Effects of Pesticides on Development of Tape 2 Diabetes Mellitus

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Abstract. Scope and quality of studies on direct or indirect (through obesity) effects of pesticides on the whole and certain drugs on type 2 diabetes mellitus (DM2) acquiring epidemic proportions vary widely, not allowing to draw firm conclusions. To identify significance and degree of dependence of incidence rates of type 2 diabetes mellitus and obesity in adult population on the use of pesticides and new till technologies at regional level. Reports of the Ministry of Health and the Ministry of Ecology of the Republic of Tatarstan for the period from 2004 to 2016 were used. Cause and effect relationships of the parameters were assessed by means of multiple correlation and regression analysis with subsequent disperse one. Out of 116 992 patients with DM2 registered in the Republic, 116 977 were from the adult population. Relationships of DM2 (r=0.85) and obesity (0.71) prevalence with use of glyphosate preparations, tillage area according to no-till (r=0.97 and 0.89) and reduced-till (0.72 and 0.63) technologies were revealed. Correlation of agricultural indices with incidence of new cases of DM2 and obesity becomes significant only during the second-third year. The model of DM2 prevalence in case of the greatest effect of the volume of glyphosate use (R²=0.98; p<0.003), which correlated closely with the area with reduced-till and no-till technology (0.93 and 0.92; p<0.0001), was identified as the only one as informative (R²=0.93) and adequate of the variants of incidence rates of DM2, obesity and use of herbicides analysis. Increase of consumption of glyphosate-containing herbicides in conditions of no-till and reduced-till technologies contributes to growth of diabetes mellitus and obesity prevalence in adult population.

1. Introduction

Modern strategy of steady development of agriculture consists in the use of pesticides, mineral fertilizers and optimization of the cropping system. The crop losses from a complex of pests, diseases and weeds can make 25-30% without carrying out proper special activities [1]. 6-10% of crops are lost annually because of weed infestation, and 20-30 million tons – from diseases [2]. Although the primary consumer of pesticides is an agricultural sector, up to 45% of their volumes are used in other spheres of economic management (disinfection, deratization, killing of weeds along the highways and the railways, and etc.) [3].

The largest volumes of using pesticides were registered at the end of 1970-ies and the beginning of 1980-ies, when preparations with a load higher than 4 kg/ha, frequently as high as 10-20 kg/ha, were mainly used. From the end of 1980-ies their consumption began to decrease due to many causes, including crisis, the appearance of new preparations with low application rates.
The growth in sales volume of pesticides, herbicides in particular, began in the years of 1998-2000. In the same years, in many countries, the incidence of diabetes mellitus, primarily of insulin-independent type 2 (DM2), making more than 95%, acquired epidemic proportions, which caused significant socio-medical and economic losses. In 90% of cases, DM2 is diagnosed in connection with overweight, which along with obesity accompanies 44% cases of DM2. High growth rates of obesity are explained primarily by increasing prevalence of high-calorie nutrition and lack of physical exercise among population, but according to the studies, chemical compounds increase the incidence of obesity and DM2 even on following a healthy lifestyle [4].

However, a number of pesticides cause pronounced effects on the adipogenesis and the adipose tissue metabolism, where they are typically deposited [5, 6]. Overlapping of the growth of DM2 cases and the gross volume of preparations from different groups is identified [7]. The effect on formation, development and outcome of DM2 is shown with the highest degree of proof as far as chloroorganic pesticides belonging to persistent organic pollutants, which are at present prohibited or limited for use [8]. Scope and quality of the carried out studies on direct or indirect effects of pesticides both on the whole, and certain classes on DM2 vary widely, preventing from drawing firm conclusions, determining the relevance of works in this field.

Aim of this work is to identify significance and degree of dependence of incidence rates of type 2 diabetes mellitus and obesity in adult population on the parameters of using pesticides and tillage technologies in farming at regional level.

