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The changes in spirometric measurements during 6 months` methadone maintenance treatment in opiate dependent patients

Zmiany wskaźników stanu czynnościowego układu oddechowego w okresie sześciomiesięcznego leczenia substytucyjnego metadonem

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The aim of the study was to evaluate the respiratory system response to individually specified doses of methadone in opiate dependent patients during 6 months' methadone maintenance treatment at the Department of Clinical Toxicology CM UJ. There were 34 persons (14 women aged from 21 to 33 years and 20 men aged 21-46 years) under examination. Examinations were performed three times: I – initial examination – before administration of methadone maintenance treatment; II – control examination after 3 months – methadone maintenance treatment; III – control examination after 6 months – methadone maintenance treatment. Ventilation efficiency was assessed on the basis of the results from a "flow-volume" loop, spirometry and the measurements of the respiratory tract resistance (R_{rs}) in a computerised system. R_{rs} was determined by means of the flow-interruption method. The parameters obtained from a "flow-volume" loop and spirometry were stabile within opiate substitution with methadone, whilst the values of respiratory resistance were significantly different. Significant increase in respiratory resistance values between initial and control examination (after 3 months) was noted. The normalisation of respiratory resistance was proved after 6 months treatment. It can indicate the impact of nervous component on spastic reaction of central bronchi.

Celem pracy była ocena odpowiedzi układu oddechowego na podawanie osobom uzależnionym od opiatów indywidualnie dobranej dawki metadonu w okresie sześciomiesięcznego leczenia substytucyjnego metadonem w Klinice Toksykologii CMUJ w Krakowie. Badaniami objęto 34 osoby: 14 kobiet w wieku 21-33 lat i 30 mężczyzn w wieku 21-46 lat. Sprawność wentylacyjna określana była w oparciu o wyniki uzyskane z krzywej „przepływ-objętość", spirometrii oraz pomiaru oporów dróg oddechowych (R_{rs}) w skomputeryzowanym systemie Lung-test. R_{rs} oznaczone jest metodą przerywania przepływu. Badania wykonywane były 3-krotnie: I – badanie wyjściowe – przed rozpoczęciem leczenia substytucyjnego metadonem; II – badanie kontrolne po 3 miesiącach trwania leczenia metadonem, III – badanie kontrolne po 6 miesiącach trwania leczenia metadonem. W okresie półrocznego leczenia substytucyjnego metadonem nie stwierdzono istotnych zmian w stanie czynnościowym układu oddechowego. Wartości wskaźników przepływowych uzyskanych z pętli „przepływ-objętość" nie wykazywały znamiennych różnic w badaniach wykonanych po 3-miesięczym oraz 6-miesięcznym okresie trwania kuracji metadonowej. Opory dróg oddechowych zachowywały się mniej stabilnie. Stwierdzono znamienny przyrost wartości oporów dróg oddechowych w początkowym okresie leczenia nawet u osób o prawidłowych wartościach tego parametru przed przystąpieniem do programu. Obniżenie się wartości oporów w późniejszym okresie leczenia do wartości wyjściowych świadczyć może o dużym wpływie komponenty nerwowej na stan czynnościowy centralnych oskrzeli.

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Introduction

Respiratory disoders are a common complication in opiate dependent persons [4,7]. Central bronchi obturation was diagnosed in 37% of patients classified to methadone maintenance treatment programme at the Department of Clinical Toxicology [5]. Expected normalization of life functioning [2,3,8] was believed to improve also the ventilatory efficiency of opiate dependent patients.

The aim of the study was to evaluate

the spirometric measurements of addicts in course of methadone maintenance treatment.

Material and methods

There were 34 study patients out of 35 examined in the previous study [5] from methadone maintenance treatment programme conducted at the Department of Clinical Toxicology. One of the examined persons stopped substitution therapy, so finally the examined group consisted of 14 women between the ages of 21 and 33 (average height: 164.8±7.6 cm; average body mass: 56.9±10.5 kg) and 20 men between the ages of 21 and 46 (average height: 177.3± 5.7 cm; average body mass: 70.9±15.75kg). Ventilation efficiency was determined on the basis of the results from a "flow-volume" loop, spirometry and the measurements of the respiratory tract resistance (R_{rs}) in a computerised system Lungtest - MES company (Poland). R_{rs} was determined by means of the flow-interruption method (measurement module made on the basis of the study of *Klass van der Plas* from University Hospital in Leiden - Holland).

