

Raynaud's phenomenon in the occupational context

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SUMMARY

OBJECTIVE: To review articles that evaluated the prevalence of Raynaud's phenomenon of occupational origin.

METHODS: The search for articles was carried out in the Medline (via PubMed), Embase, Web of Science, Scientific Electronic Library Online (SciELO), and Latin America and Caribbean Health Sciences Literature (Lilacs) databases.

RESULTS: 64 articles were obtained from the electronic search; 18 articles met the eligibility criteria. All studies discussed the exposure to vibrations in the upper limbs. In 6 of them, the thermal issue was directly or indirectly addressed. No studies have addressed exposure to vinyl chloride.

CONCLUSION: In general, a higher prevalence of Raynaud's phenomenon was found among vibratory tool operators compared to non-exposed workers, with an increase in the number of cases the higher the level of vibration and the time of exposure. Cold is a triggering and aggravating factor of the Raynaud phenomenon and seems to play an important role in the emergence of vascular manifestations of the hand-arm vibration syndrome.

KEYWORDS: Raynaud Disease. Peripheral Vascular Diseases. Vibration. Vinyl chloride. Cold Temperature.

INTRODUCTION

Raynaud's Phenomenon: General Concepts

Raynaud's phenomenon is a condition characterized by an exaggerated vasospastic response at the level of the digital arteries and cutaneous arterioles. The episodes are evidenced by a well-marked alteration of the coloration of the fingers, which may be accompanied by paresthesias and pain. The classic triad described for Raynaud's phenomenon is the sequential alteration of white, blue, and red colors¹. This triad may not be observed in all patients, and most authors suggest the need for at least pallor and cyanosis to characterize the episode².

In the primary Raynaud's phenomenon, blood

vessels are structurally normal and no trophic changes, pittings, digital ulcers, and gangrene are expected. Patients who manifest vasospastic episodes due to a condition or disease that interferes with the mechanisms of vascular reactivity have secondary Raynaud's phenomenon¹. Several conditions may be associated with this type of Raynaud's phenomenon, such as autoimmune rheumatic diseases, hematological diseases, endocrine diseases, medications (bleomycin, cisplatin, interferon), malignancies, and situations related to the occupational context^{1,3}.

According to the list of work-related diseases, adopt-

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ed as a reference by the Brazilian Ministry of Health, localized vibrations, vinyl chloride, and work in low temperatures are considered etiological agents or occupational risk factors for Raynaud's phenomenon⁴.

Vibrations and Raynaud's phenomenon

There are two forms of occupational exposure to vibrations: localized and full-body vibration. Localized vibration is transmitted to the hands and arms and can cause injury to the upper limbs, including Raynaud's phenomenon. On the other hand, whole-body vibration can be harmful to the spine⁵.

Raynaud's phenomenon, digital neuropathy, and carpal tunnel syndrome have a well-established occupational link with exposure to localized vibrations. The injuries of the upper limbs associated with this type of exposure are called "hand-arm vibration syndrome". In this syndrome, neurosensory changes and vasospastic disease may coexist or progress independently. Vascular symptoms tend to improve at variable times after withdrawal from exposure. However, advanced cases of digital neuropathy, with loss of hand functions, are usually irreversible⁵.

Occupational exposure to localized vibrations is mainly related to activities using motorized tools such as hammers, crushers, polishers, sanders, drills, lawnmowers, countersinks, and chainsaws. Exposure commonly occurs in heavy construction and civil engineering services but may be present in a variety of activities⁵.

Vinyl chloride and Raynaud's phenomenon

Vinyl chloride is a volatile substance that is quickly absorbed through the lungs and metabolized by the liver. The final product of the polymerization of vinyl chloride is the polyvinyl chloride (PVC), which is widely used in the plastic industry⁶.

Before the 1970s, workers were commonly exposed to high concentrations of vinyl chloride in occupational air. For this reason, the term "vinyl chloride disease" was used to describe cases of acroosteolysis, hepatopathy, neuropathy, thrombocytopenia, skin lesions, and vascular alterations (Raynaud's phenomenon) attributed to the occupational exposure to this substance. However, industries progressively reduced workers' exposure to vinyl chloride as its deleterious effects and close connection to the onset of cancer were recognized⁶. Since 1979, vinyl chloride has been considered by the *International Agency for Research on Cancer* (IARC) as a human carcinogen (Group 1)⁷.

