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Development of a New Treatment for Lung Diseases, Mainly Interstitial Pneumonia, Using Platinum-Palladium: A Pilot Study

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Abstract

Interstitial pneumonia is a general term for diseases in which inflammation occurs mainly in the interstitium of the lung. It is also pointed out that interstitial pneumonia reduces alveolar function and makes it difficult to take in oxygen through inspiration, causing symptoms such as dyspnea and coughing, which may eventually lead to respiratory failure. At present, there is no effective treatment, and only conservative treatment exists. This time, we report that the therapeutic effect was confirmed in patients with interstitial pneumonia who took platinum palladium. In this case, improvement tendencies were observed in patients with Idiopathic pulmonary fibrosis (IPF), but improvement tendencies were also observed in many other lung diseases. In order to explore the mechanism, AMPK was measured at the in vitro level, and blood KL-6 and hydrogen peroxide levels in the patient were measured at the in vivo level. AMPK values were significantly elevated by more than 800%, and KL-6 and hydrogen peroxide levels were also significantly decreased by drinking platinum palladium. Platinum palladium exhibits a strong antioxidant effect and is the only substance in the world that can approach all four types of active oxygen. In addition, when it was actually administered to patients, there were cases of dramatic improvement, and it was confirmed that KL-6, a parameter of lung function, decreased in 16 out of 32 patients, and furthermore, oxygen inhalation was completed. Patients were also seen. It was suggested that increasing the number of cases in the future may help improve interstitial pneumonia.

Keywords: interstitial pneumonia; platinum-palladium; functional nutritional water; KL-6; AMPK; hydrogen peroxide; case improvement; oxygen inhalation

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1. Introduction

The alveoli are covered with pulmonary arteries, pulmonary veins, and capillaries, and "gas exchange" takes place, exchanging oxygen needed by the body for carbon dioxide that is no longer needed. The "interstitium" exists in the part called the alveolar wall that is on the outside of the alveoli. Interstitial pneumonia is a general term for diseases in which the interstitium becomes inflamed and fibrotic due to some cause [1].

Currently, interstitial pneumonia is classified according to the cause as follows [2–7].

- Idiopathic interstitial pneumonia

The medical term for the inability to identify the cause of onset is "idiopathic". As the name suggests, idiopathic interstitial pneumonia is a disease that develops with unknown causes, and it is said to account for 80 to 90% of interstitial pneumonia patients.

- Autoimmune interstitial pneumonia

This is interstitial pneumonia that occurs in conjunction with autoimmune diseases, mainly collagen diseases. It develops as one of the immune abnormalities in which the immune system attacks its own cells.

- Drug-induced interstitial pneumonia

It has been pointed out that interstitial pneumonia is more likely to develop due to the influence of anticancer drugs and other therapeutic drugs.

- Occupational/environmental interstitial pneumonia (hypersensitivity pneumonitis)

This type of interstitial pneumonia develops when foreign substances, such as dust, mold, pet hair, and chemicals, are inhaled due to the influence of occupation or lifestyle.

- Interstitial pneumonia caused by other factors

This type of interstitial pneumonia includes pneumonia caused by the influence of eosinophils, a type of white blood cell, and sarcoidosis, which causes inflammation in cells throughout the body.

In all types of interstitial pneumonia, the interstitial pneumonia that has chronic inflammation gradually hardens. When it progresses to a state called fibrosis, it affects the supply of oxygen and the excretion of carbon dioxide, which are essential for maintaining life, and the entire body becomes oxygen-deficient, leading to shortness of breath, coughing, and difficulty in breathing.

In this study, we investigated the possibility of new treatments, particularly for patients with idiopathic pulmonary fibrosis (IPF). In interstitial pneumonia, inflammation gradually causes the fibrosis of the alveolar walls [8] and increases pulmonary surfactant protein-D (SP-D) levels [9,10]. As lung function declines, oxygen supply becomes difficult, causing coughing and shortness of breath, and ultimately leading to respiratory failure and death [11]. As of now, there is no effective treatment, and steroids and other treatments for interstitial lung disease are the only symptomatic treatments [12].