Examinations were performed three times:

I – initial examination – before the administration of methadone maintenance treatment.

II – control examination after 3 months – methadone maintenance treatment.

III – control examination after 6 months – methadone maintenance treatment.

The following parameters were recorded from "flow-volume" and spirometry: Forced Vital Capacity (FVC); Forced Expiratory Volume for 1 sec. (FEV_1); Peak Expiratory Flow (PEF); Forced Expiratory Flow at 25% of Forced Vital Capacity (FEF_{25}); Forced Expiratory Flow at 50% of Forced Vital Capacity (FEF_{50}); Forced Expiratory Flow at 75% of Forced Vital Capacity (FEF_{75}); Forced Expiratory Flow measured between 25% and 75% of Forced Vital Capacity (FEF_{25-75}). The results obtained were referred to their predicted values (N) regarding sex, age and anthropometrical indices (body weight and high) [1].

The rise or drop in spirometric measurements was calculated for each of the patients and then expressed as a percentage difference between the values obtained in examinations as follow: II to I; III to I; and III to II. A treshold of 20% was chosen due to large variation of individual spirometric measurements obtained from three examinations. Nonparametric *Friedman* test and *Pearson* correlation test were used to evaluate the significance of differences between the parameters obtained from each examination.

Table I

Characteristics of spirometric measurements from the initial examination (I), the examination performed after 3 months (II) and six months' (III) duration of methadone maintenance treatment of oplate dependent patients (n = 34).

Charakterystyka wartości wskaźników spirometrycznych w badaniu wyjściowym (I), w badaniu po trzech miesiącach (II) oraz po 6 miesiącach leczenia substytucyjnego metadonem (N = 34).

Parameters	Mean	Min	Max	± SD
FEV_1 I [L]	3.98	2.38	5.44	0.73
FEV_1 II	3.98	2.59	5.59	0.78
FEV_1 III	3.97	2.74	5.08	0.74
FVC_{EX} I [L]	4.76	2.70	6.99	1.03
FVC_{EX} II	4.70	2.73	7.02	1.00
FVC_{EX} III	4.77	2.91	6.78	0.99
PEF I [L/s]	8.54	4.55	12.03	2.04
PEF II	8.84	4.94	12.64	2.11
PEF III	8.64	5.10	12.76	2.00
FEF_{75} I [L/s]	7.90	4.45	11.46	1.86
FEF_{75} II	8.00	4.54	12.24	1.93
FEF_{75} III	7.79	4.21	11.97	1.86
FEF_{50} I [L/s]	5.72	3.29	7.66	1.19
FEF_{50} II	5.64	3.05	7.93	1.317
FEF_{50} III	5.47	2.52	7.41	1.18
FEF_{25} I [L/s]	2.90	1.61	5.26	0.84
FEF_{25} II	2.81	1.57	5.33	0.97
FEF_{25} III	2.69	0.91	4.42	0.80
$FEF_{25/75}$ I [L/s]	5.10	2.95	7.04	1.04
$FEF_{25/75}$ II	4.98	2.96	7.42	1.16
$FEF_{25/75}$ III	4.84	2.16	6.66	1.04
FEV_1 %FVC_{EX} I	84.69	64.27	99.53	8.45
FEV1 %FVC_{EX} II	85.12	69.95	99.76	7.04
FEV1 %FVC_{EX} III	84.27	64.50	99.75	7.46
R_{RS} I [kPa/dcm³/s]	0.28	0.18	0.42	0.06
R_{RS} II	0.29	0.20	0.50	0.07
R_{RS} III	0.27	0.18	0.42	0.07

Table II

Values of spirometric parameters expressed as a percentage of their predicted values (%N) obtained from the initial examination (I), the examination performed after 3 months (II) and six months' (III) duration of methadone programme (N = 34).

Odsetkowa wartość wskaźników spirometrycznych w badaniu wyjściowym (I), w badaniu po trzech miesiącach (II) oraz po 6 miesiącach leczenia substytucyjnego metadonem w odniesieniu do wartości należnych (N = 34).

