HIGH PREVALENCE OF EXTRAPYRAMIDAL SIGNS AND SYMPTOMS IN A GROUP OF ITALIAN DENTAL TECHNICIANS

Edito Fabrizio, Nicola Vanacore*, Marcella Valente, Alfonso Rubino,Giuseppe Meco.

Department of Neurological Sciences, "La Sapienza" University, Viale Università 30
00185 Rome, Italy

* National Centre of Epidemiology, National Institute of Health, Via Giano della Bella 34, 00161 Rome, Italy.

E-mail addresses:
Edito Fabrizio : edito@libero.it
Nicola Vanacore: vanacore@iss.it
Marcella Valente : marcella.valente@virgilio.it
Alfonso Rubino: alf-rub@libero.it
Giuseppe Meco: giuseppe.meco@uniroma1.it

Text word count: 1783 (abstract 201)

Key words: solvents, metals, parkinsonism, postural tremor

Running title: extrapyramidal signs and symptoms in dental technicians.

Competing interests: none

Corresponding author:
Prof. Giuseppe Meco
Department of Neurological Sciences
"La Sapienza" University
Viale Università 30
00185 Rome, Italy
tel +390649914706
fax +390649914840
e-mail: giuseppe.meco@uniroma1.it

ABSTRACT

Background -Occupational and chronic exposure to solvents and metals is considered a possible risk factor for onset of Parkinson's disease and essential tremor. Dental technicians are exposed during the manufacture of dental prostheses to numerous chemicals that contain toxins known to affect the central nervous system, such as solvents (which contain n-hexane in particular) and metals (which contain mercury, iron, chromium, cobalt and nickel).

Methods- We performed an epidemiological and clinical study on all 27 dental technicians working in the same school for dental technicians. We asked all the technicians to fill in a self-administered questionnaire on extrapyramidal symptoms and the General Health Questionnaire (GHQ), a self-administered screening instrument, to detect current diagnosable psychiatric disorders. We propose to all 27 dental technician also a neurological examination and a detailed occupational anamnesis in our clinic.

Results - Of the 14 subjects who underwent the neurological examination, four had postural tremor and one had a diagnosis of Parkinson's disease.

Conclusions - We found an high prevalence of extrapyramidal symptoms in a group of male dental technicians working in a state technical high school in Rome. We believe that this finding could be due to the presence of toxins in the dental technician's work.

BACKGROUND

Occupational and chronic exposure to solvents and metals is considered a possible risk factor for onset of Parkinson's disease (PD).

In particular, two case-control studies point to a role of these environmental toxins in the etiopathogenesis of PD.

The first study performed on 144 PD cases and 464 controls revealed a higher incidence of PD among subjects with more than 20 years' exposure to lead-iron (OR=2.83; 95CI% 1.07-7.50) and iron-copper (OR = 3.69; 95 CI% 1.40-9.71) combinations [1].

The second study, conducted on 341 cases and 357 controls, revealed that the incidence of PD was associated with occupational exposure to solvents (OR = 1.89; 95 CI% 1.2-2.7) [2].

Another analytical epidemiological study indicated a possible association between exposure to mercury and PD [3]. Moreover, some case reports point to a link between parkinsonism and exposure to n-hexane and mercury [4,5]. An epidemiological review on this theme has been reported [6]. Some case-control studies show different results regarding a possible link between occupational exposure to metals and solvents and essential tremor (ET) [7,8]. Dental technicians are exposed to dust and vapour during the manufacture of dental prostheses from the negative impression of the patients' teeth obtained by the dentist. Dental production entails exposure to various chemical hazards, including solvents, mineral acids, gases and vapours released during polymerisation, metal casting and porcelain baking, as well as dust from plaster, metal alloys, ceramics and acrylic resins [9]. Moreover, during the processing of resins, particles of dust of methacrylate compounds are worked with oxidative substances that release free radicals. The dust also contains inorganic pigments such as mercury sulphide. Dental technicians are consequently exposed during the manufacture of dental prostheses to numerous chemicals that contain toxins known to affect the central nervous system, such as solvents (which contain n-hexane in particular), metals (which contain mercury, iron, chromium, cobalt and nickel) and bisphenol-A [9] . In this

study, we found an high prevalence of extrapyramidal symptoms in a group of male dental technicians working in a state technical high school in Rome.