On the other hand, COPD (chronic obstructive pulmonary disease) is a chronic respiratory disease that progresses irreversibly and is characterized by inflammation and destruction of the alveoli due to smoking and environmental chemicals [13,14]. As with interstitial pneumonia, there is no effective treatment for COPD, and only symptomatic treatment is applicable. Symptomatic treatments include conservative oxygen inhalation, maintenance of ADL, and maintenance and improvement of QOL [15]. According to the WHO, COPD is the third most common cause of death in the world, so measures to combat it are urgently needed [16]. COPD is also said to be a possible background risk for lung cancer, so measures must be taken [17]. Until now, the main treatments for COPD have been smoking cessation, antioxidants, dietary therapy, and alternative therapies, but these have been aimed at slowing down the disease's progression [18]. In our clinical experience, approximately 40–50% of patients with COPD have shown improvement in symptoms after administration of platinum-palladium. Although COPD was not directly studied in this study, it is possible that it may improve respiratory disease. Although no data have been collected yet, when platinum-palladium was administered to COPD patients, some improvement was observed, so this report was made. In this study, because it was expected that the treatment would be effective for interstitial pneumonia, cases were examined as

a pilot study from multiple perspectives. For these reasons, we expected that the same therapeutic effect would be seen in interstitial pneumonia, so we examined cases.

Platinum-palladium is generally available as a soft drink (functional nutritional water), but this is a colloidal solution of platinum and palladium mixed at a ratio of 1:3 (Figures 1 and 2). It has also been confirmed to induce apoptosis in stomach cancer and colon cancer, and is the world's first functional nutrient water that is expected to have various effects, including activating immune cells (unpublished).

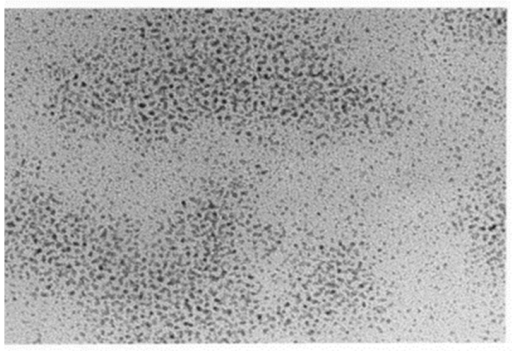

Figure 1. Platinum colloid.

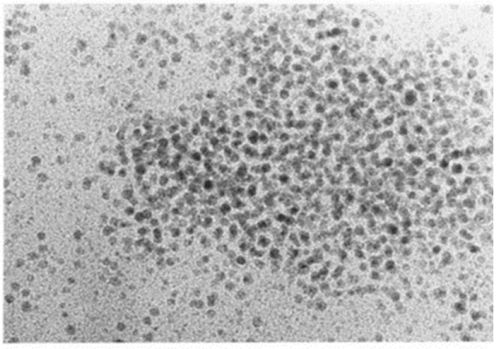

Figure 2. Palladium colloid.

Platinum is a chemically very stable element and is used for various purposes. In the medical field, its complexes are used as anticancer drugs [19]. Other uses focusing on the antioxidant properties of platinum have been reported [20]. Palladium is also one of the platinum group elements, and is widely used in industrial materials and dentistry, and in Japan, it is also treated as a food additive [21,22]. It is known that platinum causes a reduction reaction, and when palladium is added to it, it causes a reduction reaction again [23]. This time, the mixture of platinum and palladium is used in various situations [24]. Based on the chemical reaction and various properties of platinum and palladium, the mixture of platinum and palladium is expected to be useful as a material with sustained antioxidant properties compared to platinum alone [24]. Furthermore, it is known that platinum palladium moderately removes all four types of active oxygen [25]. According to a literature survey, there is no other substance that can remove all four types of reactive oxygen species (generally superoxide, hydrogen peroxide, hydroxyl radical, and singlet oxygen [26]). In addition, platinum-palladium is considered to have a low absorption rate in the intestinal tract due to its colloidal nature [27,28]. It is possible that platinum-palladium may act as a catalyst and activate AMPK (AMP-activated protein kinase) at the cellular level in the digestive tract, thereby contributing to the improvement of symptoms and lesions of interstitial pneumonia and COPD. In this study, we reported cases and measured blood KL-6 [29] and hydrogen peroxide levels [30] in patients with interstitial pneumonia and

COPD. At the same time, we confirmed whether platinum-palladium activates AMPK at the in vivo and in vitro levels.

2. Materials and Methods: A Case of Interstitial Pneumonia Improved

2.1. Patient

- 90-year-old male.
- Height 172.3 cm, weight 68.3 kg, body surface area 1800 m^2.
- Smoking history: None.
- Diagnosis: Interstitial pneumonia.
- Age at onset of interstitial pneumonia: 85 years old (as of 2020)
- Underlying diseases: None.
- Platinum-palladium intake: 18 mL/day (6 mL/1 vial × 3 vials).
- Duration: 44 months.
- Drug treatment: None.
- Oxygen inhalation: None.

