

The Effect of Methylmetacryalte Exposure on The Incidence of Asthma Bronchiale

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Abstract

Background: Asthma is one of the major health problems in the world. An estimated 300 million people worldwide suffer from asthma, with 250.000 deaths each year from asthma. The prevalence of asthma has continued to increase in recent years, Asthma affects 1 in 14 people in America in 2001 while in 2009 the rationale was 1 patient in 12 people The aim of this report is to get a systematically searching in order to get an answer about the risk factor of the Asthma bronchiale and the prevention measure.

Methods: A 40-year-old woman who works as a dental technician complains of experiencing symptoms of shortness of breath, wheezing, coughing and cold. A search was carried out to obtain clinical answers with databases obtained from: PubMed, and ProQuest. With the keyword "Worker", "Methyl Methacrylate OR Acrylic" AND "Occupational Asthma" with inclusion criteria cohort studies, case control studies, cross sectional studies, methyl methacrylate, occupational asthma, occupational, and case report.

Results: One study was found that there was a relationship between asthma and exposure to methacrylate. Risk of doctor-diagnosed asthma within 12 months (OR 27.6, 95% CI 1.19 - 7-54) and adult-onset asthma (2.65, 1.14-7.24) when compared with those not exposed to methyl methacrylate.

Conclusion: From the two studies that we have been reviewed there was a significant relationship between exposure of methyl methacrylate or acrylic to the incidence of asthma.

Keywords: asthma bronchiale, methylmetacryalte

Abstrak

Latar belakang: Asma merupakan salah satu masalah kesehatan utama di dunia. Diperkirakan 300 juta orang di seluruh dunia menderita asma, dengan 250.000 kematian setiap tahun akibat asma. Prevalensi asma terus meningkat dalam beberapa tahun terakhir, Asma menyerang 1 dari 14 orang di Amerika pada tahun 2001 sedangkan pada tahun 2009 alasannya adalah 1 pasien dari 12 orang. Tujuan dari laporan ini adalah untuk membuat pencarian secara sistematis untuk mendapatkan jawaban tentang faktor risiko Asma bronkial dan tindakan pencegahannya.

Metode: Seorang wanita berusia 40 tahun yang berprofesi sebagai teknisi gigi mengeluh mengalami gejala sesak napas, mengi, batuk dan rinore. Pencarian dilakukan untuk mendapatkan jawaban klinis dengan database yang diperoleh dari: PubMed, dan ProQuest. Dengan kata kunci "Pekerja", "Metil Metakrilat atau Akrilik" dan "Asma Kerja" dengan kriteria inklusi studi kohort, studi kasus kontrol, studi cross sectional, metil metakrilat, asma akibat kerja, okupasi, dan laporan kasus.

Hasil: Satu studi menemukan bahwa ada hubungan antara asma dan paparan metakrilat. Risiko asma yang didiagnosis dokter dalam 12 bulan (OR 27,6, 95% CI 1,19 - 7-54) dan asma onset dewasa (2,65, 1,14-7,24) jika dibandingkan dengan mereka yang tidak terpapar metil metakrilat.

Kesimpulan: Dari kedua penelitian yang kami analisis terdapat hubungan yang signifikan antara paparan metil metakrilat atau akrilik dengan kejadian asma.

Kata kunci: asma bronkiale, methylmetacryalte

Introduction

Asthma is one of the major health problems in the world. An estimated 300 million people worldwide suffer from asthma, with 250,000 deaths each year from asthma. The prevalence of asthma has continued to increase in recent years, Asthma affects 1 in 14 people in America in 2001 while in 2009 the rationale was 1 patient in 12 people.¹

Most asthma, especially in children, is related to allergies. Meanwhile, asthma in adults has more diverse characteristics of risk factors and causes. Several factors related to asthma, especially in adults, include obesity, environmental pollution, genetic changes in vitamin D receptors, psychological, hormonal, cigarette smoke, and one of the most important is occupational asthma. Occupational asthma is estimated at 15% -25% of all adult asthma cases worldwide. Occupational asthma is estimated by the CDC to be 1.9 million cases, or more than 15% of asthma cases in America. Occupational asthma cases were found mostly in the 45 - 64 years group (20.7%).²

Occupational asthma is increasingly becoming a problem in the management of asthma, the prevalence of occupational asthma tends to increase due to the many exposure to substances found in work as the cause of asthma. In addition, the demands of industrialization and consumerism have resulted in an increasingly unhealthy work environment. In addition, clinical understanding of the management of asthma is still limited, so this case tends to be difficult to control.³