METHODS AND POPULATION

A 47-year-old right handed male was referred to our specialized centre for the diagnosis and treatment of PD and other extrapyramidal diseases. The neurological symptoms in this patient, consisting of heaviness in the upper right limb, had first appeared at the age of 44 years. At the clinical examination, the patient scored 13 in the UPDRS motor scale (speech 1, facial expression 2, right-arm postural tremor 1, neck rigidity 1, right-arm rigidity 2, right-leg rigidity 1, right-hand finger taps 1, right-hand hand movements 1, right-hand rapid alternating movements 2, gait 1). He did not have a family history of parkinsonism or ET evaluated only with the anamnesis of the patient.

Magnetic resonance images of the encephalon, the electromyography, sensorimotor nerve conduction, motor evoked potential, serum copper and serum ceruloplasmin were all normal. An acute L-dopa test improved the UPDRS motor scale by 46%. In particular the patient took one tablet of levodopa and carbidopa at dosages of 250 and 25 mg, respectively. After two hour the UPDRS motor score of the patient reduced from 13 to 7.

The patient is now 50 years old and, 7 years after the onset of symptoms and 3 years after first coming to our observation, in which the disease had remained clinically stable, the parkinsonism continues to be strictly lateralized on the right side (UPDRS motor score of 12). He has, for the last 16 months, been taking antiparkinsonian drugs; he is currently on pramipexole and selegiline at dosages of 2.1mg/day and 5mg/day, respectively.

Although he has had a right hemiparkinsonism for 7 years, our patient's other clinical features meet the UK Brain Bank clinical diagnosis criteria for probable PD.

He is a dental technician who had taught in a state school for dental technicians in Rome.

He had, for the previous 30 years, always worked in this environment in which numerous toxic substances, such as mercury sulphate, metals and solvents, were used. The patient had never used any protective clothing, nor had he ever undergone any biochemical tests to assess his level of exposure to solvents and metals.

Moreover, the patient referred that many of his colleagues had similar symptoms.

We performed an epidemiological and clinical study on all 27 dental technicians (including the above patient) working in the same school for dental technicians.

We asked all the technicians to fill in a self-administered questionnaire on extrapyramidal symptoms used as a screening instrument to detect parkinsonism cases in the general population [10]. This questionnaire contained nine questions on symptoms (presence or absence of a symptom) and two questions regarding the diagnosis of PD and treatment. Using a cut-off of four positive answers, this questionnaire achieves a sensitivity of 90% and a specificity of 94% [10].

We also used also the General Health Questionnaire (GHQ), a self-administered screening instrument, to detect current diagnosable psychiatric disorders [11]. The GHQ was designed to cover four identifiable elements of distress: depression, anxiety, social impairment and hypochondriasis (indicated above all by organic symptoms). We used a GHQ-28 item version. Items were scored using conventional of 0,1,2,3 likert scores for the response categories. When a two point score (present or absent) was used for the GHQ, a cut off score of 6 or above was the best threshold for sensitivity (79.2%) and specificity (79.6%)[11].

Lastly, all 27 dental technicians were offered a neurological examination and a detailed occupational anamnesis in our clinic.

Ethical committee approved this study, and written consent was obtained from all subjects

Statistical analysis

A Student's t-test was used for the comparisons. The frequency analysis was performed by means of the chi-square test. A p value of 0.05 was considered as statistically significant. All statistical analyses were carried out by means of SPSS software (Version 13.0).

RESULTS

The 27 male dental technicians had a mean age of 49.1± 5.5 years (range 41-64 yrs) and a mean duration of exposure to toxins in dental work of 24.7± 3.1 years (range 17-31 yrs).

Twelve subjects responded positively to at least four questions in the self-administered questionnaire on extrapyramidal symptoms. Fifteen subjects has a score of 6 or above at the GHQ. Fourteen subjects accepted the offer of a clinical evaluation (neurological examination and administration of UPDRS) and an accurate occupational anamnesis in our clinic.

There were no significant differences in age, duration of exposure to toxins, positive screening for extrapyramidal symptoms or the total and subtotal and cut-off scores in GHQ between the 14 subjects that came to the clinic and the 13 that did not (Table 1).

