Recent epidemiological studies on boron exposure – contradiction between hazard and risk-based assessments

Introduction

Boric acid and inorganic borates are abundant in nature and widely used in industrial, agricultural, cosmetic and many different applications since a long time. According to the above mentioned results in animal experiments mediate decreased sperm count and/or lack of viable sperm were reported in boron administered male rats and 17.5mg B /kg bw/day was identified as the NOAEL for these adverse effects. On the other hand decreased fetal body weight was reported in female rats treated with high level of boron. The NOAEL for this adverse effect was 9.6mg B /kg bw/ day. Boron mediated decreased reproductive toxicity indicators. The study group was exposed to boron through inhalation (occupational exposure) during their work shift and additionally by drinking water (environmental exposure). Boron concentration in the drinking water of the study area was 9.5mg/L. The workers were classified into control, low, medium and high exposed groups according to their blood boron concentrations. However statistically significant correlations between these parameters and blood/urine boron concentrations. However statistically significant correlations between these parameters were not reported.

The results of the epidemiological study in Turkey

The study was conducted in boron exposed male workers employed in Bandirma Boric Acid Production Plant in order to investigate boron mediated effects on reproductive toxicity indicators. The study group was exposed to boron via inhalation (occupational exposure) during their work shift and additionally by drinking water (environmental exposure). Boron concentration in the drinking water of the study area was 9.5mg/L. The workers were classified into control, low, medium and high exposed groups according to their blood boron concentrations. The calculated mean daily boron exposure was 14.45mg/day for the high exposure group. The reproductive toxicity parameters (FSH, LH, testosterone levels, DNA damage in sperm cells, sperm concentration, motility and morphology parameters) were compared between control and exposed groups. However, boron mediated unfavorable effects were not reported. Additionally, the correlations between blood/urine boron concentrations and the above mentioned parameters were statistically not significant.

The results of the epidemiological study in Argentina

Argentina have also some boron rich areas. In recent years some studies were conducted on boron exposure through drinking water in pregnant woman and the birth size in population living in the Andean part of the Salta province of northern Argentina (altitude 3180-4070m above sea level). Drinking water is reported as the major source of boron exposure (377-10929µg B/L) for this Study area. The results of this study reported an inverse association between elevated boron
Recent epidemiological studies on boron exposure – contradiction between hazard and risk-based assessments

Exposure and birth size. This is the first and only epidemiological study that support the boron mediated decreased fetal bodyweight in boron exposed females. However, some major confounders have not been considered in interpreting the results of this study. The studied population co-exposed to boron and lithium at the same time. The authors reported an inverse association also between lithium exposure during pregnancy and fetal size in their earlier published study at the same sampling area. On the other hand, the study area is located 3180-4070m above the sea level. There are many published studies on the relation between low birthweights and high altitude. In a study conducted in Colorado (970-3550m above the sea level) birth weight declined 121g for every 1000m gain when the effect of altitude was considered alone. However, the negative effect of the high altitude on the body weights of newborns has not been taken into account in the study published by Igra et al. Under the above mentioned circumstances the decreased birth size couldn’t be attributed to the boron exposure.

What did we learn from epidemiological studies?

Boron exposed males

The recently published epidemiological studies reveal that daily boron intake can be much higher in some special geographic areas than the daily boron intake levels calculated for some developed countries. Extreme boron exposure levels were reported in both epidemiological studies in China and Turkey. These exposure levels were far above the daily boron intake levels for humans in daily life. However, unfavorable effects on sperm quality parameters were not reported in epidemiological studies in contrast to the animal experiments. In other words, hazard based assessment in male experimental animals are not in line with the epidemiological studies in male workers even under worst case exposure conditions. On the other hand, the daily boron exposure levels provided by the epidemiological studies made it possible to perform risk based assessment for reprotoxic effects in men as shown below.4–14

\[
\text{RfD}_{\text{boron}} = \text{NOAEL}_{\text{boron}} / \text{UF}_{\text{boron}} \text{ (chemical specific uncertainty factor of boric acid=60)}
\]

\[
\text{RfD}_{\text{boron}} = 17.5/60 = 0.29\text{mg B/kg-bw/day}
\]

\[
\text{RfD}_{\text{boron}} = 0.29\times 70 \text{ (average body weight of a man)}
\]

\[
\text{RfD}_{\text{boron}} = 20.3\text{mg B/day}
\]

Accordingly, the daily boron exposure lower than the RfD should be safe for adult males and boron mediated reproductive toxicity shouldn’t be expected. The mean daily boron exposure in the epidemiological study conducted in Turkey is lower (14.45mg B/day) than the RfD. Under these circumstances the lack of boron mediated reprotoxic effects in male workers shouldn’t be considered as a surprise. However the mean daily boron exposure reported in Chinese study (37.0mg B/day) is above the RfD calculated above. In spite of the reference dose of boron is being exceeded, reprotoxic effects have not been reported in Chinese study. From this point of view boron mediated reprotoxic effects does not seem possible for men under normal handling and use conditions in daily life.

Boron exposed females

Epidemiological studies on boron exposure in pregnant woman and the body weights of newborns in highly boron exposed areas are inadequate. Recently Igra et al., reported inverse association between boron exposure during pregnancy and birth size in northern Argentina. This study, however, shouldn’t be considered as a supportive evidence for boron mediated developmental toxicity in females. As mentioned above lithium exposure and the high altitude of the sampling area have not been taken into consideration in that study. Therefore comprehensive epidemiological studies are needed especially on body weights of newborns in highly boron exposed populations.

Conclusion

Hazard identification is an early step in risk assessment and may offer benefit for regulatory decisions. However, hazard based classification and labelling of chemicals can be misunderstood and used to draw false conclusions about risk, without any consideration of potency or exposure. On the other hand, risk-based approaches provide practical information concerning the probable risk to the exposed population. The study conducted in Turkey provided daily exposure levels under worst case exposure conditions. Even under this exposure conditions boron mediated reprotoxic effects have not been reported. Additionally, boron mediated reprotoxic effects in male workers were not reported even in the Chinese study. The mean daily boron exposure level in this study was far above the RfD calculated above. Accordingly, risk assessment of boron in occupational settings reveal that boron mediated reprotoxic effects does not seem possible for men under normal handling and use conditions in daily life. Risk-based assessment for boron mediated developmental toxicity in females is unfortunately not possible in present time due to the lack of comprehensive epidemiological studies. Therefore, epidemiological studies on highly boron exposed females are strongly needed.

Acknowledgements

None.

Conflict of interest

The author declares no conflict of interest.

References


