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# "Effect of human occupational exposure to organic solvents: An Electrophysiological Study."

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**ABSTRACT:**

**Introduction:** Exposure to solvents is ubiquitous in modern industry and the workers are commonly exposed to mixtures of solvents.

**Aim & objectives:** This study aims to assess the effect of prolonged occupational exposure to organic solvent mixtures on peripheral nerve conduction parameters of workers employed in automotive spray paint industry by using nerve conduction studies. **Material & Methods:** The recordings were done in a standard way using Medelec Synergy EMG and EP systems. The exposed group consisted of 100 workers professionally exposed to chemical noxae, while the control group also consisted of 100 workers with no contact with such noxae at their workplace, working/living in the same area, matched for age, height and working conditions. Nerve conduction studies (NCS) of ulnar, median, common peroneal, tibial and sural nerves were performed in both groups. The sensory nerve conduction velocity and sensory nerve action potential (SNAP) of median, ulnar and sural nerves showed significant decline in exposed workers in comparison to the control group. Similarly, there was a significant increase in minimum F-wave latency and a significant decline in motor nerve conduction velocity and compound muscle action potential (CMAP) of the median, ulnar, common peroneal and tibial nerves of the exposed workers in terms of increasing duration of exposure.

**Conclusion:** It is concluded that the present study suggests peripheral neurodegeneration in workers of paint and lacquer industry.

**Key words**: occupational exposure, organic solvents, nerve conduction.

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**Introduction:** Exposure to solvents is ubiquitous in modern industry (1) and therefore the health impact of workplace solvent exposure remains an issue of substantial interest and concern to occupational health professionals. Organic solvents are chemically heterogeneous compounds that all share the property of dissolving fats, oils, resin, cellulose acetate and cellulose nitrate (2). These compounds are often discussed as a group because of their similar toxicological effects and a frequency of exposure

to their various combinations (3, 4).

Our study is based on the concept that solvent induced long term nervous system disease could involve damage to peripheral nervous system tissue by a process/mechanism related to the chemical properties of organic solvents and that this damage is detectable by diagnostic techniques. In the commonest circumstance of exposure to solvent mixtures, such as that encountered by painters, epidemiologic studies done earlier have shown significant increased rates of adverse peripheral nervous system (PNS) symptoms and electrophysiologic abnormalities on nerve conduction testing (2,5,6,7,8,9). Only a few of them could not replicate this relationship (10).

**Material and methods :** 100 subjects working in spray painting industries involved in automobile and railway coach painting constituted the study subjects. The control comprised of 100 workers with no contact with harmful chemical at their workplaces, working/living in the same area, matched for age, height and working conditions.

Within the exposed group separately, the subgroups were defined according to the length of exposure: a) <20 years and b) ≥20 years. Subgroups represent subsets of subjects according to the length of exposure (years) in the exposed group.

The nerve conduction study that involves the motor and sensory nerve conduction was done in a standard way using Medelec Synergy EMG and EP systems.

The following indices were used and defined as:

4. MNCV: maximum nerve conduction velocity of the motor fibres of the ulnar and median nerve between the wrist and elbow and common peroneal and posterior tibial between the knee and ankle.
1. SNCVd: distal conduction velocity of sensory fibres of the ulnar and median nerve between the wrist and 1st and 5th metacarpophalangeal joint and the sural nerve between the calf and foot.
2. Amplitude: amplitude of maximum sensory nerve action potential (SNAP) of the ulnar, median and sural nerves and maximum motor nerve action potential (CMAP) of ulnar, median, common peroneal and tibial nerves.
3. F-wave: for ulnar, median, common peroneal and posterior tibial nerves.

Surface electrodes were used both for stimulating and recording. The recording electrodes were in the form of disc for motor conduction tests and in the form of ring for sensory conduction tests. Tests were conducted with the subject in lying down position.

In motor nerve conduction studies, the active electrode was placed over the motor point which is usually at the midpoint between the origin and insertion of the muscle. The reference electrode was placed on the tendon. Their distance was standardized.

In sensory nerve conduction studies, both active and reference electrodes were placed on the innervation area of nerve with an inter-electrode distance of 4 cm. The nerve was stimulated antidromically.