The proportion of subjects examined by us at the clinic was greater among the subjects who reported positive shaking in the arms or legs at specific item of the questionnaire than those who did not (8/6 vs 2/11 ; p= 0.02).

Of the 14 subjects who underwent the neurological examination, four had postural tremor and one PD (the aforementioned patient described in detail). The age, clinical and occupational variables of these five dental technicians are shown in Table 2.

From a clinical point of view, three subjects had bilateral postural tremor, while one had monolateral postural tremor [12]. Only one patient had a positive family history of postural tremor.

Two subjects (49 and 46 years old) with a positive screening for parkinsonism and shaking in the arms or legs, according to the self-administered questionnaire, were both found to be negative at the neurological examination, even though the 49-year-old subject and his family reported postural and kinetic tremor.

Among the subjects that underwent the neurological examination, there were no statistically significant differences in age, duration of exposure to toxins, total and subtotal and cut-off scores at GHQ between subjects with neurological signs and those without (data not shown); the only

statistically significant difference between these two groups was in the frequency of subjects with at least four positive answers in the questionnaire on extrapyramidal symptoms (5/1vs 2/6; p= 0.03).

DISCUSSION

We found an high prevalence of extrapyramidal signs and symptoms in a group of dental technicians working in a state technical high school in Rome (one subject with PD, three with bilateral postural tremor and one with monolateral postural tremor).

Although the mean age of the dental technicians included in this study was not very high (49.1± 5.5 yrs), the frequency of bilateral postural tremor (3/27 = 11.1%) and PD (1/27= 3.7%) in this group were markedly higher than those reported in epidemiological studies on these pathologies (0.4-3.9% for ET and 0.17- 0.25% for PD)[12].

Disease progression in our young patient with sporadic PD was atypical since his hemiparkinsonism had been present for seven years and had been stable for at least three years. This clinical picture has frequently been associated with parkinsonism of probable toxic origin, though a genetic origin cannot be ruled out.

The proportion of ET cases with a family history of ET ranges from as low as 17% to as high as 100% [12]. In this study only one subject had a familiar history of ET (1/27= 3.7%).

All five dental technicians with extrapyramidal signs at neurological examination had been exposed for many years to toxins known to affect the extrapyramidal system (solvents and metals, particularly mercury and n-hexane, chemicals such as para-nonylphenol, and bisphenol-A) that significantly stimulate hydroxyl radical (*OH) formation in the striatum [13]. Moreover, the technicians worked in a particularly difficult environment in which there was inadequate ventilation, insufficient light, a large number of people (up to 25) working in an area of 30-40 metres squares, and excessive noise due to the use of drills, vibrators, mixers and a casting machine.

We have not performed an assessment of exposure level and/or biological markers of neurotoxins present in this workplace.

We also examined a 44-year-old male dental technician who had worked in this school for 16 years. This subject had bilateral postural tremor that had first appeared approximately 10 years ago.

We cannot exclude the presence of other cases with such pathologies among the dental technicians who tested positive in the screening phase for parkinsonism but refused the clinical examination.

CONCLUSIONS

On the basis of the epidemiological, occupational and clinical data described above, we believe that the high prevalence of extrapyramidal signs and symptoms found in these 27 dental technicians working in the same school was not a chance occurrence, but this phenomenon could be due to the presence of known neurotoxins in the dental workers' profession.

In Italy, there are estimated to be approximately 1000 dental technicians working in 30 state technical high schools and 15000 dental technicians working in 5000 dental laboratories.

An epidemiological study designed to assess the possible risk of parkinsonism, PD and ET in a large cohort of dental technicians is warranted.

The authors declare that they have no competing interests

Authors ' contributions

EF carried out the clinical and epidemiological study and conceived of the study,

NV participated in the design of the study and performed the statistical analysis

MV carried out the clinical study

AR carried out the clinical study

GM conceived of the study, and participated in its design and coordination and helped to draft the manuscript.

All authors read and approved the final manuscript.

REFERENCES

[1] Gorell JM, Johnson CC, Rybicki BA Peterson EL, Kortsha GX, Brown GG, Richardson RJ : **Occupational exposures to metals as risk factors for Parkinson's disease.** Neurology 1997,**48**:650-658.

