

Adverse outcomes of uncompleted pregnancy following insulin exposure: What the analysis of Egyptian postmarketing pharmacovigilance data tells us

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Introduction

Diabetes mellitus is a major public health burden particularly in developing countries. Egypt is one of the leading countries in terms of prevalence of the disease¹. Insulin products are widely used in diabetic patients and may be used as the first line of treatment in pregnant women.

Objective

To analyse and characterise Egyptian case reports of **foetal death/abortion** events in pregnant women following insulin exposure.

Methods

These combinations were analysed during the Signal Detection and Causality Assessment Workshop organised by Uppsala Monitoring Centre in May 2023. Data analysis, based on case reports from participants' country-specific data, was performed in VigiBase, WHO's global database of reported potential side effects of medicinal products. Case series were analysed using the Bradford Hill criteria for causation. A literature search was performed and product information reviewed.

Results & Discussion

Cumulatively through 16 April 2023, 74 unique cases were retrieved in VigiBase, with insulin as a suspect or interacting drug and relevant MedDRA preferred terms including foetal death/stillbirth/abortion related-adverse events.

After in-depth assessment no well-documented cases were found. Age ranges between 18 and 49 (median 33) years, with the highest percentage of cases (n=56, 76%) in the age group below 40 years. Time-to-onset was reported in 20 cases (27%) with no consistent pattern identified. Reported concomitant medications represented drugs routinely used during pregnancy. Many of the cases indicated poor control of diabetes during pregnancy with or without a medical history of miscarriages. The suspected products included basal, prandial, and premixed insulin variants. The dose-response relationship couldn't be determined using the available dataset since the needed insulin doses differ among trimesters². As a result, most Bradford Hill criteria did not support causality in the underlying case series.

A review of the literature didn't identify any relevant article correlating events of uncompleted pregnancy with insulin use. Rather, numerous studies associate diabetes with risks of congenital anomalies, maternal and foetal adverse pregnancy outcomes, including uncompleted pregnancy events. A recent prevalence study conducted in 449 Egyptian diabetic patients has shown poor control of diabetes in the general population¹⁻².

Conclusions

The weighted cumulative evidence isn't sufficient to support a causal association between insulin use and events of uncompleted pregnancy. Rather, confounding by indication and poor diabetes management in pregnancy among Egyptian women were implied. Accordingly, communicating the importance of proper diabetes control during pregnancy and a call for expanding the national pregnancy registry for medication safety monitoring are recommended.

References/further sources of information

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