Cold environment and Raynaud's phenomenon

Concerning the work at low temperatures, it is known that cold is a triggering and aggravating factor of Raynaud's phenomenon of any etiology. Individuals with Raynaud's phenomenon are at increased risk of developing frostbite when exposed to low temperatures. Similarly, after frostbite, the affected limb may remain sensitive to cold, manifesting Raynaud's phenomenon^{3,4}. Thus, avoiding exposure to cold is an essential measure for the management of Raynaud's phenomenon in all patients¹.

Rationale and objective

The determination of occupational exposures is an essential element in the investigation of all patients with Raynaud's phenomenon. Therefore, it is important to know the prevalence of Raynaud's phenomenon in workers exposed to occupational risk conditions. On the face of it, the objective of this study was to conduct a review of articles that evaluated the prevalence of Raynaud's phenomenon of occupational origin, with emphasis on exposure to localized vibrations, vinyl chloride, and work in low temperatures.

METHODS

Eligibility criteria

Observational studies investigating the prevalence of Raynaud's phenomenon in workers with exposure to localized vibration, vinyl chloride, or low temperatures were considered eligible. Articles published since 1998 in English, Spanish, or Portuguese were searched. We excluded articles about occupational risk factors for the development of autoimmune rheumatic diseases with secondary Raynaud's phenomenon.

SEARCH STRATEGY

The search for articles was carried out in the following databases: Medline (via PubMed), Embase, *Web of Science*, *Scientific Electronic Library Online* (SciELO), and Latin America and Caribbean Health Sciences Literature (Lilacs).

The search strategy for Medline (via PubMed) was "raynaud disease"[All Fields] AND ("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH

Terms]) AND (“occupational exposure”[All Fields] OR “occupational diseases”[All Fields] OR “occupational injuries”[All Fields]) AND (“cold temperature”[All Fields] OR (“vibration”[MeSH Terms] OR “vibration”[All Fields]) OR “vinyl chloride”[All Fields]) AND (English[lang] OR Portuguese[lang] OR Spanish[lang]) AND (“1998/01/01”[PDAT] : “2018/01/31”[PDAT]).

This strategy was adapted to the other databases.

The searches were conducted from September 2017 to January 2018.

Selection of articles and data extraction

The studies were selected in two steps. The first step involved the screening of studies based on titles and abstracts. For the following evaluation, the full texts of the selected articles were retrieved. Information was recorded on: title, authors name, year of publication, country of origin, type of study, characteristics of subjects, occupation, type of exposure, type of evaluation and prevalence of Raynaud's phenomenon.

RESULTS

We obtained 64 articles from the electronic search. A total of 11 duplicate articles were excluded. After evaluation of the titles and abstracts, 19 articles were selected for full-text evaluation. Of these, one was excluded because it did not estimate the prevalence of Raynaud's phenomenon in the group of workers. In the end, 18 articles met the eligibility criteria and were included in the review (13 cross-sectional studies and 5 cohorts) — Figure 1.

The studies are highly heterogeneous. There are important differences in the analyzed populations, occupations, ways of estimating exposure to risk factors, definitions/evaluations of the Raynaud's phenomenon, and outcomes. All studies discussed exposure to localized vibrations. In 6 of them, the thermal issue was directly or indirectly addressed. No studies have addressed the exposure to vinyl chloride. The main features of the studies are presented in Tables 1 and 2.

DISCUSSION

The search strategy of this review contemplates three occupational risk factors for Raynaud's phenomenon according to the list of work-related diseases

(Brazilian Ministry of Health): localized vibrations, cold, and vinyl chloride⁴. Despite the broad scope of the research, there is a marked predominance of the topic “localized vibration of hands and arms” among the articles included. The cold was not addressed as an isolated risk factor in any article, and vinyl chloride was not discussed in any study.

In general terms, the literature review reiterates some expected data such as a higher prevalence of Raynaud's phenomenon among vibratory tool operators compared to non-exposed workers^{9,13,14}, an increased prevalence of this event the longer the exposure time to vibration^{8,21,23}, as well as among those exposed to higher levels of hand and arm vibration^{13,17,23}.

The studies that addressed the thermal issue suggest that the cold environment is an important synergy factor in the emergence of vascular manifestations of vibration syndrome^{10,12,13}. In the articles evaluated, temperature measurements were not performed in the workplace, but some studies considered metrological information to estimate exposure to colder environments^{12,13}.

In a study with construction electricians¹², among whom 95% used vibration tools at work, the

FIGURE 1.

