

Type 2 diabetes in Mexican workers exposed to a potential source of dioxins in the cement industry determined by a job exposure matrix

Diabetes tipo 2 en trabajadores Mexicanos expuestos a una fuente potencial de dioxinas en la industria del cemento determinado a través de una matriz de exposición ocupacional

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Abstract

Purpose: To identify association between type 2 diabetes (DM2) with occupational exposure to potential dioxins source in Mexican cement industry workers.

Materials and Methods: 56 medical files of cement industry workers with diagnosis of DM2 were included; 56 medical files of workers from the same industry without DM2 were the controls. The daily dose of exposure (DDE) to the potential dioxins source per work years was estimated by a job exposure matrix and categorized as low, moderate, and high. Logistic regression model that correlated high exposure to potential source of dioxins (cement clinker confinement) per work years and presence of DM2 was adjusted by work seniority, patient age at which DM2 diagnosis was established and DM2 familiar background.

Results: the OR for the presence of DM2 in workers with moderate and high exposure to potential source of dioxins in the cement industry was 3.25 (1.10–9.57), $p= 0.03$, adjusted by work seniority, worker age at which DM2 diagnosis was established, and DM2 familiar background.

Conclusions: In according with the data explored in the medical files of cement industry workers, there is an association between high exposure to the industrial confinement of the cement clinker as a potential source of dioxins and presence of DM2 in a modest dose-response gradient.

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Key Words: *Dioxins, Occupational exposure, Type 2 diabetes.*

Resumen

Propósito: Identificar asociación entre diabetes tipo 2 (DM2) en trabajadores Mexicanos con la exposición ocupacional a una fuente potencial de dioxinas de la industria cementera.

Material y métodos: Se incluyeron 56 expedientes clínicos de trabajadores de la industria cementera con diagnóstico de DM2; los controles lo constituyeron 56 expedientes clínicos de trabajadores de la misma industria pero sin DM2. La dosis diaria de exposición (DDE) a la fuente potencial de dioxinas por años trabajados se estimó a través de una matriz de exposición ocupacional y fue categorizada como baja, moderada y alta. El modelo de regresión logística que correlacionó la alta exposición a la fuente potencial de dioxinas (confinamiento de la escoria o *clinker* de cemento) por años trabajados y presencia de DM2 fue ajustada por antigüedad en el trabajo, la edad del paciente en la que se estableció el diagnóstico de DM2 y antecedente familiar de DM2.

Resultados: la razón de momios para la presencia de DM2 en trabajadores con exposición moderada y alta a la fuente potencial de dioxinas en la industria cementera fue de 3.25 (1.10–9.57), $p= 0.03$, ajustada por antigüedad en el trabajo, edad del trabajador en la que se estableció el diagnóstico de DM2, y el antecedente familiar de DM2.

Conclusiones: De acuerdo con los datos explorados en los expedientes clínicos de trabajadores de la industria cementera, existe asociación entre la alta exposición al confinamiento industrial de la escoria o *clinker* de cemento, como fuente potencial a dioxinas, y la presencia de DM2 con un modesto gradiente de dosis-respuesta.

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Palabras clave: *Dioxinas, Exposición ocupacional, diabetes tipo 2.*

BACKGROUND

Dioxins are ubiquitous substances considered practically anthropogenic that have arisen as undesirable product of industrial processes employing incineration at high temperatures.¹⁻⁵ From the biochemical point of view, dioxins are organic, aromatic, and chlorinated compounds that are extremely lipophilic, with a bioaccumulative capacity adjudged as possessing toxic power, among others, to change glucose cell transportation and synthesis, as well as to diminish insulin efficiency, with the consequent negative effect on the general carbohydrate metabolism.⁶⁻¹⁶

Lethal doses of 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) —a type of dioxins, but with the greatest toxic power— in experimental animals produces abrupt weight loss, rejection of food, and inactivity, all these accompanied by reduction of adipose tissue, hypertriglyceridemia, and redistribution of fatty acids. This battery of effects has been explained by changes exerted by 2,3,7,8-TCDD on the lipoprotein lipase, which under normal conditions regulates insulin production and liberation in pancreas, and which in liver is assigned the task of controlling glucose metabolism and fatty acid synthesis.⁷