Parameters	Mean	Min	Max	± SD
FEV_1 I [L]	96.68	64.00	120.00	12.61
FEV_1II	96.27	70.00	116.00	11.71
FEV_1III	96.21	74.00	119.00	11.53
FVC_{EX} I [L]	98.65	66.00	122.00	13.09
FVC_{EX} II	97.62	67.00	125.00	12.13
FVC_{EX} III	98.97	71.00	123.00	12.36
PEF I [L/s]	93.65	58.00	122.00	16.82
PEF II	96.77	63.00	126.00	15.50
PEF III	94.71	65.00	128.00	15.77
FEF_{75} I [L/s]	98.94	60.00	136.00	20.33
FEF_{75} II	99.74	64.00	143.00	19.33
FEF_{75} III	97.32	60.00	140.00	19.44
FEF_{50} I [L/s]	103.35	56.00	144.00	23.22
FEF_{50} II	101.38	53.00	149.00	23.04
FEF_{50} III	98.53	47.00	148.00	22.75
FEF_{25} I [L/s]	101.59	40.00	178.00	32.95
FEF_{25} II	96.85	40.00	158.00	31.74
FEF_{25} III	93.06	36.00	146.00	28.12
$FEF_{25/75}$ I [L/s]	112.00	87.00	141.00	14.52
$FEF_{25/75}$ II	107.33	73.00	138.00	17.39
$FEF_{25/75}$ III	101.86	47.00	144.00	20.97
R_{RS} I [kPa/dcm³/s]	108.10	37.94	200.2	61.30
R_{RS} II	113.94	43.86	238.3	67.20
R_{RS} III	107.58	38.14	200.6	59.40

Results

The values of spirometric measurements from initial examination and from the examinations performed after 3 and 6 months of methadone treatment are presented in table I.

Table II presents the spirometric measurements referred to their predicted values (N).

Only the values of respiratory resistance (R_{rs}) were significantly different while comparing the results obtained from the three examinations performed. Significant increase in mean respiratory resistance expressed as a percentage of predicted value (R_{rs} %N) between the initial and second examination was noted. The differences be-

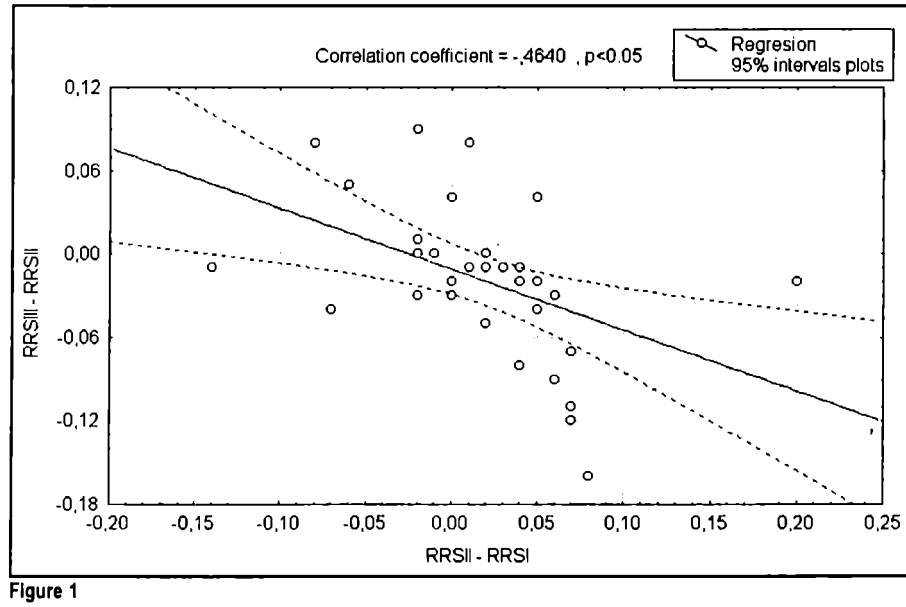

Figure 1

Scatter plot of individual differences between the values of respiratory resistance (R_{rs}) obtained from examinations II vs. I, and III vs. II.