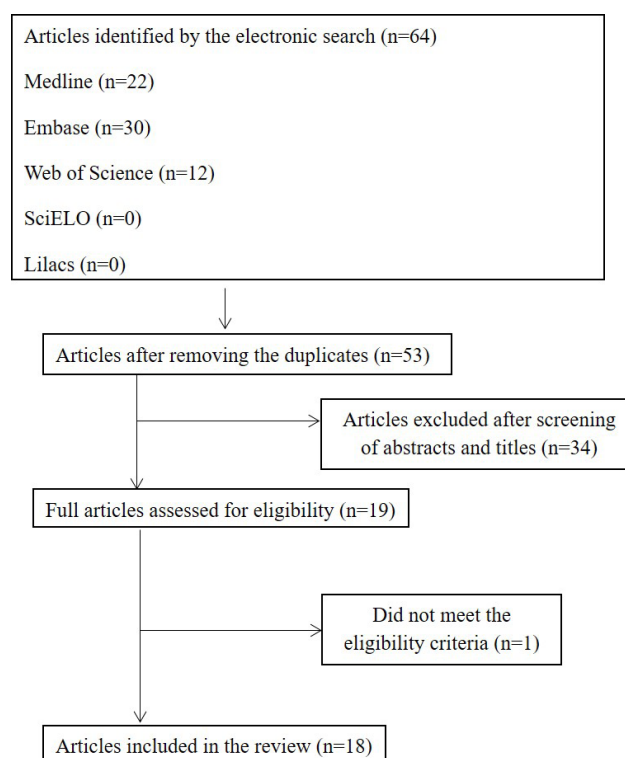


TABLE 1. RAYNAUD PHENOMENON IN WORKERS WITH EXPOSURE TO LOCALIZED VIBRATIONS, LOW TEMPERATURES, OR VINYL CHLORIDE.

First author	Year	Study design	Country	Characteristics (population)	Characteristics (occupation)	Type of exposure
Kluger ⁸	2017	Transversal	Finland	1000 people invited by email; response rate: 45%, 98 women and 350 men	Tattoo artists who are members of the French Union of Tattoo Artists	Vibration: tattoo gun
Pettersson ⁹	2014	Transversal	Sweden	Workers with ONIHL*; received the questionnaire: 246 men/78 women; response rate: 41%	Most common occupations: teachers, military, and welders	Vibration: questions to estimate minutes/day and years of exposure. Cold: time outdoors when working
Roquelaure ¹⁰	2012	Transversal	France	3.710 workers, 2.161 men (58%) and 1.549 women (42%)	Almost all occupations except farmers, artisans, tenants, self-employed	Vibration tools (≥ 2 hours/day): 460 workers. Cold temperature $< 15^{\circ}\text{C}$ (≥ 4 hours/day): 220 workers
Aiba ¹¹	2012	Cohort	Japan	704 workers (685 men and 19 women). Mean observation time: 10.6 ± 7.4 years	Workers using an impact wrench	Vibration: 8 vibrating tools selected to be evaluated during work. Acceleration: 4.9 - 22.6 m/s ²
Inaba ¹²	2010	Transversal	Japan	120 men; 74 answered a questionnaire in the winter and 83 in the summer	Electricians (construction workers)	Vibration: 95% of electricians used vibration tools. Cold: local metrological information
Burström ¹³	2010	Transversal	Sweden	Cases: 19,251 men exposed to vibration of hands/arms. Controls: 3,350 office workers	Cases: construction workers with exposure to hand and arm vibration	Vibration: 0-5 scale (occupational hygienists). Cold: local metrological information
Bovenzi ¹⁴	2010	Cohort	Italy	Cases: 249 workers with exposure to vibration. Controls: 138 workers without exposure	Forestry workers (chainsaws with anti-vibration device) and quarry workers	Vibration: ISO 5349. Estimation of daily exposure: direct observation for one week (chronometer)
Bovenzi ¹⁵	2008	Cohort	Italy	Cohort of 128 forestry workers. At the end of the follow-up, 57 workers (44.5%) had retired	Forestry workers: chainsaw operators	Vibration: sample of 9 chainsaws during operating conditions as per ISO 5349
Bovenzi ¹⁶	2008	Cohort	Italy	183 forestry workers and 33 quarry workers completed the follow-up	Forestry workers: chainsaws. Quarry workers: tools for processing marble	Vibration: measurements taken during tool operating conditions as per ISO 5349