**Observations and Results :**

Table I: Anthropometric profile of controls and subjects of different groups :

| Parameter | Control (n=100) | Subjects with duration of exposure | |
|---|---|---|---|
| | | <20 years (n=50) | ≥20 years (n=50) |
| **Age (yrs)** | 42.85± 6.12 | 35.8±3.48*** | **53.87± 5.25*** ** |
| **Height (cm)** | 168.42 ±4.4 | 166.13±10.79 | **166.72±16.23** |
| **Weight (kg)** | 65.25±12.25 | 66.21±1.33 | **63.21± 10.64** |
| **BMI** | **24.41 ± 6.34** | **23.5±4.04*** | **22.04± 3.52** |

Data presented are mean±SD. Analysis of data was done by one-way ANOVA and post hoc by Tukey-Krammer test. The control group was compared with both the study groups. *Significant at p<0.05 and *** significant at p<0.001

Significant association was observed in age and BMI of control and study subjects only.

Table II: Motor conduction velocity (m/s) of nerves among exposed and controls relative to the length of occupational exposure:

| Parameter | Control (n=100) | Subjects with duration of exposure | |
|---|---|---|---|
| | | <20 years (n=50) | ≥20 yrs (n=50) |
| **Right median nerve** | 59.80± 2.32 | 57.6±2.93 | **54.4± 2.65*** ** |
| **Right ulnar nerve** | 61.24± 3.33 | 59.55±6.24 | **56.45± 3.01*** ** |
| **Left common peroneal nerve** | 45.3± 2.14 | 43.86±3.05* | **41.80± 4.12*** ** |
| **Left tibial nerve** | **51.21± 2.78** | **48.25±3.38*** ** | **43.64± 3.22*** ** |

Data presented are mean±SD. Analysis of data was done by one-way ANOVA and post-hoc by Tukey-Krammer test. The control group was compared with both the study groups. *Significant at p<0.05 and *** significant at p<0.001

Table III: Maximum action potential (mV) of nerves among exposed and controls relative to the length of occupational exposure

| Parameter | Control (n=100) | Subjects with duration of exposure | |
|---|---|---|---|
| | | <20 years (n=50) | ≥20 yrs (n=50) |
| **Right median nerve** | 7.42± 1.96 | 7.04±2.27 | **5.85± 1.65*** ** |
| **Right ulnar nerve** | 7.72± 1.38 | 7.02±1.19* | **5.62± 1.72*** ** |
| **Left common peroneal nerve** | 4.15± 1.96 | 3.49±1.00* | **2.10± 0.88*** ** |
| **Left tibial nerve** | **3.66± 0.95** | **3.28±0.75*** | **1.95± 0.92*** ** |

Data presented are mean±SD. Analysis of data was done by one-way ANOVA and post-hoc by Tukey-Krammer test. The control group was compared with both the study groups. *Significant at p<0.05 and ** significant at p<0.01 *** significant at p<0.001

Table IV: Sensory nerve conduction velocity (m/s) of nerves among exposed and controls relative to the length of occupational exposure

| Parameter | Control (n=100) | Subjects with duration of exposure | |
|---|---|---|---|
| | | <20years (n=50) | ≥20 yrs (n=50) |
| **Right median nerve** | 43.59± 3.55 | 41.25±3.99*** | **36.65± 2.77*** ** |
| **Right ulnar nerve** | 52.84± 4.26 | 50.74±3.81** | **47.35± 3.50*** ** |
| **Left Sural nerve** | **47.45± 4.21** | **45.6±3.32** ** | **41.66± 2.12*** ** |

Data presented are mean±SD. Analysis of data was done by one-way ANOVA and post-hoc by Tukey-Krammer test. The control group was compared with both the study groups. *Significant at p<0.05 and ** significant at p<0.01 *** significant at p<0.001

Table V: Sensory nerve action potential (μV)) of nerves among exposed and controls relative to the length of occupational exposure

| Parameter | Control (n=100) | Subjects with duration of exposure | |
|---|---|---|---|
| | | <20 years (n=50) | ≥20 yrs (n=50) |
| **Right median nerve** | 7.95± 3.24 | 6.77±1.98* | **4.26± 2.06*** ** |
| **Right ulnar nerve** | 5.66± 1.54 | 5.16±2.23 | **3.66± 2.52*** ** |
| **Left Sural nerve** | **9.25± 1.32** | **8.5±1.2**** | **7.28± 1.55*** ** |

Data presented are mean±SD. Analysis of data was done by one-way ANOVA and post-hoc by Tukey-Krammer test. The control group was compared with both the study groups. *Significant at p<0.05 and ** significant at p<0.01 *** significant at p<0.001