Other elements to consider comprise irregularities in glucose uptake due to defects in type 4 glucose transporters (GLUT-4), which under normal conditions are those responsible for supplying glucose to muscle and other tissues. This alteration has been cited as the most important mechanism in DM2 pathogenesis induced by experimental exposure to 2,3,7,8-TCDD.⁷⁻¹¹ Despite this evidence, epidemiologic studies that have attempted to associate the presence of DM2 in workers chronically exposed to dioxinogenous sources, or even in populations acutely and accidentally exposed to high concentrations of these substances due to industrial disasters, have yielded not very conclusive results, which has placed in doubt the diabetogenic power of dioxins in humans.¹²⁻¹⁶ However, it is recognized that there are not yet enough information to discard this proposal, due on the one hand to the complex participation of multiple factors that trigger DM2, which should be controlled, and on the other hand to the difficulties in establishing environmental or occupational exposure, this due to the temporal and spatial fluctuations to which a worker performs his/her job.^{6,7,17,18}

Based on what has been referred herein and because at present the cement industry is considered one of the main dioxin sources in the modern industrial world, the objective of the study was aimed to determine the association between occupational exposure to potential dioxins source in the Mexican cement industry and presence of DM2 in their workers.

METHODS

From 2,714 medical files of workers at the Occupational Health Services of the Mexican Institute of Social Security in which DM2 and its complications are depicted as diagnosis between July, 1999 and June, 2003; 276 of them were identified with ≥ 1 year of occupational life performed in any cement industry workplace. Finally, 56 medical files of workers with diagnosis of DM2 established at work in this type of industry and fulfilled inclusion criteria were included to the study. In addition, 56 files of workers who also worked in the cement industry but without DM2 diagnosis were utilized to make up the comparison group.

The daily dose of exposure (DDE) to dioxins in all workers—partly based on the job exposure matrix proposed by Piaciatelli and collaborators—was estimated.¹⁹ In the reliability process of the instrument, staff who had worked in this type of industry supported with the workplace and job descriptions; this information improved the consistency in determination of the daily fraction of workers exposed to potential sources of dioxins expressed in terms of percentage (exposure length) and level of occupational contact with 2,3,7,8-TCDD; in the case of our study was considered the location where the cement clinker material —an

intermediate product obtained after incineration in rotary furnaces manufactured from pre-triturated and standardized material and prepared for final milling, application of additives, and cooling prior to packaging and final shipment—is deposited. The subrogated concentration considered for this dioxinogenous source comprises that indicated by US Department of Health & Human Services based on average total dioxin-like toxic equivalents per kg of cement clinker produced.²⁰

The final result of the estimated DDE to dioxins was based on the equation proposed by Piacitelli et al.,¹⁹ i.e., 2,3,7,8-TCCD concentration x level of contact (0.01–1.5 based on what is demonstrated in Table 1) x time of exposure (the fractional percentage in 1 work day), which was applied for each particular case; with this the DDE to potential source of dioxins in the cement industry was calculated, and for estimation of the DDE/years worked in this type of industry, job seniority expressed in years that the worker performed in the cement industry was also identified in the workers medical files. Internal reliability of the instrument proposed measured by Kuder-Richardson coefficient was > 0.80 (“good internal reliability”).²¹

Table 1. Occupational contact level with TCDD and daily fraction (%)