Bovenzi ¹⁷	2005	Transversal	Italy	Cases: 100 female workers using orbital sanders. Controls: 100 female office workers	G(A) orbital sanders; (B) orbital sanders/hand sanding; (C) hand sanding	Vibration: measurements performed on 9 orbital sanders. Acceleration: 6.8 m/s ²
Futatsuka ¹⁸	2005	Transversal	Japan	73 quarry drill operators; 29 controls: manual tasks in the same companies	Quarry drill operators (rock drill)	Vibration: ISO 5349. Acceleration (drills): 45-55 m/s ² ; 160-210 min/day. Temp: South of Vietnam $> 25^{\circ}\text{C}$
Barregard ¹⁹	2003	Transversal	Sweden	900 car mechanics received a questionnaire; 806 replied	Mechanics of cars	Vibration: working time (average): 12 years. Exposure: 14 minutes/day. Vibration level: 3.5 m/s ²
Allen ²⁰	2002	Transversal	Ireland	Three groups of men (79 riveters, 52 healthy controls, and 79 claimants)	Workers: riveters. Controls: no vibration. Claimants: yard/public services	Vibration: exposure time of 0.2 - 18 years among riveters and 1.5 - 48 years among claimants
Palmer ²¹	2000	Transversal	United Kingdom	Questionnaires answered by 12.907 people aged 16-64 years (6.913 men/5.994 women)	Unspecified, random selection of record lists	Vibration: exposure assessed by questionnaire
Aiba ²²	1999	Cohort	Japan	383 workers (men): use of impact wrench in electric light pole factory, 1982 to 1999	Workers using an impact wrench	Vibration: ISO 5349 and JIS B 49000. Exposure: 102 to 117 minutes/day. Cold: not characterized
Palmer ²³	1998	Transversal	England	153 gas distribution agents (response rate 81%). Average of 16 years using vibrating tools	Gas distribution agents (pneumatic tools)	Vibration: ISO 5349. Vibratory tools (time of use - questionnaire): 1.2 to 5.5 hours/week (on average)
Bovenzi ²⁴	1998	Transversal	Italy	Cases: 822 workers exposed to vibration, Controls: 455 healthy men not exposed	Grinders, mechanics, quarry drillers, construction/forestry workers, etc.	Vibration: ISO 5349; 8.3 m/s ² (percussion); 2.8-4.7 m/s ² (percussion/rotary); < 2 m/s ² (rotary hand tools)
Miyashita ²⁵	1998	Transversal	Japan	4652 private forestry workers (at least 1 medical examination for VS** from 1974 to 1996)	Forestry workers exposed to hand and arm vibration (chainsaws)	Vibration: estimation of career time operating vibratory tools

