Vorhabensbeschreibung, Arbeitsziele (max. 1.800 Zeichen)
project description, objectives

This systematic review of the scientific medical literature about the causation of chronic-obstructive pulmonary disease (COPD) by the inhalation of inorganic dust and the accompanying metaanalysis of spirometric results were performed to explore the evidence for a causal relationship.

Review and metaanalysis aimed at summarizing the present stage of knowledge on the topic to provide a basis for further evaluation of the "Bundesministerium für Arbeit und Soziales" and the Medical Advisory Board for new occupational diseases.

Durchführung, Methodik, Gender Mainstreaming
implementation, methodology, gender mainstreaming

On the basis of the PICOS criteria (= Participants, Intervention, Comparison, Outcome, Study Design) the sort of study type and participants were defined in advance (Stroup 2000, Liberati 2009). Also it was defined a priori which occupational inhalative exposure to inorganic dust and which endpoints of obstructive airway restriction should be considered in the review. Publications fulfilling certain validity criteria were selected for the review/metaanalysis, which was divided into four areas: (1) population-based studies, (2) studies dealing with biopersistent granular dust (BGD), (3) silica- or (4) fiber containing dust. Tables in the annex provide information about first author, publication year, country, study type, number of exposed and not exposed study subjects, quantification of exposure, and parameters considered in the metaanalysis. If a study was part of the review but not considered for metaanalysis, it is justified why.

The publicly available data file of the US-American National Center for Biotechnology Information (NCBI) as well as EMBASE (Excerpta Medica Database) were used for retrieval of publications. On the exposure side the applied MeSH-terms were: ("occupational exposure" OR "air pollutants, occupational") and on the outcome side the Mesh-terms ("pulmonary disease, chronic obstructive" OR "pulmonary function test") supplemented by text fields related to lung function test. Defined search string: ("pulmonary disease, chronic obstructive" OR "respiratory function tests" OR "respiratory function" OR “lung function” OR “pulmonary function”). After inspection of title and abstract by two independent reviewers (Brüske/Nowak) 496 publications were ordered as well as two publications retrieved "by hand". Inclusion
criteria were checked, which left 257 publications for evaluation of validity (Brüske/Huster/Nowak). The quality was assessed on the basis of the Newcastle-Ottawa Scale (NOS) and the recommendations of the Cochrane Collaboration. Abstraction sheets were created and applied for the most important features of each study.

Ergebnisse, Schlussfolgerungen
results, conclusions

Review

The population-based studies predominantly showed a positive association between exposure to dust and signs of airway obstruction. This was considered as an important evidence for a causal relationship between airway obstruction and dust exposure at the workplace in the general population.

Biopersistant granular dust (BGD): Early studies from the US, Jordan and Norway showed no detrimental effect of dust exposure on lung function in cement workers. But, later studies with a higher dust exposure of cement workers from Tansania and Iran showed a strong association with impaired lung function. Especially, a new large and prospectively designed study of the European Cement Association (Nordby et al. 2011) with 4265 exposed participants was very informative. Alle studies related to carbon black/soot/rubber/talcum showed adverse effects of dust exposure on lung function with stronger effects for early studies with high dust exposure compared to late studies with low exposure. The evidence from studies with workers in the aluminum, iron and steel industry was inconsistent. Negative or only weakly positive (and not statistically significant) impact of dust exposure on lung function was seen in studies from Canada, Finland and the US. The mining industry was varied a lot in regard to sort, composition and intensity of dust exposure. Whereas workers in a large open pit mining of Bauxite in Australia were only slightly exposed and showed no lung function abnormalities, there was a high dust exposure in manganese mining underground in Iran. Spirometry showed a significant decrease of FEV1 and FVC of exposed workers compared to non-exposed workers with a stronger effect in smokers. The longitudinal study of Lotz et al. (Lotz et al. 2008) performed in potash mining underground in Germany showed a significant decrease in lung function over time.

Silica containing dust: Granite quarry workers have been investigated in Sweden, Spain, and in a controversially discussed study in Vermont, US. The results were inconsistent. Two studies from the Netherlands, one in potato sorter with a high exposure to respirable dust containing silica, and one in concrete workers showed significantly lower values for FEV1 and FEV1/FVC in the cross-sectional comparison to non/exposed workers. Several Norwegian studies of tunnel workers showed an increased risk of obstructive airway disease, which could not be assigned to the exposure to silica dust without ambiguity. In the US, a cohort of employees in a foundry showed decreasing % predicted values for FVC and FEV1 as well as FEV1/FVC dependent on the cumulative exposure to respirable silica dust, however only for smokers. In underground uranium mining in the former German Democratic Republic (Möhner et al. 2012) the cumulative exposure to 1 mg/m³•year pure respirable silica dust was associated with a 2.75% decrease in FEV1/FVC (p<0.001). An imbedded case-control study showed that the risk of COPD stage I was associated with an odds ratio of 1.81 per 1 mg/m³•years respirable silica dust.