2.2. Progress

In daily life, the patient walked 2–3 km every day to maintain and improve his health. No smoking history, alcohol history. Suddenly, frequent coughing was confirmed, and cough suppressants were prescribed, but there was no sign of improvement. When he returned to the city hospital for a follow-up visit, chest X-rays and other tests showed findings specific to interstitial pneumonia, and he was diagnosed with interstitial pneumonia. His doctor told him he had two years to live. His condition gradually progressed, and he experienced difficulty breathing even when performing everyday activities such as climbing the stairs at home or going to the toilet, and he would often collapse. He lost the will to move, but by taking platinum-palladium, his respiratory function improved on the 18th day, his coughing almost disappeared, and his difficulty breathing decreased. At his final visit, he had improved to the point where he was able to resume walking. However, during a period when he temporarily stopped taking platinum-palladium, he experienced difficulty breathing again.

3. Measurements at In Vitro and In Vivo Levels

3.1. AMPK Measurement

Examination of AMPK activity by platinum-palladium.

In this experiment, the aim was to measure activity at an in vitro level without using humans. The reason for this is that in order to observe the time-dependent AMPK activity of platinum-palladium, if humans are used, AMPK activity will change due to eating and sleep, so the experiment was performed using cell cultures that can be measured under certain conditions. Using the CycLex® AMPK Kinase Assay Kit (MEDICAL & BIOLOGICAL LABORATORIES Co., Ltd., Tokyo, Japan), AMPK activity was examined in the platinum-palladium addition group (final concentration 1%). The PBS addition group was used as a control. Since the kit's instructions stated that measurements were performed using breast cancer cell lines, a comparative evaluation was performed using the purchased human breast cancer cell line (MCF-7). In addition, in order to measure the current activity of AMPK in this kit, three flasks were prepared, and AMPK activity was confirmed 1 h, 12 h, and 24 h after addition. In addition, the evaluation was performed using statistical processing software (IBM SPSS Statistics Ver. 29) and, since there was no correspondence, a statistical evaluation was performed using the Mann–Whitney U test. The investigation of AMPK activity was conducted by platinum-palladium.

3.2. Measurement of Blood KL-6

Study of KL-6 fluctuations due to platinum-palladium.

This study involved 16 patients (hereafter referred to as subjects) who visited Hino Kosei Clinic, were diagnosed with idiopathic interstitial pneumonia, and agreed to participate in this study. As this was a pilot study, no control group was set up. KL-6 was measured before and after administration and compared. The evaluation was performed using statistical software (IBM SPSS Statistics Ver. 29) with the paired *t*-test.

KL-6 was measured by enzyme immunoassay (EIA) as per the standard method, with a standard value of less than 500 U/mL [31,32].

3.3. Measurement of Blood Hydrogen Peroxide (Figure 3)

Study of changes in hydrogen peroxide due to platinum-palladium.

This study included 12 subjects (hereafter referred to as subjects) who visited Hino Kosei Clinic and agreed to participate in this study. Each subject was given platinum-palladium for 28 days (4 weeks). The subjects were given three vials in the first week, two vials in the second week, and one vial in the last 2 weeks. Hydrogen peroxide was measured before and after administration and compared. In addition, the results were statistically evaluated using a paired *t*-test with statistical processing software (IBM SPSS Statistics Ver. 26).

Qualitative measurement of hydrogen peroxide was performed using the peroxidase-diaminobenzidine method.

