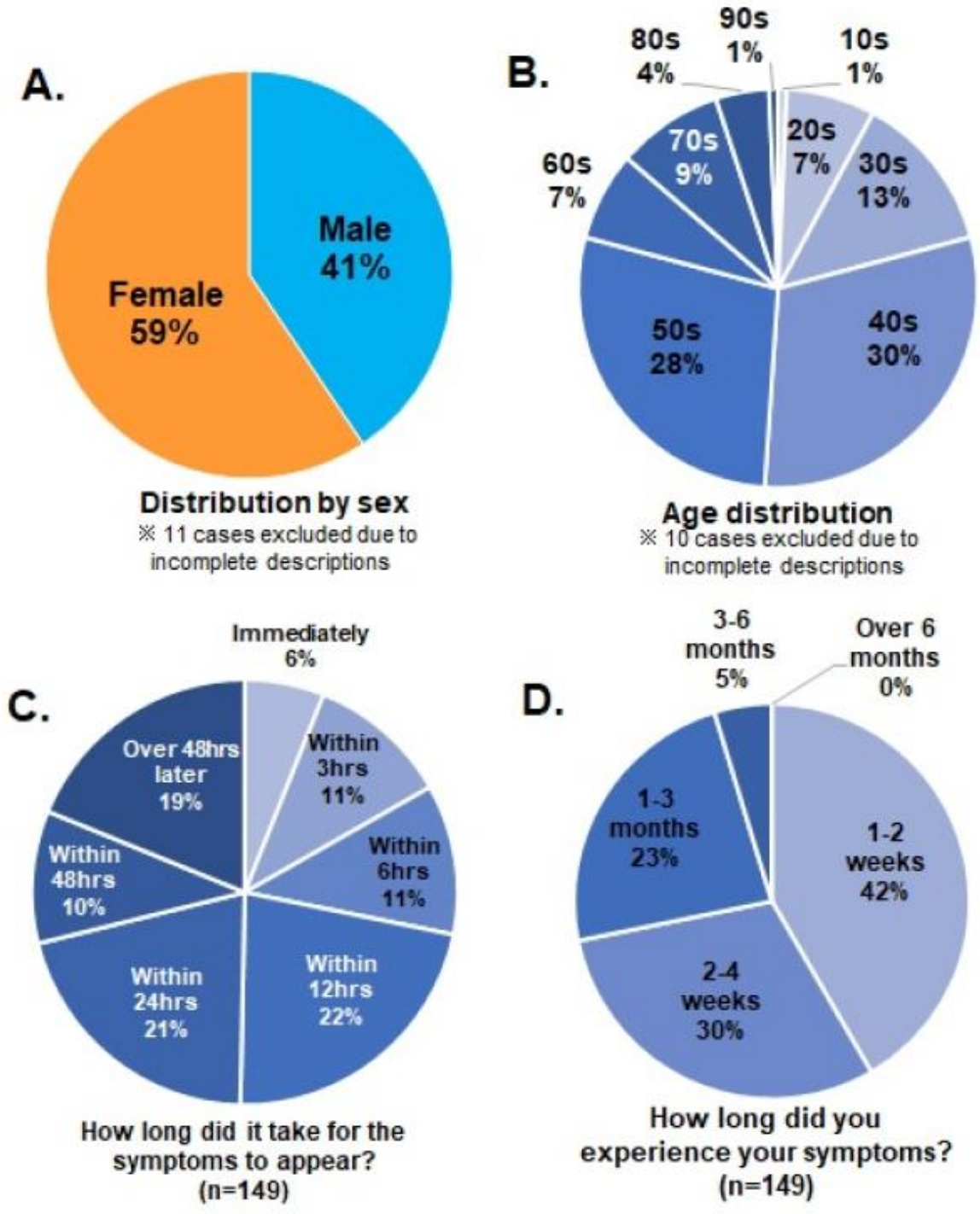

Fig. 1: Patient Characteristics & Symptom Distribution

Results

In the interim report (compiled between September 2 and October 18, 2021), 149 valid responses were received. Sixty percent of respondents were female (Fig .1A). In terms of age, the largest group consisted of individuals in their 40s (30%). This group combined with respondents in their 30s (13%) and 50s (28%), accounted for more than half of all respondents (Fig. 1B). Adverse reactions occurred in some individuals as early as immediately after vaccination, 22% had symptoms occur within 12 hours, and 21% with 24 hours; these two groups accounted for nearly