Level	Level value	Work profile	%
1	0.01	Workers have practically null contact with the potential dioxin source and workers with only general instructions on the company's safety. Industrial security personnel, backhoe operators, and cargo workers are found at this level.	0.05
2	0.05	Workers perform in areas that are not dioxin sources but have exceptional contact with it; probably wear contaminated clothing. Workers in administrative and office areas fall within this category.	0.10
3	0.10	Workers have very low contact with the potential exposure source, but wear the same work clothing that is probably contaminated. At this level are found mill hopper operators, who only occasionally are mobilized to other areas.	0.10
4	0.25	Workers have low contact in company areas outside of the company's potential dioxin-generating process and where the contaminated product accumulates. Probably wear clothing that is contaminated. This level includes superintendents, packers, and cargo elevator workers.	0.15
5	0.50	Workers are in moderate contact. This level includes chemists and laboratory assistants, who are exposed with relative frequency to the potential dioxin source and who can have areas of dermal or respiratory contact on managing industrial samples for their daily analysis.	0.30
6	0.75	Workers are in high contact with the potential dioxin exposure source. Production-area engineers and maintenance supervisors are included at this level, and have some dermal or respiratory contact.	0.40
7	1.00	Workers are in considerably high contact with the potential exposure source. This level includes the company's laboratory technicians who routinely daily production-area samples, and who routinely are in dermal or respiratory contact with dioxin-contaminated contact.	0.60
8	1.25	Workers are in very high contact with the potential dioxin source. Included in this level are technicians who routinely carry out supervisory tasks and who occasionally perform heavy manual tasks with potential contact with large amounts of dioxin-contaminated material.	0.80
9	1.50	Workers are in extraordinary high contact with the potential dioxin source. This includes the general laborers who are in very close and permanent contact with the production process and with the pre-established dioxin-exposure source and potentially with others. This level also includes tasks involving removal of dioxin-contaminated material, carrying out heavy manual tasks, and routinely cleaning automatized but very contaminated areas in the company.	1.00

Worker age, total work years of the worker, fraction of total work years devoted to the cement, worker's age when the DM2 diagnosis was established, years of disease evolution, and familiar background of DM2 also were explored.

From values of DDE/years worked in the cement industry, two cut-off points were established to configure three levels: low DDE (<percentile₂₅); moderate DDE (between percentile₂₅ and percentile₇₅), and high DDE (>percentile₇₅). To determine the dose/response gradient presence of DM2 according to DDE/occupational years to which the worker was subjected in this type of industry, the category denominated as low was took as baseline. The associations were measured by odds ratio (OR) with 95% confidence intervals (95% CI), and the Mantel-Haenszel χ test with critical p value at 0.05.

Logistic regression model that correlated high occupational exposure to the cement clinker as a potential source of dioxins and DM2 was adjusted by work seniority, patient age at which DM2 diagnosis was established and DM2 familiar background.

RESULTS

The 112 analyzed medical files corresponded to male workers with 51.3 ± 8.1 of age with 31.9 ± 9.4 total years of work life, which 31% were devoted to cement industry. Average of job seniority in this type of industry according to that consigned in the medical files included in the study was 11.1 ± 6.3 years.

Regarding workplace types, the following were identified: 32 general laborers; 23 supervisors; two chemists; one chemical laboratory technician; five superintendents; four packers who also performed as load elevator workers and storage workers; two mill hopper workers; 12 employees who carried out diverse activities in the company's administrative services; six security employees; eight backhoe operators; 10 load workers, and seven maintenance workers.

The data obtained from the medical files concerning worker age, years worked at the cement industry, total worker occupational-life duration, the fraction dedicated to cement industry work, and DM2 familiar background, are shown in Table 2.

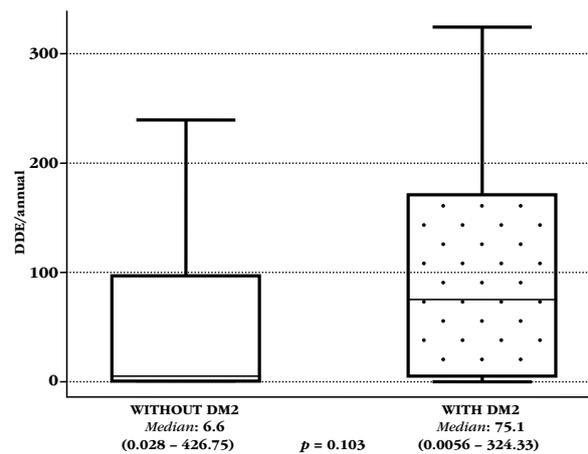
Table 2. Occupational characteristics, backgrounds, and disease evolution according to the DM2 diagnosis

