HAEMODYNAMIC DISTURBANCES IN PATIENTS WITH CHRONIC COR PULMONALE

By Junichi Mise

Haemodynamic disturbances in patients with chronic cor pulmonale will be represented by pulmonary artery hypertension and right ventricular hypertrophy and/or right heart failure. These abnormalities are caused by two major factors, that is, pathologic morphological change of the lung tissue and respiratory functional disorders, and these changes must be precipitated by chronic lung diseases such as pulmonary emphysema. In this presentation effects of aging upon the pulmonary circulation and its possibility to be a causal factor of haemodynamic disturbances were investigated. Furthermore, levels of the pulmonary hypertension were observed in regard to prognosis of the patients with chronic cor pulmonale and effects of therapy by reserpine administration and oxygen inhalation combined were investigated.

1. First of all, effects of the aging upon pulmonary circulation were observed, and haemodynamic disturbances in elderly normal subjects and patients with pulmonary emphysema especially chronic cor pulmonale were comparatively investigated.

Subjects were 55 hospitalized normal persons and 69 emphysema patients including 20 cases with chronic cor pulmonale who were catheterized and investigated about pulmonary haemodynamic and respiratory functions. And in 20 normal subjects and 24 emphysema patients a mild bicycle-type leg exercise was performed (about 25 Watts) and changes of haemodynamic values were observed.

These cases were divided into 3 groups by age: First group is aged below 49 years old, second group aged from 50 to 59, and the third aged above 60 years old.

Cardiac output index (CI) measured by Fick's direct method showed some lower levels on an average in normal subjects of groups II and III aged above 50 years old. No significant difference of CI, however, was there between the normal and emphysema groups. Pulmonary artery mean pressure (PAm) was higher in general on emphysema group than on the normal group as a matter of course. The emphysema group had increasingly higher levels of PAm by age, and especially cases aged above 60 showed high level of 23 mmHg on an average and included as many as 16 chronic cor pulmonale patients. On the other hand, however, even in normal cases PAm also showed a tendency to increase with age. Pulmonary artery wedge pressure (WP) showed slight tendency to increase in emphysema group aged above 50, and right ventricular end-diastolic pressure (RVD) also showed increase over 6 mmHg in many emphysema cases aged above 60 years old. In normal subjects, however, no significant change was observed in both WP and RVd. Calculated pulmonary vascular resistance index (PVRI) was high in the emphysema group, and in normal subjects also a tendency of increase of PVRI as well as PAm was seen with increase of the age. Arterial blood gases, that is, oxygen saturation (SaO_2) and carbon dioxide tension (PcO_2) at rest showed no change with age in normal subjects.

During a mild leg exercise test cardiac index increased, but the increase was lower in emphysema patients than in the normal subjects, and rate of the increase of cardiac index reduced with age. On the other hand, it was evident that even in the normal cases rate of the increase also reduced with age, especially in the group aged above 60 it was almost same to that in the emphysema group on an average value. PAm elevated in normal cases during the exercise and it was apparent in the group aged over 60, which increment was 7 mmHg on an average. In emphysema patients each group of the age showed elevation of PAm 6 mmHg on an average, and some cases aged over 60 showed increase of WP which increment was over 5 mmHg during the exercise. Calculated vascular resistance index increased in all groups of emphysema patients. On the other hand it was reduced in young normal, but increased in older normal over 50 years old in the same way to emphysema cases.

As described above, in emphysema patients PAm and vascular resistance are evidently higher than in normal subjects in the same age group. However, even in the normal cases effects of the aging upon the increase of cardiac index, elevation of pulmonary artery pressure and vascular resistance are apparent. These changes are more marked during the exercise test, that is, between the pulmonary artery pressure and cardiac index a significant correlation was found and ratio of the increase of PAm to the increase of cardiac index is marked and greater in the group aged over 60 years old than in the young group.

All 20 cases with chronic cor pulmonale indicated by double circle mark were included in the groups II and III and 16 cases of them were in the group III aged above 60. Although haemodynamic disturbances in emphysema patients must be caused by emphysematous morphological changes and respiratory functional disorders such as hypoxia and hypercapnea, effect of aging will accelerate these disturbances as a major casual factor. Emphysema patients associated with chronic cor pulmonale are mostly situated in the elderly group, especially above 60 years old.

2. As reported previously, clinical course and prognosis were observed on 65 emphysema patients. From viewpoint of the pulmonary hypertension, among 8 chronic cor pulmonale cases with PAm over 30 mmHg 5 cases died from right heart failure, whose survival time was in a range from 1 year and 2 months to 3 years and 7 months, 2 years and 3 months on an average, and 2 cases became worse, 1 remained unchanged, but none showed any improvement during the period of the observation. Eighteen cases with PAm over 22 mmHg developed their clinical course as follows: Seven cases died from right heart failure, whose survival time was in a range from 1 year and 2 months to 3 years and 8 months, average survival time was 3 years and 3 months, "worse" in 4 cases, "unchanged" in 3, "improved" in 3, and "dead" from other cause in only 1 case during the observation.