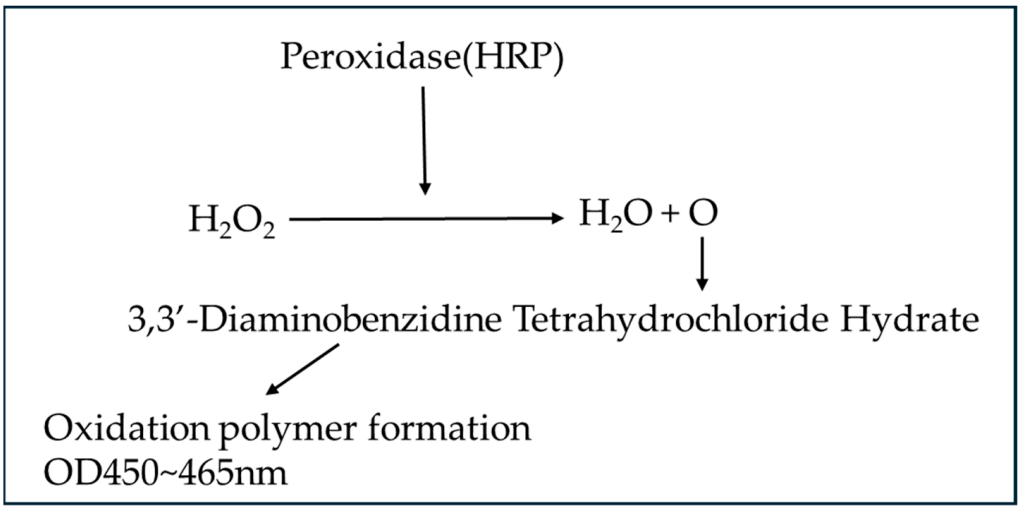

Figure 3. Hydrogen peroxide measurement principle.

3.4. Study on the Effect of Platinum-Palladium on Symptom Improvement in Patients with Interstitial Pneumonia

A total of 32 patients with interstitial pneumonia were given platinum-palladium for one to three months, three vials for the first week, two vials for the second week, and one vial for the last two weeks, and clinical judgment was made. In this study, the subjects were patients with KL-6 > 500 U/mL, crepitus + in breath sounds, and + in X-ray reading. It should be noted that since this is a pilot study, no control group was set up.

4. Results

4.1. AMPK Measurement

To measure the activity of MPK, platinum palladium was administered to MCF-7, and the percentage was calculated from the absorbance, with the following results being

obtained. With the control group taken as 100%, it was confirmed that the activity had increased significantly in all groups at a significance level of 1%. (Table 1 and Figure 4)

Table 1. AMPK activity when compared to the control group (100%).

1 h		**12 h**		**24 h**	
Cnt	Pt:Pd	Cnt	Pt:Pd	Cnt	Pt:Pd
100%	809.80%	100%	763.92%	100%	886.74%

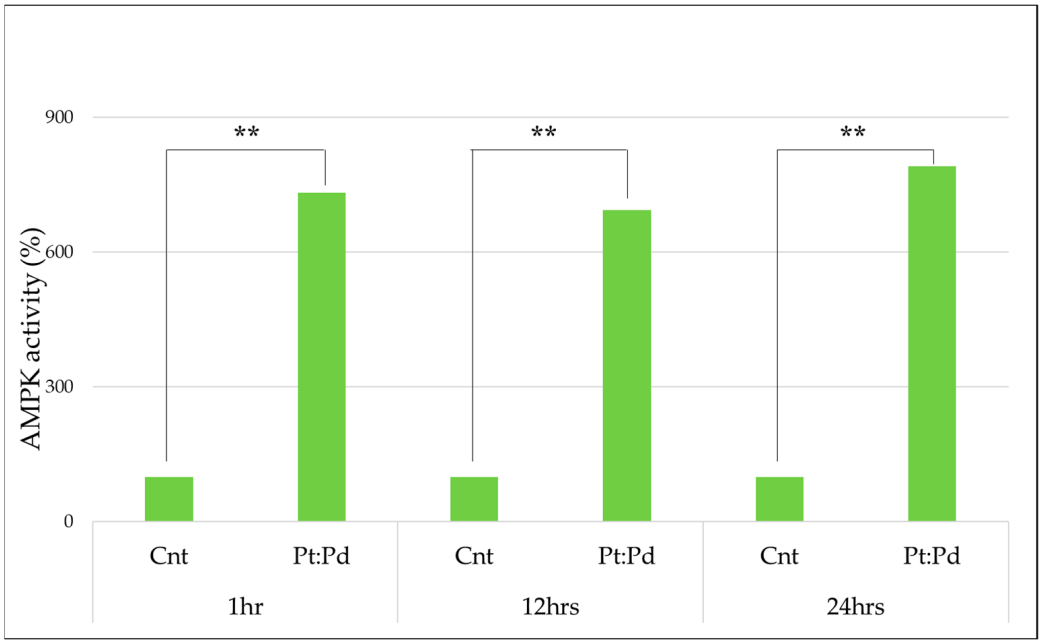

Figure 4. AMPK activity in platinum-palladium compared to the control group (100%) (Mann–Whitney U test., **: $p < 0.01$).

4.2. Measurement of Blood KL-6

In $n = 16$ subjects, a tendency for the KL-6 value to decrease was observed, as shown in Table 2 and Figure 5 below. Furthermore, statistical processing revealed a significant decrease at a significance level of 5%. This suggests that the escape of KL-6 from the alveoli is suppressed, suggesting the possibility of improved alveolar function (Table 2 and Figure 5).