The influence and psycho-socioeconomic impact of occupational asthma is also a separate issue regarding this condition. Occupational asthma patients often still experience decreasing quality of life, even though they have been transferred from a place where the cause of their asthma is predicted. There are also psychological problems experienced by patients, such as depression and anxiety. There is an economic impact of occupational asthma cases. This economic impact can be directly related to the cost of health services and indirectly due to the inability of workers to maintain productivity in the company.⁴ Polymethyl methacrylate (PMMA) is a type of polymer derived from the monomer methyl methacrylate. Methyl methacrylate is a non-biodegradable monomer. The process of forming methyl methacrylate into PMMA, which is now known as polymerization, was first discovered in 1877 by

two German chemists, Fittig and Paul. PMMA also has another name, poly methyl 2-methylpropenoate (IUPAC name). In addition, the trade name of this polymer can be Lucite, Perspex, Oroglass, Goldglas, Altuglas, or Plexiglas. This polymer is amorphous and is a thermoplastic material that is hard, stiff, and brittle at room temperature. In addition, PMMA is also a biocompatible material due to its wide application but is non-biodegradable because it comes from monomers with similar properties. PMMA is slightly hydrophobic but will become more hydrophilic after reacting with water.⁵

A dental laboratory is a place where the process of producing, processing, mixing and changing chemicals to support the work of licensed dentist. Dental technician is a specialized profession for individuals who are devoted to the manufacture of dentures, orthodontic and maxillofacial devices, in partnership with dentists and specialist dentists. One of the products that dental technicians produce is a removable orthodontic appliance made from acrylic. Although at present there is a great need for the use of fixed orthodontic appliances, there are still many loose orthodontic appliances made mainly as retention devices and appliances for simple orthodontic treatment.^{5,6}

Case Description

A 40-year-old woman who works as a dental technician complains of experiencing symptoms of shortness of breath, wheezing, coughing and cold. This complaint occurred 6 months after the patient came into contact with a substance containing methyl-methacrylate. Previously, patients were often exposed to substances containing methyl methacrylate for about 13 years. Complaints are felt to be reduced after the patient breathes fresh air, the patient does not have a history of asthma as a child and does not have a family history of asthma, the patient also does not have a history of smoking.

A skin test performed by applying methyl methacrylate to the skin yielded negative results. When a provocation test was performed with methyl-methacrylate, the patient experienced shortness of breath with decreased Forced Expiratory Volume (FEV1) and Peak Expiratory Flow Rate (PEFR). From the results of taking samples of nasal fluid, it was found an increase in leukocytes, eosinophils, basophils, albumin, eosinophils cationic

protein (ECP) and mast cell tryptase after bronchial provocation tests.

The authors concluded that methyl-methacrylate can cause (non-atopic) asthma in people exposed to the effects at work.

Evidence

A search was carried out to obtain clinical answers with databases obtained from: PubMed, and ProQuest. With the keyword “Worker”, “Methyl Methacrylate OR Acrylic” AND “Occupational Asthma” with inclusion

criteria cohort studies, case control studies, cross sectional studies, methyl methacrylate, occupational asthma, occupational, and case report and also for exclusion criteria article that have no population sample, inappropriate exposure, and studies in animals. The searching was done on 16 Nov 2020.

Result

Based on online search, it was found that articles that match the inclusion and exclusion criteria, cross sectional study M.S jaakkola, T.Leino, Tammilehto, P

Table 1. Searching keywords used on several databases

Electronic database	Search strategy	Hit	Selected
PubMed	(((worker[MeSH Terms])) OR (job)) AND ((methyl methacrylate) OR (Acrylic)) AND ((asthma[MeSH Terms]) OR (occupational asthma[MeSH Terms]))	16	2
ProQuest	(((worker)) OR (job)) AND ((methyl methacrylate) OR (Acrylic)) AND (occupational asthma) NOT ((nail) or (rhinitis) or (cancer) or (radiologist) or (Pneumoconiosis) or (Nitric oxide) or (isocyanate) or (Dermatitis) or (Heart Disease))	10	0