In addition to this level of PAm above 22 mmHg, it will be likely that WP above 12 mmHg, PVRI over 500 dyne, sec, cm^{-5}/M^2 or TPRI over 600, and RVd above 6 mmHg are useful indices in predicting the prognosis.

On the other hand, phonocardiographic Q-IIp interval was measured in young normal, elderly normal subjects and emphysema patients including chronic cor pulmonale cases. Between Q-IIp interval and heart rate there was a close inverse correlation giving a linear regression line, and Q-IIp was shorter in elderly persons than in young normal subjects. In emphysema patients with pulmonary hypertension above 17 mmHg Q-IIp were evidently shorter than those in cases with normal PAm below 16 mmHg. Thus Q-IIp interval is shortened with increase of the age and pulmonary hypertension, mainly due to shortening of ejection time of the right ventricle.

Professor of Internal Medicine, Yamaguchi University School of Medicine, Ube, Japan.

And then relationship of per cent predicted Q-IIp interval (% Q-IIp) to the pulmonary artery pressure was searched. % QIIIp reduced linearly with the elevation of PAm up to 22 mmHg, at this point the reduction of Q-IIp interval seemed to cease and situate stationally making a plateau thereafter, that is, no more shortening of Q-IIp occurred with the elevation of pulmonary artery pressure. A similar relation was found between % Q-IIp interval and PVRI, and the critical value was seen from 250 to 500 dyne, sec, cm^{-5}/M^2.

These data suggest that in emphysema patients a limitation of Q-IIp shortening, in other words, reduction of ejection time of the right ventricle could be reached and thereafter right sided heart failure might start. It is interesting that in regard to clinical course and prognosis of the emphysema patients including chronic cor pulmonale PAm of 22 mmHg and PVRI of 250-500 dyne, sec, cm^{-5}/M^2 were somewhat critical levels as described above.

3. In therapy, we used reserpine administration and oxygen inhalation combined on patients with chronic cor pulmonale mainly caused by chronic pulmonary emphysema, and obtained some good results on acute experimental and long term observations.

(i) Acute experimental observation: A relatively uniform reduction of PAm occurred 90 minutes after intra-muscular injection of 1 mg reserpine, and SaO2 showed significant reduction in majority of the cases. Furthermore PAm reduced 20 minutes after 40% oxygen inhalation in succession to reserpine administration, and SaO2 improved as a matter of course.

(ii) Reserpine 0.5-0.2 mg daily and oxygen inhalation (about 3 liters pure oxygen per minute through nasal catheter one hour a day) combined were given for long term at least for 40 days on 14 patients with chronic cor pulmonale including less evident cor pulmonale. These 14 cases had been treated by bronchodilators, antibiotics, steroids etc., and their conditions were stational or tended to worsen before administration of reserpine and oxygen inhalation.

This treatment was considered to get benefits not only on the several findings of blood gases, ventilatory functions and electrocardiogram, but also much significant improvement on physical activity (Fig. 13). Physical activity graded by our modified Hugh-Jones classification improved significantly on 6 cases, other 4 patients showed a tendency to improve, and the remaining 4 cases had no change. One second forced expiratory ratio improved slightly in a few cases, but in severe cases there was almost no change. Arterial oxygen saturation increased in many cases, and heights of P wave in ECG reduced in 3 cases, which will suggest reduction of the load on the right heart.

The treatment by oxygen inhalation and reserpine administration combined for long term would have an effect upon patients with pulmonary hypertension and/or chronic cor pulmonale to improve physical activity, to support his life and to make its prognosis better.

REFERENCES

1. Junichi Mise: "Pulmonary circulation—pulmonary blood pressures in Japanese." Respiration and Circulation, 18, 623, 1970.
2. Junichi Mise, Iwao Fujino and Satoshi Yokochi: "Recent treatment of chronic cor pulmonale in Japanese." Internal Medicine 29, 1097, 1972.
3. Katsutoshi Moriyama and Iwao Fujino: "Pathophysiological studies on pulmonary circulatory responses to exercise test." Jap. Circulation J., 45, 35, 1971.
4. Nobuhiro Oota: "Studies on the Q-IIp interval in chronic obstructive lung disease." Jap. Circulation J., 37, 1973, in press.
5. Shozo Itagaki: "Prognostic evaluation of pulmonary circulatory disturbance in patients with chronic obstructive ventilatory disturbance," Jap. J. Med., 9, 59. 1970, J. Jap. Soc. Int. Med., 58, 127, 1969.