4.3. Measurement of Blood Hydrogen Peroxide

When blood hydrogen peroxide levels were measured in $n = 12$ subjects, a decrease was observed at a significance level of 5%, as shown in Table 3 and Figure 6. Since there is thought to be a relationship between interstitial pneumonia and hydrogen peroxide, these results suggest that interstitial pneumonia caused by hydrogen peroxide may improve (Table 3 and Figure 6).

Table 2. Comparison of KL-6 before and after administration of platinum-palladium ($n = 16$) KL-6 (IU/mL).

Case No.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**
Before	583	276	509	253	679	268	321	224	726	137	103	674	168	787	752	89
After	351	203	367	272	474	315	298	205	622	171	189	422	193	525	473	91

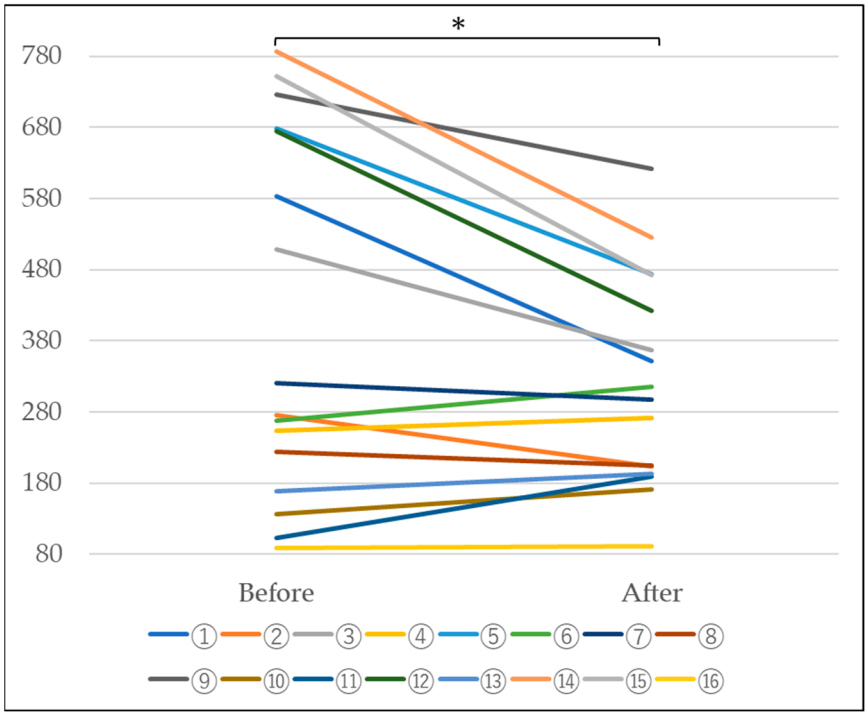

Figure 5. Changes in KL-6 before and after platinum-palladium administration (Paired-samples *t*-test, *: $p < 0.05$).

Table 3. Changes in blood hydrogen peroxide levels due to platinum-palladium (U).

Case No.	1	2	3	4	5	6	7	8	9	10	11	12
Before	284	243	368	311	307	267	363	307	311	240	289	297
After	250	224	282	212	314	206	247	274	279	206	295	283