*ONIHL = Occupational noise-induced hearing loss; VS** = Vibration Syndrome

TABLE 2. RAYNAUD PHENOMENON IN WORKERS WITH EXPOSURE TO LOCALIZED VIBRATIONS, LOW TEMPERATURE, OR VINYL CHLORIDE: EVALUATION OF THE RAYNAUD PHENOMENON AND OUTCOME.

First author	Evaluation of the Raynaud phenomenon	Outcome
Kluger ⁸	Questionnaire by e-mail. RP*: finger whitening related to cold. No evaluation was performed by a physician	448 questionnaires: 30 reported symptoms of RP*; 11 appeared after the beginning of tattooing activity. Daily work hours: association with RP*
Pettersson ⁹	RP* classified by the questionnaire (with image)	RP* considered in 37% of those who reported exposure to hand and arm vibration and in 15% of those who did not report the exposure
Roquelaure ¹⁰	Doctor asked about RP* features (last 12 months), defined as finger whitening episodes triggered by exposure to cold	87 cases of RP* diagnosed, 56 (women) and 31 (men). Female: association with psychosocial factors. Male: association with exposure to cold
Aiba ¹¹	Medical evaluation with questions about the signs/symptoms related to RP* and typical image to aid in reporting	RP*: 39 workers during the period. Incidence of RP*: 6.27 people per 1000 individuals-year. Prevalence: 0.6% (1982), 6.2% (1987), 4.9% (2008)
Inaba ¹²	Self-administered questionnaire. "White finger in response to cold environment". No evaluation by a physician and no picture of RP*	Prevalence of RP* among construction electricians: 43.2% (winter) and 7.2% (summer)
Burström ¹³	Self-administered questionnaire. Prevalence of RP* estimated by the questionnaire, without medical evaluation	Prevalence of white fingers: 13.4% (hand/arm vibration); 8.4% (controls). Higher odds ratio: intense vibration categories and workers in the North
Bovenzi ¹⁴	Criterion 1: reliable history (images of RP*). Criterion 2 (more restrictive): history of "white fingers" and cold provocation test	Prevalence of RP*: Criterion 1: 21.7% (vibration) and 7.3% (controls). Criterion 2: 10.8% (vibration) and 0.7% (controls)
Bovenzi ¹⁵	Physical examination; RP* related to occupation if provoked by cold and first episode after the beginning of occupational exposure	Prevalence of RP* related to vibration (beginning of the study): 26.6%; 11 new cases during the follow-up; cumulative incidence: 11.7%
Bovenzi ¹⁶	Physical examination; RP* related to occupation if provoked by cold and first episode after the beginning of occupational exposure	Prevalence of RP* related to vibration (beginning of the study): 18.1% (forest workers:14.8%; quarry workers:36.4%). Incidence:1.7% (3 cases)
Bovenzi ¹⁷	Physical examination; RP* related to occupation if provoked by cold and first episode after the beginning of occupational exposure	Daily vibration: higher in group A (4.7 m / s ²) than in group B (3.9 m / s ²); no significant difference (RP*) between furniture sander and controls
Futatsuka ¹⁸	Subjective complaints assessed by interview. Peripheral circulation and neurosensory tests	No workers suffering from "white fingers". Hypoaesthesia, weakness, and coldness in fingers/hands: significantly higher in the drill operators
Barregard ¹⁹	Diagnosis based on the history of well-marked pallor episodes on the fingers or parts of the fingers (induced by cold)	Estimated prevalence of RP* related to vibration: approximately 15% among car mechanics
Allen ²⁰	Questionnaire: medical and occupational history. Vasospasm: provocative test (cold) and systolic pressure of the finger	Riveters (6.3%) and claimants (83.5%) reported RP* symptoms. Positive test for vasospasm (finger cooling): riveters (30.4%); claimants (19%)
Palmer ²¹	Questionnaire considering well-marked alterations of finger coloration caused by cold conditions	Pallor of the fingers (history): 14.2%. Cold-induced: 11.8%. Clear demarcation: 4.6%. Time of exposure (vibration): associated with symptoms
Aiba ²²	Questionnaire: medical and occupational history. Doctor asked about RP* related factors (images of RP*)	Prevalence of RP* related to vibration: 1.7% (1982), 4.86% (1986), disappearing in 1994. During the period: preventive measures introduced
Palmer ²³	Interview with doctor or nurse, questionnaire, physical examination, and hand immersion test in cold water (2-8oC for 4 minutes)	Prevalence of pallor of the fingers: 24%. Risk increased significantly with the hours of use of vibratory tools and the level of vibration
Bovenzi ²⁴	Diagnosis: positive history for pallor episodes involving at least 1 finger and occurring after exposure to localized upper limb vibration	Prevalence of RP*: 17.2% among workers exposed to vibration, ranging from 9.0% among grinders to 51.6% among foundry workers
Miyashita ²⁵	Medical evaluation records	Prevalence of workers who complained of "white fingers" induced by vibration: 25.9% (1978), 25.7% (1988) and 15.1% (1996)

RP* = Raynaud phenomenon

prevalence of subjective symptoms of Raynaud's phenomenon was found in 43.2% of them during the winter (temperature of 5.5°C on average) and only in 7.2% during the summer (temperature of 24.4°C on average). A Swedish study¹³ in which the contrast of the cold environment was made by

choosing a northern and a southern region of the country, suggested that the factors mainly related to the Raynaud's phenomenon were the two most intense categories of exposure to vibration in workers living farther north (colder weather) compared to the south.

Regarding the manifestations of hand-arm vibration syndrome, it is known that neurosensory alterations and vasospastic disease can coexist or progress independently⁵. A Japanese study¹⁸ evaluating quarry workers (drill operators) from southern Vietnam did not identify cases of Raynaud's phenomenon. However, the prevalence of peripheral neurologic symptoms such as hypoaesthesia and weakness of the hands were significantly higher among the drill operators than in the controls. The hypothesis raised by the authors is that cold is an essential factor to trigger vascular manifestations of hand-arm vibration syndrome, and the workers evaluated did not develop them because they remained in environments with temperatures higher than 25°C throughout the year. In this way, the authors of this study suggest that, in a tropical environment, workers exposed to high levels of vibration could develop a dominant neurosensory form of hand-arm vibration syndrome, reinforcing the theory that circulatory and neuropathic symptoms may be independent¹⁸.