Wykres rozrzutu indywidualnych różnic między wartościami oporów dróg oddechowych otrzymanych z badania II w stosunku do badania I oraz badania III w stosunku do badania II.

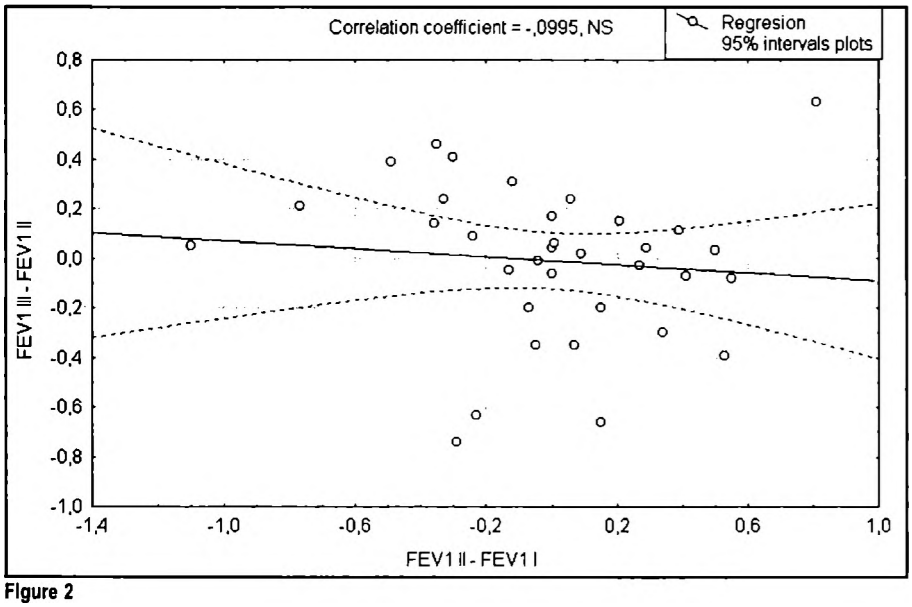

Figure 2
Scatter plot of individual differences between the values of Forced Expiratory Volume per 1 sec. (FEV_1) obtained from examinations II vs. I and III vs. II.
Wykres rozrzutu indywidualnych różnic między wartościami natężonej objętości wydechowej 1s. (FEV_1) otrzymanych z badania II w stosunku do badania I oraz badania III w stosunku do badania II.

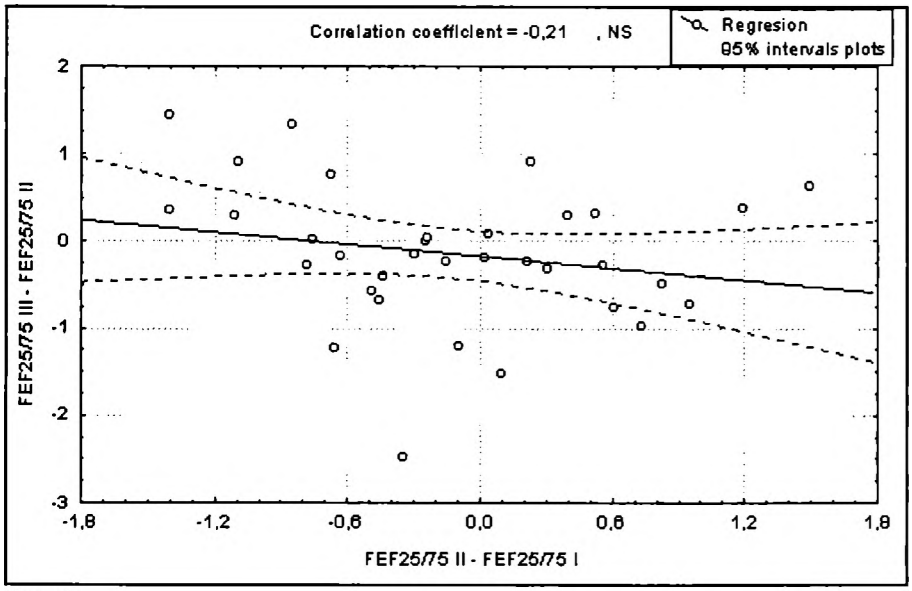

Figure 3
Scatter plot of individual differences between the values of Forced Expiratory Flow measured between 25% and 75% of Forced Vital Capacity (FEF_{25-75}) obtained from examinations II vs. I and III vs. II.
Wykres rozrzutu indywidualnych różnic między wartościami natężonego przepływu wydechowego między 25-75% natężonej pojemności życiowej (FEF_{25-75}) otrzymanych z badania II w stosunku do badania I oraz badania III w stosunku do badania II.