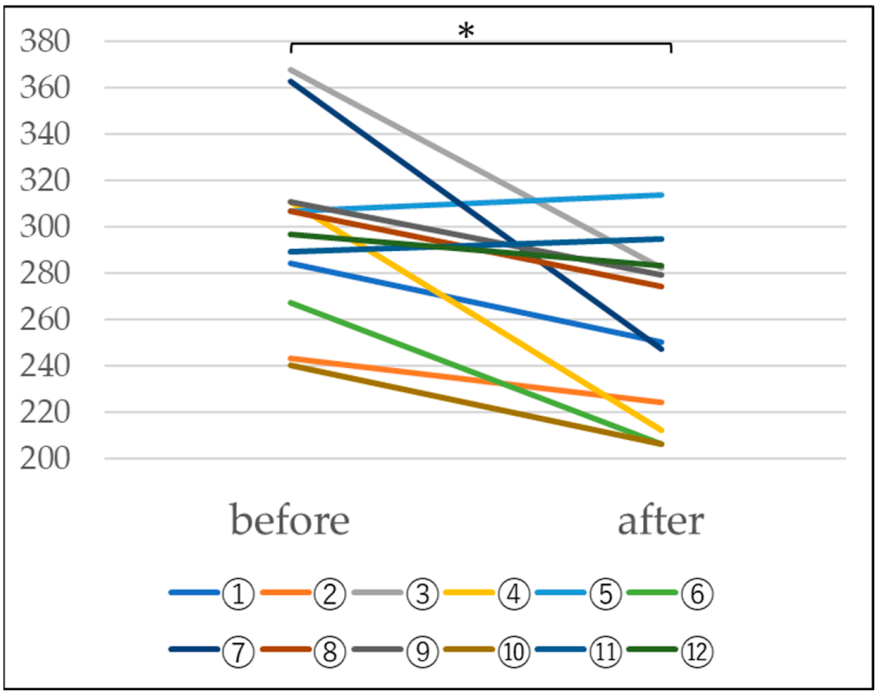

Figure 6. Changes in blood hydrogen peroxide levels before and after administration of platinum-palladium (Paired-samples *t*-test, *: $p < 0.05$).

4.4. Investigation into the Effectiveness of Platinum-Palladium in Improving

Symptoms in patients with interstitial pneumonia (Figure 7).

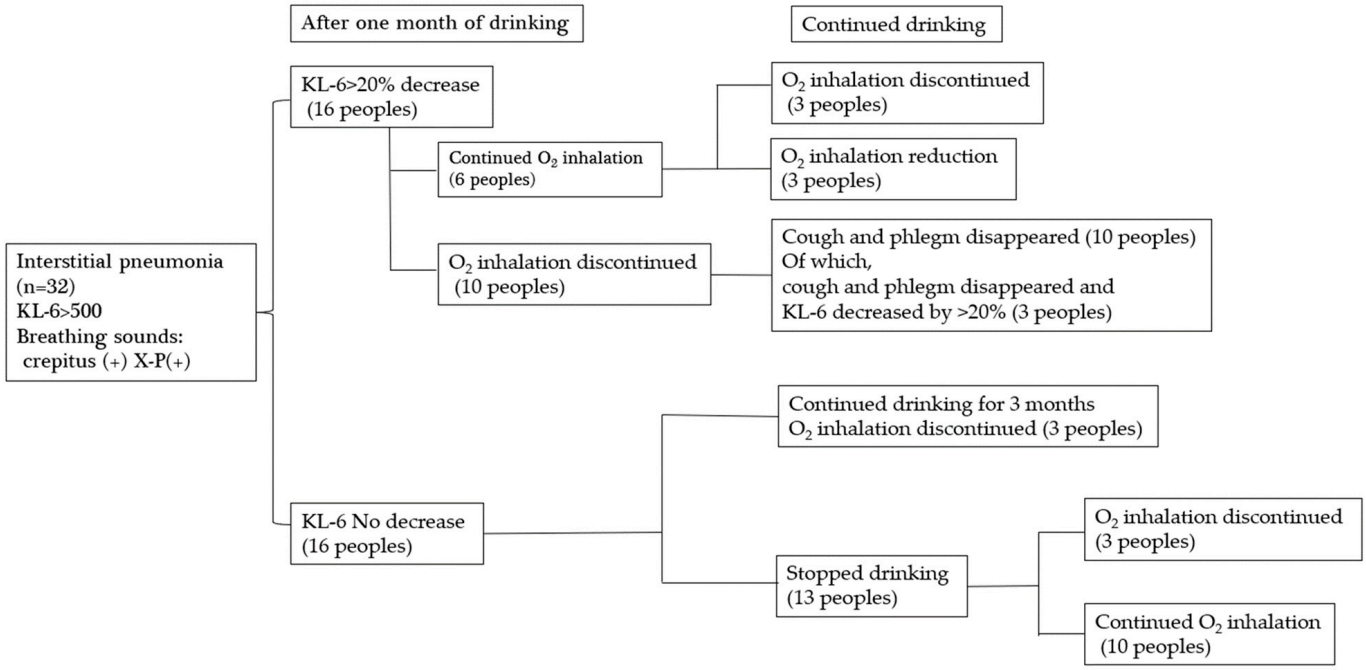

Figure 7. Changes after drinking platinum-palladium.