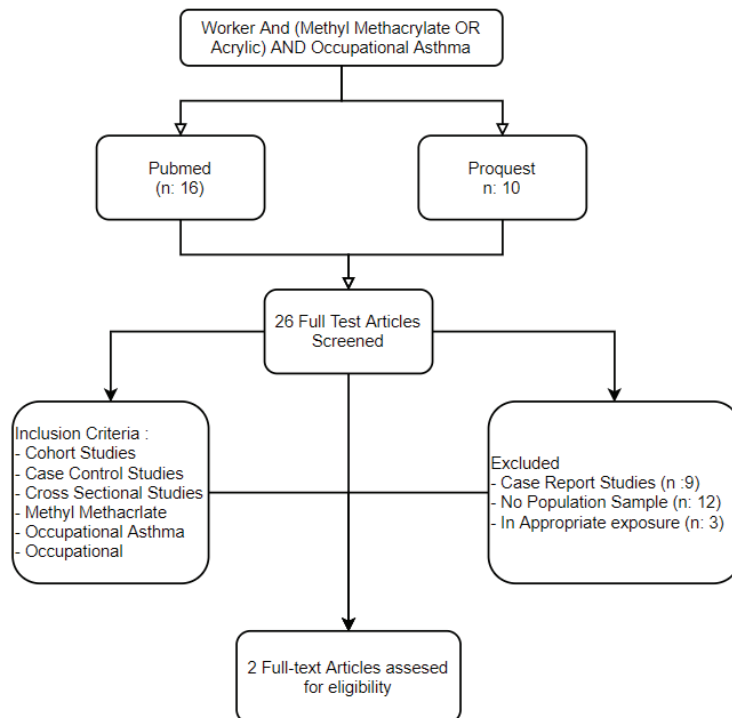


Figure 1. Literature searching flow chart

Ylatalo, E. After conducting a critical appraisal, it can be concluded that all articles are valid. The results of the critical appraisal can be assessed in Table 2

The first article, a cross sectional study conducted by M. S. Jaakkola et al, was conducted by the institute of occupational and environmental medicine, University of Birmingham, Finnish Institute of Occupational Health, Department of Periodontology, Institute of Dentistry, University of Oulu. This case control study was conducted to see the effect of exposure to methacrylate on dental assistants respiratory problem, the subject of this study was 779 female dental assistants who were interviewed with a questionnaire containing exposure to methyl methacrylate and asthma.¹

The subject were asked whether they have Exposure to methyl methacrylate Every day for the last 3 months with main job is making dental filling, cementing orthodontal brackets, veneers cementing, crowns and bridges, and repairing dentures. The duration of exposure was divided into 4 categories, with no exposure, 5 years of exposure, 5 - 10 years, and more than 10 years. For the category of asthma, if subject answered yes in "have you ever had asthma" and "whether it was diagnosed by a doctor" question from questionnaire. Then the participants were also asked whether in the last 12 months they had an asthma attack or not.

From these results, it was found that there was a relationship between asthma and exposure to methacrylate. Risk of doctor-diagnosed asthma within 12 months (OR 27.6, 95% CI 1.19 - 7-54) and adult-onset asthma (2.65, 1.14-7.24) when compared with those not exposed to methyl methacrylate.

The second article, a Cohort Retrospective study conducted Lilienberr L, Et Al, Occupational and Environmental Medicine, Sahlgrenska Academy, University of Gothenburg. In this article using 21802 workers born in 1945 to 1973, the study was carried out in 1989-1992. Then followed up again with a questionnaire from 1999 to 2001. New Onset Asthma is defined if you have a positive answer to the question "do you have asthma after the age of 16 years" and "has it been diagnosed by a doctor" for atopy means if you have a positive answer to the question "do you have hay fever or nasal allergy" The subject was also classified as having never smoked and had ever smoked.²

From the results of the study, it was found that the increased risk of developing asthma in men without a history of atopic was HR = 3.3; 95% CI = 1.4-7.5.

Discussion

Making dentures requires certain materials, one of the chemical material is methyl methacrylate or often referred to as acrylic. Acrylic is a material that is often used in the manufacture of dentures, but this material can also cause new problems, namely bronchial asthma.⁷ From the results of a study conducted by MS Jaakkola et al was carried out cross sectional on dental assistants who were exposed to methacrylate every day for more than 3 months, it was found that the increase in OR on risk Respiratory disorders are 1.47, 95% CI 1.02-1.84) and cough due to work is OR 1.69, 1.08 - 2.71), while for the risk of Doctor diagnosed asthma in the last 12 years, OR 2 was obtained , 76, 95% CI 1.19-7-7.54) and adult onset asthma (2.65, 95% CI 1.14-7.24) were very significant.¹

In this study there was also a comparison of the duration of exposure to the methacrylate substance, namely 0-5 years having an OR of 7.61 95% CI: 1.66-55.36; 5-10 years have OR: 4.20 (95% CI 0.98-29.21) and > 10 years have OR 3.02 with 95% CI (0.80-19.75). This may occur due to methacrylate type occurring within a period of 5 years or the second possibility that workers who already have a history of asthma or their asthma has worsened have been advised to be transferred.^{9,10}

The next article is an article by Linnea Lillienberg et al, with a large population of 13284 subjects born from 1945 to 1973, which was administered by giving a questionnaire. in 1989-1992 and 1999-2001.² From the observation, it was found that 429 subjects with new onset asthma were inclined 1.4 cases per 1000 people per year for men and 2.4 for women. When examining the risk of exposure from acrylates, it was found that the HR value was 3.3 with 95% = 1.4 -7.5.^{10,11}