Table VI: F-wave latency (ms) of nerves among exposed and controls relative to the length of occupational exposure

| Parameter | Control (n=100) | Subjects with duration of exposure | |
|---|---|---|---|
| | | <20 years (n=50) | ≥20 yrs (n=50) |
| **Right median nerve** | 29.81± 2.67 | 30.8±2.57 | **33.14± 2.64*** ** |
| **Right ulnar nerve** | 29.32± 7.65 | 31.86±2.09* | **33.10± 2.25*** ** |
| **Left common peroneal nerve** | 57.5± 2.55 | 61.14±4.27*** | **65.36 ±5.35*** ** |
| **Left tibial nerve** | **58.61± 2.34** | **61.49±2.43*** ** | **67.52± 4.45*** ** |

Data presented are mean±SD. Analysis of data was done by one-way ANOVA and post-hoc by Tukey-Krammer test. The control group was compared with both the study groups. *Significant at p<0.05 and ** significant at p<0.01 *** significant at p<0.001

**Discussion:** When interpreting the results of this study, several factors were considered. First, the selection criteria were based on previous medical history. Due to the effects of confounding variables some workers were excluded from the study and hence we believe that our data are correct but cannot be absolutely free from reporting bias. Second, since the major exposures, which can be anticipated in the work environment of a painting industry, are a cocktail of chemicals and the specific effect of each chemical is very difficult to pinpoint in such a multi-exposure scenario, so, instead of taking individual solvents into account, we conducted our study on a group of organic solvents that had toxicological effects on the nervous system. So, there was a possibility of having additive/amplifying effect because of the superimposition of solvents.

In the previous studies on this topic, few observed no difference (5) while others found slight reduction in the NCV in the exposed workers (6,7,8,9). Our results are consistent with a previous study that reported a significant positive association with long length of exposure to toxic agents leading to a change in the motor and sensory conduction velocity as well as distal latency of exposed workers in comparison to those of the control group (10).

We had taken F- wave latencies as unlike most other nerve conduction studies that are segmental; F-wave gives an idea of conduction in whole of the motor nerve starting from anterior horn cell and also gives an idea of the health of anterior horn cell. The latency of F-wave of the median, ulnar, common peroneal and tibial nerves increased with the increasing duration of exposure; the result being significant after 20 years of exposure. We have not come across a single study that gives an account on F-wave latency in relation to organic solvent exposure, so our results on F-wave could not be compared with previous studies.

Two basic forms of damage of peripheral nerves have been identified as responsible for the peripheral neuropathies associated with occupational exposure to organic solvents. Segmental demyelination results from primary destruction of the neuronal myelin sheath, with the relative sparing of the axons. This process begins at the nodes of Ranvier and results in the slowing of nerve conduction. Axonal degeneration is associated with metabolic derangement of the entire neuron and is manifest in degeneration of the distal portion of the nerve fiber. Myelin sheath degeneration may occur secondarily. This form of axonal degeneration was originally described as “dying back” neuropathy. In many instances, axonal degeneration and segmental demyelination may coexist, presumably due to the secondary effects derived from damage to each system (11). The clinical manifestations of neuropathy in exposed individuals may represent a combination of both pathologic processes (11, 12).

A possible underlying mechanism for solvent-induced long-term nervous system disease could involve damage to peripheral nervous system tissue by a process related to the chemical properties and dose of organic solvents. Following absorption, organic solvents undergo biotransformation (which occurs primarily in the liver), or they accumulate in lipid-rich tissues such as those of the nervous system. Metabolism in the liver generally consists of oxidative reactions catalyzed by the cytochrome P-450 mixed-function oxidase system followed by conjugation with glucuronic acid, sulfuric acid, glutathione, or glycine. Metabolism usually results in the detoxication of the organic solvent through formation of water-soluble compounds that are excreted through urine or bile (14,

15). However, metabolism may also produce reactive intermediate metabolites that are more toxic than the parent compound (14, 15). For example, n-hexane and methyl n-butyl ketone (solvents that produce peripheral neuropathies in exposed workers (16) are both metabolized to 2,5-hexanedione (17), which has been shown to have a greater neurotoxic potency (18,19) than either parent compound (20).

**Conclusion:** We conclude that there is a decline in the sensory and motor NCV, CMAP and SNAP amplitude and increase in the F wave latency of median and ulnar nerves of workers exposed to organic solvents used in paint industry as compared to the matched reference groups in accordance with increasing duration of exposure to organic solvents. Similar trend in MNCV, CMAP amplitude and F wave latency of common peroneal and tibial nerves was observed. The SNCV and SNAP amplitude of the sural nerve also declined significantly with increasing duration of exposure to organic solvents. The organic solvents used in paint industry pose a serious threat to the neurological health of workers.

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