2. Materials and methods
The analysis included data from the Center for Information and Analysis of the Ministry of Health of the Republic of Tatarstan (RT), the Ministry of Ecology and Natural Resources of the RT for the period from 2004 to 2016. The value of 0.05 was taken as a critical significance level at all stages of statistical analysis. The non-parametric Spearman rank-order correlation coefficient was determined year in and year out, and with 1-4 year lag (the time lag) with an indication of the 95% confidence interval (CI). Cause and effect relationships and the contribution of agricultural parameters to incidence rates of DM2 and obesity were assessed according to results of multiple correlation and regression analysis with subsequent application of disperse one by means of AtteStat and PSPP software.

3. Results of study and discussion
Out of 116 992 patients with DM2 registered in the RT as on January 1, 2017, 116 977 patients were from the adult population (18 years and older). The proportion of insulin-independent diabetes in DM on the whole varied over a period of 2004-2016 from 90% to 96.7%, which corresponds to global statistics. If relative indices of primary and total DM2 incidence in the RT in the year of 2016 were somewhat higher (Table1) than on the average in the RF (265.2 and 3606.4 per 100 thousand of population correspondingly), then those of obesity were lower (292.3 and 1188.9 cases per 100 thousand of population correspondingly).

Table 1. Indices of primary and total incidence of type 2 DM and obesity among adult population of the Republic of Tatarstan.

| Index                                      | Primary | Total |
|--------------------------------------------|---------|-------|
| DM2                                        | Obesity | DM2   | Obesity |
| Growth rate (2004-2016), %                 | 44.1    | 121.9 | 158.9   |
| Per 100 thous. population (2016), cases    | 280.7   | 3806.9| 882.0   |

The highest growth rate in the given period was observed as far the frequency of new cases of obesity and the lowest – DM2. The range value of primary DM2 incidence in the years under study
between administrative units of the Republic increased from 4.6 (2005) to 34.1 (2015); and that of prevalence - from 2.8 (2005) to 3.5 (2015).

A highly significant and strong relationship was determined between prevalence of DM2 and obesity in adult population (r=0.92; the 95%-th CI: 0.76±0.98; p<0.0001), whereas it was moderate (r=0.5; the 95%-th CI: 0.07±0.82; p=0.04) between indices of primary incidence.

The results of statistical processing can be regarded as an evidence for the appearance of a new factor having an effect on the indicated two ICD codes (nosologies) to different extents and significance, and the non-uniform distribution of this factor over the territory. Preliminary analysis of dynamics of quantitative and qualitative characteristics of the technogenic (man-made) burden on the environmental compartments of the region from different sources shows that the most significant changes took place in farming during the period indicated.

The pesticide application area varied from 1923.7 to 3889 thousand ha; the gross consumption – from 1380.9 tons to 2310.8 tons; the median of specific gravity of herbicides in total amount of preparations corresponded to 70.7%.

During these years, the application of new tillage technologies increased by a factor of 21.9: from 42.3 thousand to 928.1 thousand hectares. The determination factor of the trend line approximation of the area (R²) according to reduced-till technology (up to 30% of crop residues remain on the soil surface – reduced-till) was determined as 0.73, and according to no-till technology (the soil is not cultivated, and the sowing is carried out directly into stubble or bands – no- till) – 0.95, characterizing steady and very high growth rates

Glyphosate-based herbicides (26.0-34.2%), phenoxaprop-P-ethyl (16.1-19%), desmedipham and phenmedipham (12-18%), 2,4-dichlorophenoxyacetic acid (10.5%), dicamba (3-4.1%), MCPA and others began to be used more often. The use of glyphosate preparations (glyphos, glyphor, glyder, glyphogold, roundup, tornado, argument, fakel) increased by a factor of 25.4 (from 13.2 to 334.8 tons).

Correlation analysis revealed statistically highly significant correlation of DM2 and obesity prevalence with the consumption volume of glyphosate-containing preparations and the areas for cultivation of agricultural lands according to no-till and reduced-till technologies, and zero correlation – with the area and the consumption of pesticides, herbicides (Table2). It is important that dependence of DM2 and obesity incidence on glyphosate consumption and the areas for using new technologies persisted for up to two-four years

**Table 2.** Spearman rank-order correlation coefficient between agricultural indices and incidence of type 2 DM and obesity.