Another issue that deserves attention when evaluating the results of the studies included in this review refers to the methodological limitations of certain forms of research. Some studies only used information obtained through questionnaires to define the presence of Raynaud's phenomenon related to vibration^{8,9,12,13}. However, the self-reported symptoms alone may not be sufficiently specific to assess whether Raynaud's phenomenon is primary or secondary, and as a result, there may have been incorrect classification in some cases. Likewise, the quantification of the duration of exposure to hands and arms vibration is not an easy task and is subject to recall biases when estimated through questionnaires or even by direct interview⁹.

Questionnaire responses about symptoms suggestive of Raynaud's phenomenon may be influenced by the context in which they are obtained. An Irish study²⁰ comparing riveters to a group of claimants for vibration-related injury showed that 6.3% of riveters and 83.5% of claimants reported symptoms of Raynaud's phenomenon. However, 30.4% of the riveters and only 19% of the claimants had a positive test for vasospasm after cooling the finger at 10°C for 5 minutes. The authors argued that only the lack of sensitivity and specificity of the cold provocation test would not explain the large discrepancy between the riveters and the claimants²⁰. Thus, some contexts

could underestimate, and others overestimate the symptoms.

In order to reduce the prevalence of Raynaud's phenomenon by localized upper limb vibration, measures such as limiting working hours with vibrating tools, using anti-vibration technology, and maintaining the working environment warm are performed²². In a Japanese study, technical improvements in tool motors with the introduction of anti-vibration mechanisms dramatically reduced the vibration transmitted to the hands of workers using impact wrenches²². In this study, the prevalence of Raynaud's phenomenon among workers was 4.86% in 1986 and gradually declined until disappearing in 1994. During this period, impact wrenches with anti-vibration mechanisms and measures to regulate the environment and protect workers from the cold were introduced (curtains to protect against outside cold, hand washing with warm water and impact wrench with heated handle)²².

Articles exploring vinyl chloride as an occupational risk factor for Raynaud's phenomenon were not found in our search. This fact is probably due to two reasons. The first to be considered is that vinyl chloride disease is a rare event, and most of the studies are case reports or cases series, which were not considered in our search strategy. The second, and possibly even more important, is related to the fact that our electronic search was restricted to the last 20 years. Since 1979, vinyl chloride has been classified as carcinogenic to humans⁷, and industries have made interventions to reduce the concentration of this substance in occupational air drastically. This allowed "vinyl chloride disease" to have only a historical significance today.

CONCLUSION

Localized vibrations of the upper limbs, low temperatures, and vinyl chloride are considered occupational risk factors for the development of Raynaud's phenomenon. There is a higher prevalence of Raynaud's phenomenon among vibratory tool operators compared to non-exposed workers. The higher the level of vibration and the time of exposure to it, the greater the risk of developing the disease. Cold is a triggering and aggravating factor of Raynaud's phenomenon and plays an important role in the onset of vascular manifestations of hand-arm vibration syndrome. The reduction of the time

using vibrating tools, the acquisition of equipment with anti-vibration technology, and the adoption of measures to protect workers from the cold environment should be considered to reduce the prevalence of work-related Raynaud's phenomenon.

RESUMO

OBJETIVO: Realizar um estudo de revisão dos artigos que avaliaram a prevalência do fenômeno de Raynaud de origem ocupacional.

MÉTODOS: A busca pelos artigos foi realizada nas bases de dados Medline (via PubMed), Embase, Web of Science, Scientific Eletronic Library Online (SciELO) e Literatura Latino-Americana e do Caribe em Ciências da Saúde (Lilacs).

RESULTADOS: Sessenta e quatro artigos foram obtidos a partir da busca eletrônica, dos quais 18 cumpriram os critérios de elegibilidade. Todos os estudos discutiram sobre a exposição a vibrações localizadas em membros superiores. Em seis deles, a questão térmica foi direta ou indiretamente abordada. Nenhum estudo abordou a exposição ao cloreto de vinila.

CONCLUSÃO: De maneira geral, constatou-se maior prevalência do fenômeno de Raynaud entre operadores de ferramentas vibratórias em comparação aos não expostos, com aumento do número de casos quanto maior o nível de vibração e tempo de exposição. O frio é fator desencadeante e agravante do fenômeno de Raynaud e parece exercer papel importante para o surgimento das manifestações vasculares da síndrome de vibração de mãos e braços.

PALAVRAS-CHAVE: Doença de Raynaud. Doenças vasculares periféricas. Vibração. Cloreto de vinil. Temperatura baixa.

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