From the results of the search for the article, it was found that there was a significant increase in workers exposed to methyl methacrylate of OR 2.65 or more than 2 times the incidence of asthma when exposed to methyl methacrylate compared to not exposed. As well as the acrylic Hazard Ratio number with the number 3.3 with 95% CI = 1.4 - 7.5. Based on the article, it was found that the results of searching for journal articles critically found that from clinical questions it could be answered that Methyl methacrylate or acrylic could cause adult onset asthma.¹⁰

Table 2. Results of study characteristics and critical study

Studies	Method	Subject	Intervention	Impact and Results	The same treatment	Follow-up	Causal diagnostic test	Level of evidence *
M. S. Jaakkola et al (2017)	A cross-sectional study	923 Female dental assistants of Finnish Association of Dental Hygienist and Assistants with daily exposure to methacrylates in the past 3 months	Exposure to Metyl methacrylate	Impact: - Effects of exposure to Methacrylates on respiratory symptoms Results: - The risk of doctor diagnosed asthma in the last 12 months (adjusted OR 2.76, 95% CI 1.19–7.54) and adult-onset asthma (2.65, 95% CI 1.14–7.24)	Yes	No	No	4
Linnea Lillienberg et al (2012)	Cross sectional study about occupational exposure and New onset Asthma	21802 subjects born between 1945 and 1973, in 1999-2001 the subjects were mailed a follow up questionnaire which was answered by 16202 subjects (74%)	Exposure to HMW agents, LMW agents (Acrylic), irritating agents, accidental peak exposure to irritant, uncertain or low exposed	Impact: - Effects of exposures to New Onset Asthma Results: - Significantly increased asthma risks were seen among non-atopic men exposed to acrylates (HR = 3.3; 95% CI = 1.4–7.5),	Yes	No	No	4

* Level of evidence (etiology):

- 1 : Systematic review of randomized trials, systematic review of nested case-control studies, n-of-1 trial with the patient, you are raising the question about, or observational study with dramatic effects
- 2 : Individual randomized trial or (exceptionally) observational study with dramatic effects
- 3 : Non-randomized controlled cohorts / follow-up studies (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient)
- 4 : Case-series, case control, or historically controlled studies
- 5 : Mechanism-based reasoning

Conclusion

From the two studies that we analyse there was a significant relationship between exposure of methyl methacrylate or acrylic to the incidence of asthma.

References

1. Jaakkola MS, et al. Respiratory effects of exposure to methacrylates among dental assistants. *Journal Allergy*. 2007; 62:648–54.
2. Lillienberg L, Et al. Occupational Exposure and New-onset Asthma in a Population-based Study in Northern Europe (RHINE). *Ann Occup Hyg*. 2013;57(4):482–92.
3. Hagberg S, Ljungkvist G, Andreasson H, Karlsson S, Barregard L. Exposure to volatile methacrylates in dental personnel. *J Occup Environ Hyg*. 2005;2:302–6.
4. Peutzfeldt A. Resin composites in dentistry: the monomer systems. *Eur J Oral Sci* 1997;105:97–116.
5. Henriks-Eckerman M-L, Alanko K, Jolanki R, Kerosuo H, Kanerva L. Exposure to airborne methacrylates and natural rubber latex allergens in dental clinics. *J Environ Monit* 2001;3:302–5.
6. Vallittu PK, Ruyter IE, Buykuilmaz S. Effect of polymerization temperature and time on the residual monomer content of denture base polymers. *Eur J Oral Sci* 1998;106:588–93.
7. Andersson E, Knutsson A, Hagberg S *et al*. Incidence of asthma among workers exposed to sulphur dioxide and other irritant gases. *Eur Respir J*. 2006;27:720–5.
8. Pattaro C, Locatelli F, Sunyer J et al. Using the age at onset may increase the reliability of longitudinal asthma assessment. *J Clin Epidemiol*. 2007;60:704–11.
9. Suarathana E, Heederik D, Ghezzi H et al. Risks for the development of outcomes related to occupational allergies: an application of the asthma-specific job exposure matrix compared with self-reports and investigator scores on jobtraining- related exposure. *Occup Environ Med*. 2009;66: 256–63.
10. Holm M, Omenaas E, Gíslason T *et al*. RHINE Study Group. Remission of asthma: a prospective longitudinal study from northern Europe (RHINE study). *Eur Respir J*. 2007;30: 62–5.
11. Karjalainen A, Kurppa K, Martikainen R *et al*. Work is related to a substantial portion of adult-onset asthma incidence in the Finnish population. *Am J Respir Crit Care Med*. 2001; 164:565–8.