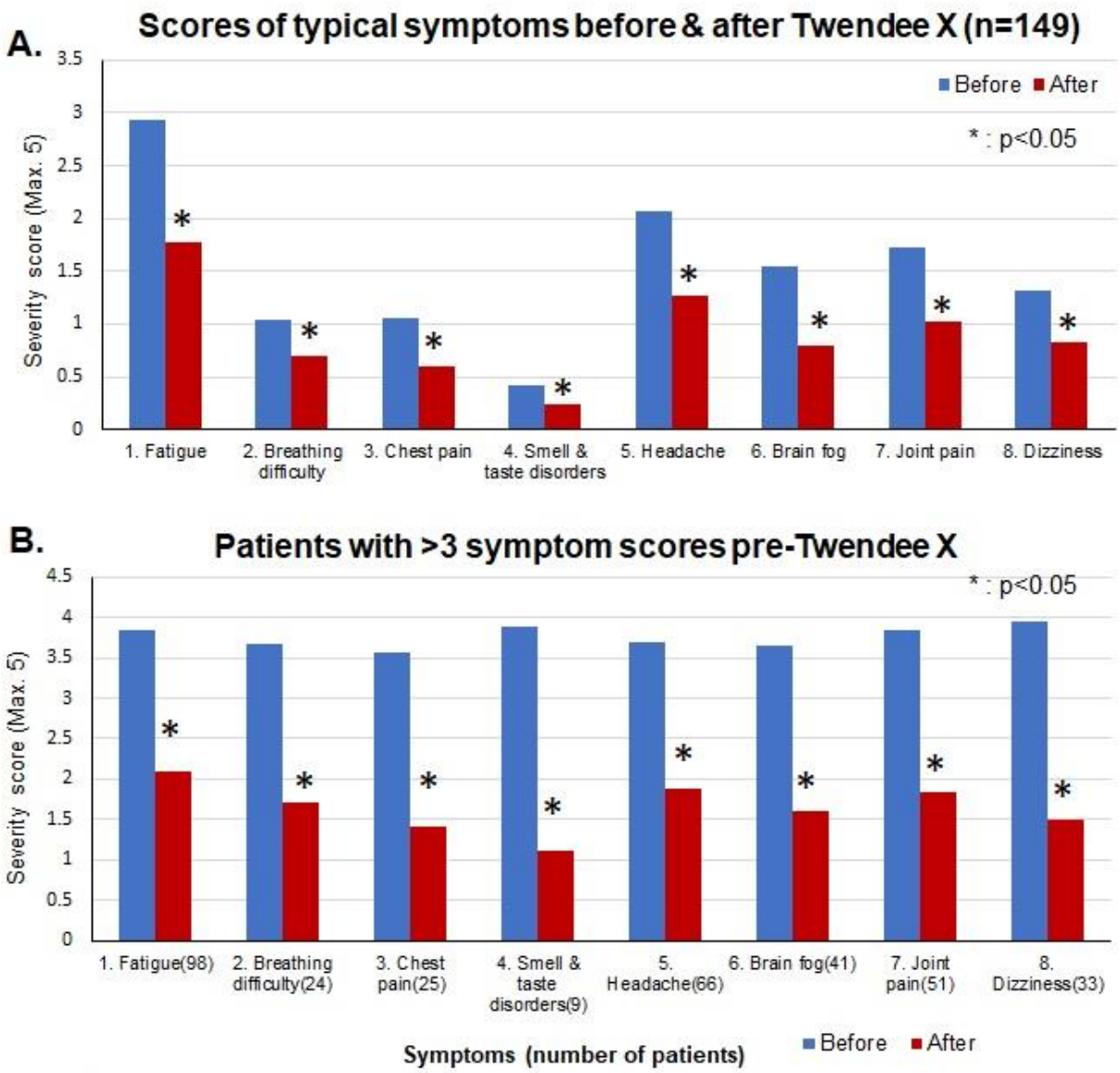

Fig. 2: Symptom Severity Scores Before and After Twendee X

half of all cases. Twenty percent experienced onset of symptoms after 48 hours (Fig. 1C). The most common duration of symptoms before taking the TwX formula was 1 to 2 weeks (42%), next 2 to 4 weeks (30%) and 1 to 3 months (23%) (Fig. 1D).

In the questionnaire, the main adverse reactions symptoms were listed as fatigue, breathlessness, chest pain, distortion of taste/smell, headache, brain fog, arthralgia and dizziness, and the results of the symptom scores before and after taking TwX were tabulated by symptom (Table. 1). The most common complaints before taking TwX were fatigue, followed by headache, joint pain, brain fog, dizziness, chest pain, breathing difficulty and distortion of taste/smell. The overall mean symptom scores (n=149) before and after treatment showed a significant decrease in all symptoms during the first month of treatment with TwX (Fig. 2A). In particular, the mean score of the participants with relatively high severity of illness, who responded with a score of 3-5, was less than half of the pre-treatment score in all cases ($p<0.05$) (Fig. 2B). Comparing the distribution of all scores by case before and after taking the TwX, the percentage of patients with "no symptoms" increased, as symptoms were reduced after one month of taking TwX for all symptoms (Fig. 3).

Discussion

This study shows that adverse reaction symptoms after SARS-CoV-2 vaccination can present