Thirty-two patients with interstitial pneumonia who visited Hino Kosei Clinic and Kisaragi Soken Clinic took platinum palladium supplements, and their progress was monitored. Sixteen of the 32 patients showed a 20% or greater decrease in KL-6 after one month. Ten of them stopped inhaling oxygen after one month, and all ten patients also stopped coughing and sputum. Three of them showed a further 20% decrease in KL-6. Six patients continued to take oxygen after one month, even though their KL-6 had decreased by more than 20%, but three of them stopped taking oxygen, and three had their dose reduced after continued intake. This suggests the need to continue taking the platinum palladium supplement. Sixteen of the 32 patients showed no decrease in KL-6 after one month, but they were able to stop taking oxygen after three more months of continued intake. Of the patients who stopped drinking the water after one month, three subsequently stopped oxygen inhalation, and ten continued oxygen inhalations; however, this does not mean that the platinum-palladium solution was ineffective, but rather that the patients discontinued the solution due to unavoidable circumstances. Therefore, it is possible that their condition would have improved if they had continued drinking the solution.

5. Discussion

This is a case report of platinum-palladium improving the condition of interstitial pneumonia. In addition to this case, there have been many reports of improvement in interstitial pneumonia and COPD at other clinics, and platinum-palladium has been used in many cases. Therefore, platinum-palladium may be an effective treatment for interstitial pneumonia. Currently, symptomatic treatment for interstitial pneumonia is focused on preventing the progression of interstitial pneumonia or administering oxygen inhalation to treat symptoms as they arise, but it is difficult to improve the condition. However, in this case, the patient was finally able to drive a car and perform daily activities, so it is possible that the lung function itself may have improved. Although the mechanism is still largely unknown, we have considered the possibility. Although the cause of interstitial pneumonia

is often unknown, it is thought that interstitial pneumonia may produce reactive oxygen species in the interstitium, causing inflammation [33]. Reactive oxygen species, such as superoxide present in neutrophils, act as a defense mechanism against antigens, while excessive reactive oxygen species have a detrimental effect on normal cells, causing lifestyle-related diseases, aging, and chronic inflammation [34,35]. In this case, platinum-palladium was used, but it is possible that platinum-palladium does not completely act as an antioxidant, but rather removes only the amount of reactive oxygen species necessary for the body, and removes only the excess. In addition, it was statistically found that platinum-palladium activates AMPK, although at an in vitro level. AMPK (AMP-activated protein kinase) is an enzyme that maintains homeostasis in the body and is a serine/threonine kinase in the metabolism of carbohydrates and lipids [36]. Generally, AMPK is activated in starvation, but it is said that the passive activation of AMPK, as in this case, maintains energy homeostasis and is currently attracting attention as a potential treatment for metabolic diseases, including diabetes and chronic inflammation-related cancer [36]. Energy is essential for human beings to maintain biological functions, and the source of this energy is ATP (adenosine triphosphate), which is generated when ATP is hydrolyzed and converted to ADP (adenosine diphosphate) [37]. AMPK regulates this ATP level to maintain homeostasis and is expected to be effective against metabolic diseases such as cancer, type 2 diabetes, and obesity [38–40]. It is thought that AMPK regulates metabolism by inhibiting the ATP consumption pathway [41,42]. Therefore, AMPK contributes to maintaining health in the body by suppressing chronic inflammation [43,44]. It promotes autophagy [45]. It contributes to the production of NAD+, which in turn activates mitochondria [46], and may increase intracellular ATP levels by activating mitochondrial biosynthesis [47,48].

In other words, it is expected that increased AMPK activity can prevent lifestyle-related diseases, including cancer. It is thought that AMPK regulates metabolism by blocking the process of consuming ATP, an energy source. It has been reported that AMPK activation suppresses chronic inflammatory responses, and further reduces cellular aging due to the activation of autophagy, which can lead to the treatment of interstitial pneumonia [49], so it was suggested that this effect could be used to play a part in the improvement of interstitial pneumonia caused by platinum-palladium.

In addition, blood tests were performed on patients at the in vivo level to measure the aforementioned KL-6 and blood hydrogen peroxide levels. KL-6 is a high molecular weight sialylated glycoprotein contained mainly in type II alveolar epithelial cells that is strongly involved in the production and secretion of pulmonary surfactant [50]. It correlates with the activity (severity) of chronic respiratory diseases [51] and is released into the blood due to inflammatory damage to the alveoli [52], so it is widely used clinically to determine the severity [53]. It is strongly correlated with the severity of interstitial pneumonia, but it has also been reported to correlate with the severity of lung cancer and mixed disorders (combined with emphysema) [54] and is used clinically [55]. In this experiment, the KL-6 value was significantly decreased, suggesting that the severity of the disease had improved. In the future, we plan to examine what action in the body's dynamics is suppressing the deviation of KL-6, but we hypothesize that the alveolar function in patients with interstitial pneumonia has improved. At the same time, we examined hydrogen peroxide. Hydrogen peroxide (H_2O_2) is one of the representative reactive oxygen species (ROS) [56]. In normal physiological actions, it plays an important role in cell signaling, etc. [57], but on the other hand, it induces oxidative stress in the body and causes cell and tissue damage [58,59]. When glucose is ingested in the body, it enters the TCA cycle through the glycolysis process and produces ATP through the electron transport chain [60], but when glucose cannot be ingested, ATP is produced by burning fat and protein. In other words, ATP is essential for human life-sustaining activities [61]. A lot of oxygen is required to produce this ATP, and

