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LETTER

Comment on the case report "Possible association between acetazolamide administration during pregnancy and multiple congenital malformations"

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Dear editor

We read with interest the case report in the April 2016 issue of *Drug Design Development and Therapy* by Al-Saleem and Al-Jobair.[1] The authors have presented a boy with oligodontia, ectrodactyly, and syndactyly who was exposed to acetazolamide in utero. Although the discussion was well balanced with a mention to possible confounders such as family and obstetric history and lack of a genetic analysis, two important papers regarding prenatal exposure to acetazolamide were not cited by the authors. In this letter, we would like to mention these studies in order to expand the current context provided by Al-Saleem and Al-Jobair.[1]

Scott et al suggested that non-rodent species such as monkeys[2] were shown to be resistant to the forelimb reduction inducing effect of acetazolamide that was seen in the offspring of rodents[3,4] (mice, rat, hamster) which were prenatally exposed to this agent. Low carbonic anhydrase enzyme activity in this species during the sensitive period of development or poor bioavailability/passage of the drug was proposed as the mechanism of resistance to the aforementioned effects.[2]

Heinonen et al[5] have evaluated and presented the outcomes of the largest number of pregnant women exposed to acetazolamide during their pregnancies. The authors included 1,024 mothers who used acetazolamide anytime during pregnancy and reported 18 infants with a malformation, a result that was not higher than the expected value (18.06) (relative risk 1.00, 95% confidence interval 0.59−1.57). However, the number of the exposures in the sensitive period of development was low; there were only 13 mother and child pairs who were exposed to carbonic anhydrase inhibitors (12 pairs to acetazolamide and one pair to ethoxyzolamide) during 1−4 gestation months and none of them had any malformation. Finally, we are in agreement with the suggestion of Al-Saleem and Al-Jobair[1] regarding the verification of the absence of pregnancy before initiating acetazolamide to women of reproductive age. Nevertheless, the successful use of acetazolamide has been described in a limited number of pregnant women with intracranial hypertension.[6,7] As previously remarked by Falardeau et al, clinicians should be aware that "The avoidance of acetazolamide during the first trimester has very little medical justification and is mainly guided by medical–legal rationale".[7] Therefore, each pregnant patient should be counseled individually with a careful risk−benefit assessment regarding the necessity of acetazolamide treatment during pregnancy in order to ensure the appropriate management of their diseases.

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Disclosure

The authors report no conflicts of interest in this communication.

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Authors' reply

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Dear editor

Thank you for the opportunity to respond to the letter from Dr Keskin-Arslan and Dr Kaplan, which contained positive comments on our case report titled "Possible association between acetazolamide administration during pregnancy and multiple congenital malformations" published in *Drug Design, Development and Therapy* Journal in April 2016.[1]

We thank the authors for their comments which served as an update on our paper and as they mentioned, expanded the current context of what we provided in the article. At the time, we chose to include only full-text articles and not just rely on abstracts. The articles the authors mentioned may be those papers that we could not access at the time.

Having provided the additional information makes the paper more informative and interesting now, and we are grateful to both of the authors.

Disclosure

The authors report no conflicts of interest in this communication.

Reference

1. Al-Saleem AI, Al-Jobair AM. Possible association between acetazolamide administration during pregnancy and multiple congenital malformations. *Drug Des Devel Ther*. 2016;10:1471–1476.