	Workers with DM2	Workers with other diagnoses	p
Workers age (years)	48.9 ± 8.1	53.7 ± 7.5	0.0015*
Seniority at the cement industry	11 (1–30)	11 (1–32)	0.73**
Total work life (years)	31.5 (2–46)	30.5 (12–50)	0.05**
Fraction (%) of total work life devoted to the cement industry	22 (0.5–79)	21.5 (1–94)	0.19 [†]
Workers (%) with familiar background of DM2	54	46	0.56 [†]

*Student t test; **Mann-Whitney test; [†] χ^2 test.

The median DDE of workers of the cement industry exposed to the confinement of the cement clinker and took this as a potential source of dioxins was identified as significantly higher among workers with type 2 diabetes [11.38 (Q_{25%}, 0.26) – (Q_{75%}, 17.07)], in comparison with those without DM2 [1.70 (Q_{25%}, 0.0569) – (Q_{75%}, 17.07)]; ($p = 0.001$). In a similar way, globally DDE/years worked in the cement industry between the work group determined to have DM2 and the group determined not to have this is shown in Figure 1.

Figure 1. DDE/years worked in the cement industry and presence of type 2 diabetes mellitus



Percentiles₂₅ and ₇₅ distribution values of DDE to dioxins/years worked in the cement industry were utilized as cut-off points to establish exposure levels proposed as low (DDE/years worked ≤0.40), moderate (DDE/years worked >0.40–135.0), and high (DDE/years worked >135.0). The low level was established as baseline from the level that determined the association of DM2 with levels of DDE to dioxins/work years categorized as moderate and high; with this, we established the dose-response gradient (Table 3).

Table 3. DDE levels of exposure to dioxins/years worked and their association with presence of type 2 diabetes mellitus in cement industry workers

Level of exposure	With DM2*	Without DM2*	OR	95% CI	p
High	18	8	4.05	1.30– 12.61	0.016
Moderate	28	30	1.68	0.66–4.25	0.274
Low	10	18	—	—	—
TOTAL	56	56			

DDE, daily dose of exposure; DM2: type 2 diabetes mellitus; OR: odds ratio; 95% CI: 95% confidence interval.

With the exception of chemist and laboratory assistant (Table 4), all workplaces were distributed in both study groups. The worker identified as general laborer was the sole workplace with DDE/years average worked at an exposure level qualified as high. Supervisor, chemist, laboratory assistant, superintendent, packer-load elevator operator-storage worker, and maintenance personnel are found at the moderate exposure level, while those identified as security employees, back hoe operators, mill hopper operators, administrative staff, and load workers are found at the low exposure level.

Table 4. DDE to dioxins/years worker by job position according to the diagnosis of DM2

Workplace	Workers with DM2		Workers without DM2	
	n1 (%)	DDE/years worked*	n2 (%)	DDE/years worked*
General laborer	23 (41)	171.0	9 (16)	239.0
Supervisor	11 (19)	114.0	12 (20)	108.0
Chemist	0 (0)	—	2 (4)	20.0
Laboratory assistant	1 (2)	82.0	0 (0)	—
Superintendent	3 (5)	6.0	2 (4)	3.0
Packer-load elevator worker-storage worker	2 (4)	6.0	2 (4)	5.0
Maintenance personnel	2 (4)	6.0	5 (10)	31.0
Mill hopper operator	1 (2)	3.0	1 (2)	0.3
Administrative staff	3 (5)	1.0	9 (15)	0.3
Security employee	2 (4)	0.03	4 (7)	0.06
Back hoe operator	4 (7)	0.03	4 (7)	0.08
Load worker	4 (7)	0.03	6 (11)	0.1
Median and range, DDE/years worked in all workplaces [§]		75.1 (0.005–324.33)		6.6 (0.028–426.75)

DDE, daily dose of exposure; DM2, type 2 diabetes mellitus; *Percentile50 of DDE/years in workplace; ** $p = 0.196$ in distribution of 12 workplace by study group; [§] $p = 0.10$ (Mann-Whitney test).