Dust containing fibers: Studies among workers in the asbestos industry showed a clear dose-response relationship between asbestos exposure and a restrictive ventilation pattern. Obstructive impairment measured as a decrease in FEV1 was also observed to some extent. Overall, the classic parameter of a COPD diagnosis: FEV1/FVC < 70% was not fulfilled. The parameter FEV1/FVC < 70% seemed not appropriate in the context of existing restrictive ventilatory defects.

Metaanalysis

To allow for the variability between studies, a random-effects model was chosen. The results of the metaanalysis in regard to parameters of cross-sectional and longitudinal evaluation are presented graphically (forest plots). There were no signs of publication bias in the funnel plots.

For the metaanalysis BGD and silica containing dust are considered each as a disjunct group and evaluated in a cross-sectional and longitudinal approach. It was not possible to use data from population-based studies or data from studies about fiber-containing dust for the metaanalysis.
The cross-sectional analysis of workers exposed to biopersistent granular dust at the workplace revealed a mean decreased FEV1 of 160 ml or 5.7 % reduced predicted value compared to non/low exposed workers. The ratio FEV1/FVC was also significantly reduced.

The longitudinal comparison showed that the average decrease in FEV1 was significantly higher (6.3 ml/year) for exposed compared to non/low exposed people. In regard to the cumulative exposure to respirable biopersistent granular dust FEV1 decreased by 1.6 ml per mg/m³•year. The odds ratio for the obstructive impairment of lung function was increased by 7% per mg/m³•year of BGD. Obstructive impairment of lung function was defined as a ratio of FEV1/FVC <70% or chronic bronchitis.

Exposure to respirable silica at the workplace gave rise to 4.6% decreased predicted value. The ratio of FEV1/FVC as a standardised mean difference between silica exposed and non exposed people was decreased (statistically significant). In the longitudinal analysis there was a higher decrease (11.8 ml/year) of FEV1 for silica exposed persons compared to non/low exposed.

Conclusions

Review and metaanalysis showed a statistically positive association between the inhalative exposure to BGD at the workplace and a decreased FEV1 in cross-sectional as well as in longitudinal analyses. The general suitability of BGD to cause a disproportionate decrease in FEV1 and thereby the development of a work-related COPD was approved. In regard to the cumulative exposure of respirable BGD the decrease of FEV1 was 1.6 ml per 1 mg•m-3•year in the longitudinal analysis. The risk of an impaired obstructive lung function (defined by FEV1/FVC < 70%) was increased by 7% per 1 mg•m-3 BGD current dust exposure. The individual cumulative exposure was not taken into account. The studies therefore did not allow directly to define a threshold limit value for respirable BGD above which a so called doubling risk for COPD could be estimated. Spirometric investigations showed a premature aging of the lung in the sense of a younger age at diagnosis of COPD, but a valid estimation of the number of years this premature aging would amount to was not possible.

For silica dust the review and metaanalysis also showed a statistically positive association between the inhalative exposure at the workplace and a decreased FEV1 in cross-sectional as well as in longitudinal analyses. The general suitability of silica to cause a disproportionate decrease in FEV1 and thereby the development of a work-related COPD was also approved. A study was able to quantify the association: The risk of COPD in underground uranium mining was increased OR=1,42 (95% KI 0,92 – 2,20) in relation to 1 mg•m-3 silica-year (respirable dust). The risk of developing a COPD stage II+ was doubled for a cumulative exposure to 2 mg•m-3•silica-year (respirable dust).

Umsetzung
realization

In spring 2013, the results of the Systematic Review will be presented and discussed by the authors in the Advisory Medical Board "Occupational Diseases" of the Federal Ministry of Labour and Social Affairs. On the basis of these results, the Board will then take up further discussions concerning the question of whether, considering the special provisions of the legislation on occupational diseases, the legal requirements are met to introduce new or reclassify existing occupational diseases as COPD diseases caused by inorganic dust.

Literatur
references