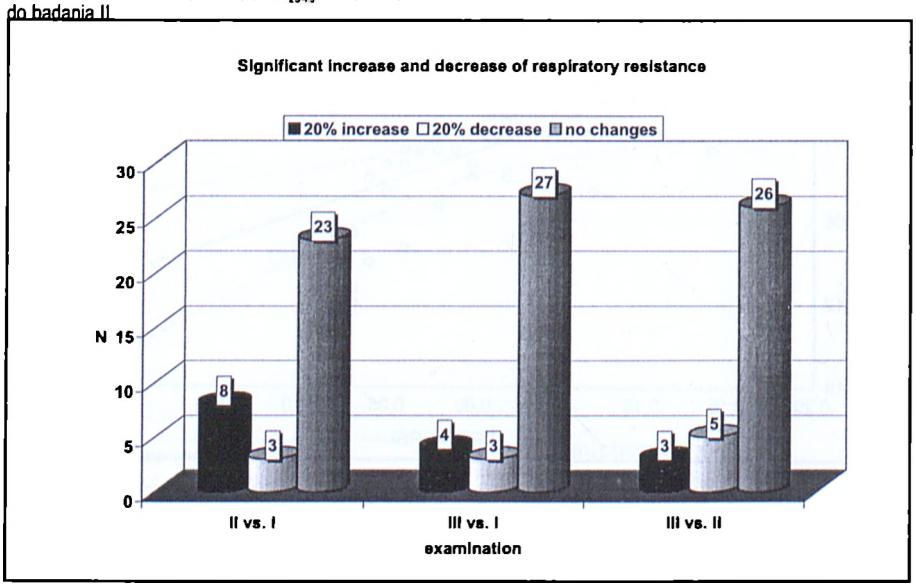

Figure 4
Over 20% variation of R_{rs} values.
Ponad 20% indywidualna zmienność wartości oporu dróg oddechowych.

tween other spirometric measurements were insignificant.

The rise or drop in R_{rs} (figure1), FEV_1, describing the central bronchi efficiency (figure 2), and FEF_{25-75} – describing the small bronchi condition (figure 3) calculated for each of the patients and expressed as a percentage of their individual differences between the values obtained in the examinations are presented in three consecutive figures.

Both the rise and drop, while comparing the results from the initial examination and the examinations performed during methadone maintenance treatment, in individual R_{rs} values were noted. They were regularly distributed and significantly correlated.

No significant differences were noted between individual changes in FEV_1 (figure 2) and MEF_{25-75} (figure 3) of opiate dependent patients during methadone maintenance treatment.

The number of patients with large (significant – 20%) variation in the values of R_{rs} (figure 4), FEV_1 (figure 5) and MEF_{25-75} (figure 6) during the methadone treatment was relatively small.

In 8 out of 34 examined opiate dependent patients, a 20% increase in R_{rs} after 3 months', and again normalisation after 6 months' methadone maintenance treatment was noted: 6 of them had the values of respiratory resistance within normal limit in the initial examination.

The lowest variation in FEV_1 - the parameter describing the central bronchi - was noted. A large worsening of MEF_{25-75} - the parameter describing the small bronchi - was noted in the examination performed after 6 months' methadone maintenance treatment.

It should be pointed up, that the examined persons were covered with the complex medical care. A full recognition of the health status was possible during 6 months of methadone maintenance. None of the examined persons suffered from cold or whether infections in the day of spirometric examination. Nobody started smoking and nobody gave up smoking either.