In Table 5 are shown the association between presence of DM2 and exposure to a potential source of dioxins in the Mexican cement industry in a logistic regression model adjusted by workers seniority at this industry, age at DM2 diagnosis, and familiar background for DM2.

Table 5. Logistic regression for the association between presence of DM2 and exposure to dioxins adjusted by seniority at cement industry, age at DM2 diagnosis, and familiar background for DM2

	Presence of DM2		
	OR	95% CI	p
High exposure to potential source of dioxins in the Mexican cement industry	3.25	1.10–9.57	0.03
Seniority at cement industry (≥ 11 years)	1.16	0.47–2.85	0.74
Age at which DM2 diagnosis was established (≥ 45 years)	0.22	0.09–0.52	0.001
Familiar background for DM2	2.65	1.13–6.20	0.02

DM2, type 2 diabetes mellitus; OR, odds ratio; 95% CI: 95% confidence interval.

DISCUSSION

The occupational exposure matrix originally proposed by Piacitelli¹⁹ for final calculation of DDE to dioxins fulfilled the purpose of serving as adequate proxy to estimate retrospectively in the Mexican cement industry workers the level of contact with 2,3,7,8-TCDD that theoretically is presented in the cement clinker.²⁰⁻²³ However, it is possible that this matrix does not strictly fulfill the oligovariability criteria of possessing a scale that proposes a range of 0.01–1.50; additionally, it is also possible that these criteria were not accurately applied because the information was through reconstructed work scenarios, verbal job performance and workplace descriptions, and were not the result from a field study conducted at companies-of-interest, basically because these refusal to permit access to their facilities, and also impeded to know the historical and current 2,3,7,8-TCDD quantification registries of the dioxinogenous source, which in theory the companies are on their own.^{19,24}

The study entailed only male workers; this is because it is common that companies at which the performance of tasks considered heavy or risky is perceived or required do not hire female workers.²⁵⁻³⁰

Although the proportion of DM2 in “active” workers in Mexico is unknown, the presence of this entity in cement industry workers through their medical files is very consistent with the prevalence described in work disability rulings of total Mexican worker population insured by the Instituto Mexicano del Seguro Social; this same consistency was observed in that regarding the proportion of workers who presented the miscellaneous diseases that conformed the control group, which render greater representativity to the sample collected for this study.³⁰⁻³² It is noteworthy that in Mexico, the economic subsector in which the cement industry is found, in conjunction with the plaster and lime industries, occupies approximately 40% of the entire personnel of the transformation industry’s economic branch.³²

From the clinic and epidemiologic point of view —with regard to age at appearance of diabetes mellitus in workers studied during the fourth decade of life and presence of family background of diabetes, which even continue to be discussed in terms of their protagonism in the appearance of diabetes— these are compatible characteristics with those found for general population. Nonetheless, negative labor-related effects have also been the reason for wide discussion,³³⁻³⁹ on the other hand, the DM2 familiar background in workers with high exposure to the potential source of dioxins demonstrated a very emphatic association.²⁹

Regarding DDE to 2,3,7,8-TCDD and congener substances, the estimation of exposure through a *job exposure matrix* was higher among workers with DM2. In addition, the estimation reinforced the idea of considering years worked in the cement industry, this despite the analysis was over the workers medical files —a secondary information source— and not due to the limitations of the study itself. It must also be accepted that the majority of these instruments are imperfect, and originated the need of delving into the study of the diverse worker tasks performed, because each of these possesses a specific exposure profile which the estimation obtained can be more accurately.^{19,40}

Despite the consistency with the modest results of association between a potential dioxinogenous source and presence of DM2 mentioned in diverse scientific literature, in no manner should it be understood, at least at present, to consider DM2 —specifically in this type of industry— as a work disease, until the diabetogenous capability of 2,3,7,8-TCDD in humans is fully elucidated.^{6-16,41}

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