| Index                        | DM2          | Obesity       | DM2          | Obesity       |
|------------------------------|--------------|---------------|--------------|---------------|
| Pesticide application area   | 0.57; p=0.03 | Insignificant | Insignificant| Insignificant |
|                              | CI :004±0.87 |               |              |               |
| Pesticide consumption        | Insignificant| 0.51; p=0.04  | Insignificant| Insignificant |
|                              | CI:-0.05±0.83|               |              |               |
| Herbicide consumption        | Insignificant| Insignificant | Insignificant| Insignificant |
| Glyphosate consumption       | Insignificant| Insignificant | 0.85; p=0.0001| 0.71; p=0.003 |
|                              |              |               | CI:0.55±0.95 | CI:0.27±0.91  |
| Reduced-till area            | 0.59; p=0.02 | Insignificant | 0.72; p=0.003| 0.63; p=0.01  |
|                              | CI:0.05±0.86 |               | CI:0.28±0.91 | CI:0.12±0.86  |
Relationships of agricultural indices with the frequency of new cases of DM2 and obesity appeared to be more complex. If primary DM2 incidence correlated with the pesticide application area, and the strength of relationship increased up to 0.81 (p=0.0001) in the second year, then the incidence of obesity – with the volume of pesticide application; and correlation with the volume of glyphosate preparations was evident only in the second year: r=0.65 (p=0.02).

Multilevel regression and dispersion analysis determined that the contribution of both the total indices of the pesticide application area, the consumption of pesticides and glyphosate preparations, and each of them, to primary incidence of DM2 and obesity was statistically insignificant. Only the contribution of the indicated parameters of pesticide application to prevalence of DM2 with a key role of volumes of glyphosate-containing herbicides use (standardized determination factor corresponded to 0.98; p<0.003) was determined as informative (according to the value of multiple determination coefficient equal to 0.93), adequate (according to the value of Fisher’s test =16.5; p<0.01) and stable (according to results of correlation matrix analysis). The complexity of pesticide effect assessment lies in the fact that the consumption, the application area, the burden per 1 ha, the spectrum of active and “inert” ingredients, and the ratio of preparations changes annually [9]. Glyphosate became the world sales leaders in the 2000-ies. In Russia, 36-39% out of 80 mln ha of the plowland are treated with pesticides, up to 58% of which are herbicides, up to 1/3 are represented by glyphosates [10]. Apart from low cost and claimed low toxicity (peroral and skin toxicity of the 3rd and the 4-th class correspondingly), the possibility of their use at all stages: during preparation of the fallow fields for full or partial substitution of tillage operations, in pre-sowing or pre-emergence periods, as a desiccator before and after harvesting is considered to be their advantage [11].

In the first year of using roundup, the content of glyphosate in the soil, when different technologies (no-till, reduced-till and traditional ones) are used, ranged from 0.112 to 0.264 mg/kg, not exceeding MAC for the soil [12]. However, in case of glyphosate consumption equal to 0.54-1.4 kg/ha as a desiccator the preparation residues were present in the wheat in concentration of 0.1-1.0 mg/kg; in the rye grains – from 1.7 to 2.2 mg/kg; in the rape – from 0.61 to 3.6 mg/kg [13].

The researchers come to conclusion that low acute peroral toxicity does not preclude the negative effect of glyphosate on its single and particularly on systematic getting into the mammals’ and the human bodies [14]. Consequently, glyphosate and its transformation product - aminomethylphosphonic acid are found in foods, water sources, soil, precipitations, and atmospheric air, in agricultural zones and biomaterial in particular in many regions of the world [15, 16]. In Denmark, glyphosate was found in the urine of all examined cows, from 0.1 to 0.3 mg of which were excreted from the body of each of them daily [17].

The results obtained by means of statistical epidemiology, with retrospective analysis of DM2 and obesity incidence in population living in a certain territory, identification of trends and interrelationships with indices of pesticide application, are of considerable practical and theoretical interest for taking actions on decrease of population risks, although the issue on the mechanisms of such effects remains open.

4. Conclusions
The use of pesticides and increase of consumption of glyphosate-containing herbicides in conditions of no-till and reduced-till technologies at the present stage can contribute to growth of diabetes mellitus and obesity prevalence in adult population, which defines the importance of following the agrotechnological rules.

5. References
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