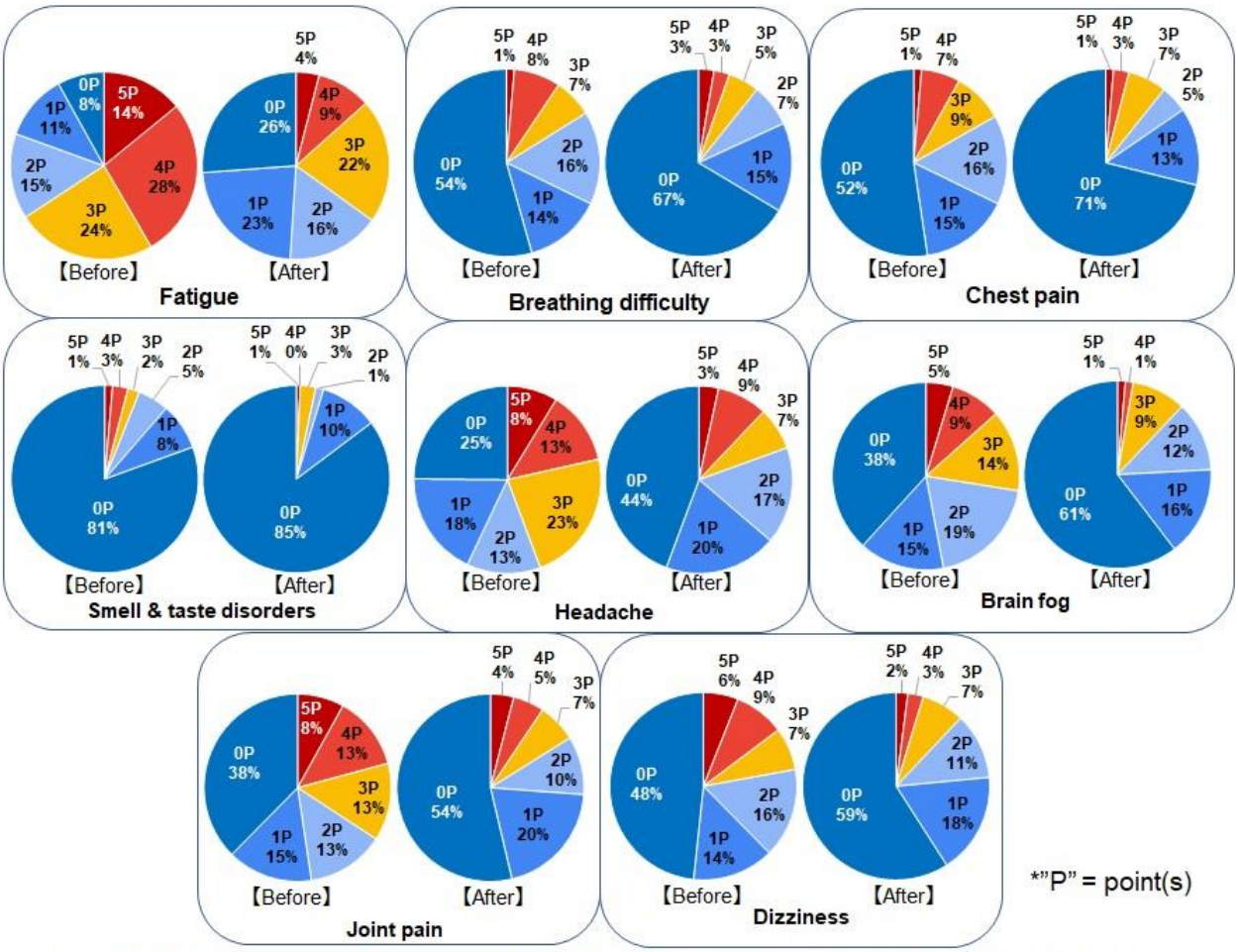

Fig. 3: Distribution of symptom Severity Scores Before and After Twendee X

simultaneously with multiple symptoms regardless of severity. Local symptoms include headache, brain fog and pain in the arm the vaccine was received. However, relatively systemic symptoms such as malaise, arthralgia, fever, shingles, urticaria and sleep disturbance are more common, suggesting that the SARS-CoV-2 vaccine affects the whole body. This study clearly shows that administering TwX, as an antioxidant for one month to patients who received SARS-CoV-2 vaccine, led to symptomatic improvements in a wide range of adverse symptoms. This suggests that patients' adverse reactions may indeed be caused by an increase in oxidative stress stemming from the SARS-CoV-2 vaccine.

The pseudouridine-modified mRNA-LNPs used by Pfizer-BioNtech and Moderna in their SARS-CoV-2 vaccine cause an inflammatory response, either by the LNPs alone or in tandem with the mRNA. It has been reported that this inflammatory response is triggered by the infiltration of neutrophils, independent of the method of administration. Inflammation occurs when the immune system triggers neutrophils and other leukocytes to scavenge bacteria and viruses through the release of reactive oxygen species (ROS). Excess ROS increases oxidative stress, leading to a vicious cycle of further inflammation. This suggests that LNP-induced inflammation causes adverse symptoms by increasing oxidative stress throughout the body, and our results show that antioxidant treatment, such as TwX, may alleviate these symptoms.

mRNA SARS-CoV-2 vaccines induces spike proteins that stimulate the immune system to produce protective antibodies. However, it is not known whether this spike protein is also associated with adverse reactions to the vaccine. As increased oxidative stress leads to decreased immunity, urgent measures should be taken to prevent the onset of diseases in patients after SARS-CoV-2 vaccination due to compromised immunity. The results of this questionnaire survey will assist in the prevention and treatment of future adverse reactions to the SARS-CoV-2 vaccine.

Conflicts of interests

The authors disclose no potential conflicts of interest.

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