of course, this oxygen is taken in through breathing. Most of them are involved in energy production, but a few percent are transformed into reactive oxygen species (ROS) [62]. ROS has advantages and disadvantages for the body. The advantage is that they play a role in the body's defense mechanism, destroying bacteria and cancer cells in granules contained in neutrophils [63]. The disadvantage is that they are known to be involved in various lifestyle-related diseases, including malignant neoplasms and aging [64]. Currently, the following four types of ROS are known to exist as representatives: ① Superoxide (O_2^-), ② Hydrogen peroxide (H_2O_2), ③ Hydroxyl radical (·OH), ④ Singlet oxygen (1O2) [65]. In recent years, methods for removing ROS for the purpose of preventing disease and combating aging have been studied both domestically and internationally [66]. Since aging has been treated as a disease since ICD-11 [67], it is expected that further research will be conducted on antioxidants in the future. In this context, platinum-palladium has been confirmed to be the only substance in the world that can remove all four types of reactive oxygen species mentioned above [25]. In this study, the plasma hydrogen peroxide level was qualitatively measured from the viewpoint that hydrogen peroxide may be generated in large amounts in patients with interstitial pneumonia before and after taking platinum-palladium [68]. A significant difference was observed in this experiment, and a tendency for hydrogen peroxide to decrease in the body was confirmed with platinum-palladium. Hydrogen peroxide is a type of reactive oxygen species [69], and it is possible that hydrogen peroxide affects the alveoli in patients with interstitial pneumonia and COPD [70]. Therefore, the fact that a decreasing trend was observed this time confirms that platinum-palladium significantly reduced KL-6 and reduced hydrogen peroxide in patients with interstitial pneumonia, suggesting that platinum-palladium may have a protective effect on the alveoli in the reduction of KL-6, suppress the effects of ROS caused by hydrogen peroxide, and also increase mitochondrial activity, thereby improving interstitial pneumonia.

6. Conclusions

In this study, the use of platinum-palladium resulted in some improvement in patients with idiopathic interstitial pneumonia. When examining the mechanism, it was found that patients with interstitial pneumonia generate a lot of reactive oxygen in their lungs [33], and the purpose of this study was to determine the need to remove this reactive oxygen. As a result, although there are four types of reactive oxygen, the use of platinum-palladium, which moderately removes all of them, was able to remove hydrogen peroxide, which is said to be closely related to interstitial pneumonia, and is thought to have led to the improvement of interstitial pneumonia. In addition, since it will be necessary to prevent and treat diseases based on "mitochondrial activity" not only in interstitial pneumonia but in all diseases in the future, AMPK was also measured as part of this. There, it was confirmed that AMPK was significantly active at the in vitro level, so it is thought that mitochondrial activity can also be expected with platinum-palladium. Since this is a pilot study, we would like to conduct further studies at the in vivo level in the future. At this stage, a certain degree of effectiveness has been observed for interstitial pneumonia, so we would like to conduct large-scale intervention trials in the future.

Author Contributions: S.K. designed this study, the main conceptual ideas, and the proof outline. T.S. and S.K. collected the data. K.S., S.W. and Y.S. aided in interpreting the results and worked on the manuscript. S.K. supervised the project. S.K. wrote the manuscript with support from S.K. and Y.F. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: This clinical research was conducted in compliance with the Declaration of Helsinki, the "Ethical Guidelines for Life Science and Medical Research Involving Human Subjects", and the research implementation plan. This study was conducted with the approval of the Hino Kosei Clinic Ethics Committee. Ethics Review Numbers HKC_N10023001 (Approved 2022/06/01), HKC_N10023002 (Approved 1 February 2023), HKC_N10023003 (Approved 3 June 2023), and HKC_N10023004 (Approved 11 July 2023).

Informed Consent Statement: Informed consent was obtained from all subjects involved in this study.

Data Availability Statement: Data are contained within the article.

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Conflicts of Interest: This study was conducted at the clinic and university to which the authors belong, and there are no conflicts of interest.

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