[2] Seidler A, Hellenbrand W, Robra BP, Vieregge P, Nischan P, Joerg J, Oertel WH, Ulm G, Schneider E : **Possible environmental, occupational, and other etiologic factors for Parkinson's disease: a case-control study in Germany.** Neurology 1996, **46**:1275-1284.

[3] Ngim CH, Devathasan G: **Epidemiologic study on the association between body burden mercury level and idiopathic Parkinson's disease**. Neuroepidemiology 1989, **8**:128-141.

[4] Vanacore N, Gasparini M, Brusa L, Meco G: **A possible association between exposure to n-hexane and parkinsonism**. Neurol Sci 2000, 21:49-52.

[5] Finkelstein Y, Vardi J, Kesten MM, Hod I : **The enigma of parkinsonism in chronic borderline mercury intoxication, resolved by challenge with penicillamine**. Neurotoxicology 1996, **17**:291-295.

[6] Gorell JM, Rybicki BA, Cole Johnson C, Peterson EL: **Occupational metal exposures and the risk of Parkinson's disease.** Neuroepidemiology. 1999;**18**:303-308.

[7] Louis ED, Applegate LM, Factor-Litvak P, Parides MK, Andrews L: **Essential tremor: occupational exposures to manganese and organic solvents.** Neurology. 2004;**63:**2162-2164.

[8] Louis ED, Jurewicz EC, Applegate L Factor-Litvak P, Parides M, Andrews L, Slavkovich V, Graziano JH, Carroll S, Todd A: **Association between essential tremor and blood lead concentration.** Environ Health Perspect. 2003;**111**:1707-1711.

[9] Torbica N, Krstev S: **World at work: dental laboratory technicians.** Occup Environ Med 2006, **63**:145-148.

[10] Pramstaller PP, Falk M, Schoenhuber R, Poewe W : **Validation of a mail questionnaire for parkinsonism in two languages (German and Italian).** J Neurol 1999, **246**:79-86.

[11] Goldberg DP, Gater R, Sartorius N, Ustun TB, Piccinelli M, Gureje O, Rutter C: **The validity of two version of the GHQ in the WHO study of mental illness in general health care**. Psychol Med 1997, **27**:191-197.

[12] Louis ED: **Essential Tremor.** Lancet Neurol 2005, **4**:100-110.

[13] Obata T: **Environmental estrogen-like chemicals and hydroxyl radicals induced by MPTP in the striatum: a review.** Neurochem Res 2002, **27**:423-31.

Table 1

Comparisons between the two groups of dental technicians included in the study

Variables	Subjects who underwent neurological examination (n=14)	Subjects who did not undergo neurological examination (n=13)	p value
Mean age (years)	50 ± 5.9	48.1 ± 5	n.s.
Mean exposure to dental work (years)	25.6 ± 3	24.0 ± 3.1	n.s.
Subjects with at least four positive answers in questionnaire for parkinsonism (y/n)	7/7	5/8	n.s.
Mean total score of GHQ*	28.7 ± 14.9	26.0 ± 12.2	n.s.
Mean score of somatic symptoms (GHQ)	8.0 ± 4.4	7.0 ± 4.5	n.s.
Mean score of anxiety (GHQ)	8.4 ± 5.2	8.0 ± 5.1	n.s.
Mean score of social dysfunction) (GHQ)	9.8 ± 3.7	8.2 ± 1.4	n.s.
Mean score of depression (GHQ)	2.5 ± 4.2	2.8 ± 2.6	n.s.
Subjects with a total score of 6 or above in the GHQ (y/n)	8/6	7/6	n.s.

* The General Health Questionnaire

Table 2

Clinical and occupational characteristic of five dental technicians with extrapyramidal symptoms

Patient	Age	Age at onset	Diagnosis	Family history for PD or/and essential tremor	UPDRS motor score	Exposure to dental work (years)
1	50	44	Parkinson's disease	no	12	30
2	64	62	Bilateral postural tremor	no	2	25
3	42	38	Bilateral postural tremor	yes	2	22
4	56	46	Bilateral postural tremor	no	3	31
5	52	46	Unilateral Postural tremor	no	1	23

Additional files provided with this submission:

Additional file 1: cover_letter_bmc_revis.doc, 38K
http://www.biomedcentral.com/imedia/1734452403145662/supp1.doc