The obtained results are similar to results obtained previously. Examinations of

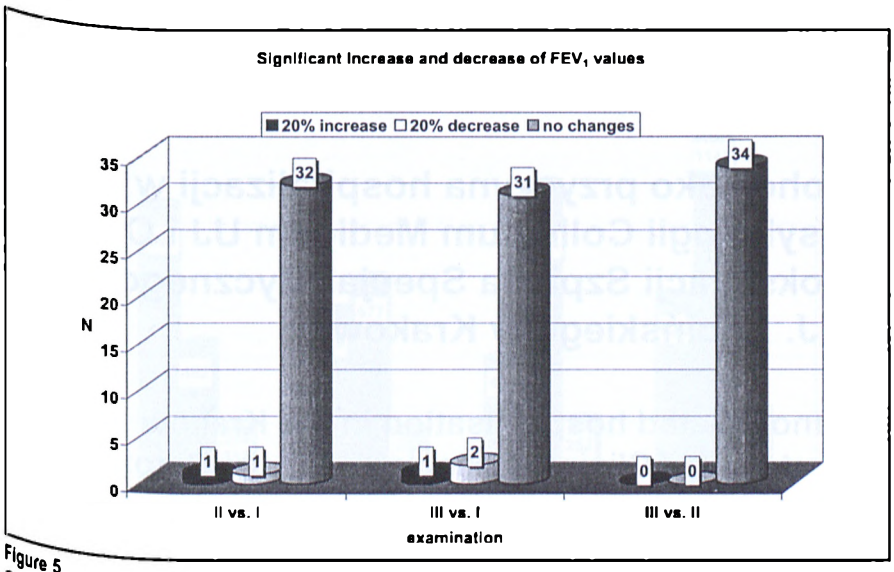

Figure 5
Over 20% variation of FEV_1 values.
Ponad 20% indywidualna zmienność wartości FEV_1.

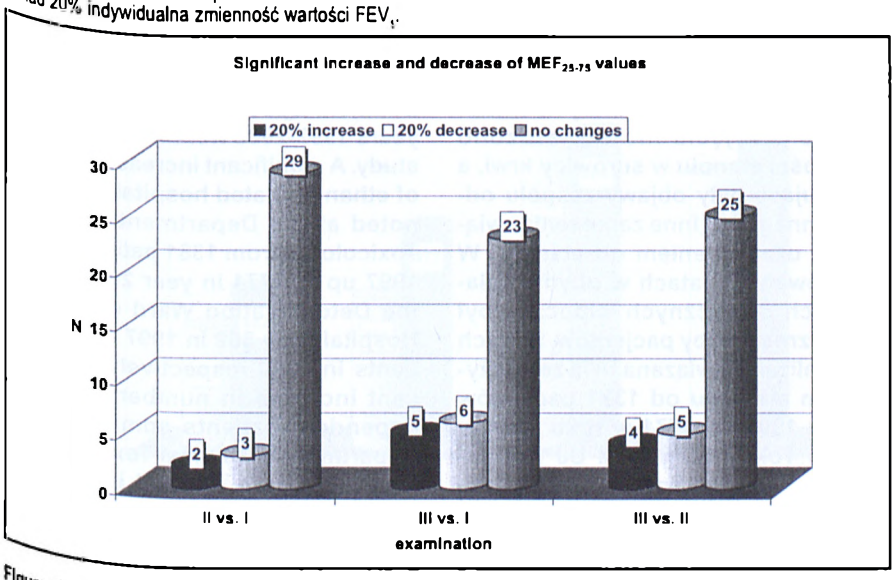

Figure 6
Over 20% variation of MEF_{25-75} values.
Ponad 20% indywidualna zmienność wartości MEF_{25-75}.

another groups of dependent persons also showed, that values of respiratory tract resistance may be increased while the spirometric parameters describing the air flow in central bronchi stays within normal limit [4,6]. Measurements of the respiratory tract resistance is very useful in clinical toxicology practice.

Conclusions

1. No substantial changes in ventilatory efficiency was noted in opiate dependent patients after 6 months' methadone maintenance treatment.

2. The parameters of respiratory flow were stable within opiate substitution with methadone.

3. The changes observed in respiratory resistance – elevation at the beginning and normalisation within a longer duration of methadone maintenance treatment can indicate a nervous component in spastic reaction of central bronchi.

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