Seawater desalination and serum magnesium concentrations in Israel
Gideon Koren, Meital Shlezinger, Rachel Katz, Varda Shalev and Yona Amitai

ABSTRACT
With increasing shortage of fresh water globally, more countries are consuming desalinated seawater (DSW). In Israel >50% of drinking water is now derived from DSW. Desalination removes magnesium, and hypomagnesaemia has been associated with increased cardiac morbidity and mortality. Presently the impact of consuming DSW on body magnesium status has not been established. We quantified changes in serum magnesium in a large population based study (n = 66,764), before and after desalination in regions consuming DSW and in regions where DSW has not been used. In the communities that switched to DSW in 2013, the mean serum magnesium was 2.065 ± 0.19 mg/dl before desalination and fell to 2.057 ± 0.19 mg/dl thereafter (p < 0.0001). In these communities 1.62% of subjects exhibited serum magnesium concentrations ≤1.6 mg/dl between 2010 and 2013. This proportion increased by 24% between 2010–2013 and 2015–2016 to 2.01% (p = 0.0019). In contrast, no such changes were recorded in the communities that did not consume DSW. Due to the emerging evidence of increased cardiac morbidity and mortality associated with hypomagnesaemia, it is vital to consider re-introduction of magnesium to DSW.

INTRODUCTION
In many regions worldwide, fresh water needs exceed the available supply, leading to the rapid development of technologies for desalinating sea and brackish water. Presently, an estimated 300 million people worldwide consume desalinated seawater (DSW) (Desalination Association 2015). Israel is among leading countries in the production of DSW, accounting now for over 50% of the country’s tap water consumption. Hence any potential health effects of DSW may have serious impact on large populations (Spungen et al. 2013).

Fresh water from the Israeli National Water Carrier (NWC) contains 20–25 mg magnesium per litre. In contrast, DSW contains virtually no magnesium due to its removal during the desalination process (Yermiyahu et al. 2007). The World Health Organization (WHO) report on drinking water, stresses that where a supply is moving to low-mineral desalinated water, one should consider replenishing with magnesium salt (WHO 2011). However, to date no analysis exists where the impact of such changes was measured directly on the body burden of magnesium. Because regular (‘hard’) water accounts for 7.5–17% of the daily requirements of magnesium (Maraveri et al. 2013), the rest coming from nutritional sources, it is critical to investigate whether this potential shortage is clinically relevant. Because in Israel the fraction of DSW in drinking water is the highest among all developed countries (Yermiyahu et al. 2007), this is a unique experimental opportunity to assess whether the massive introduction of seawater desalination has been associated with a clinically relevant decrease in the body burden of magnesium.
potentially putting people at increased risk of cardiovascular morbidity and mortality.

The aim of the present study was to quantify potential changes in serum magnesium in a large population-based study, comparing levels before and after desalination in regions that used or did not use DSW.

METHODS

The study was approved by the Assuta hospital IRB. Using anonymous data unlinked to patients, consent was waived. The present retrospective cohort study was carried out using data from the computerized files of Maccabi Healthcare Services (MHS), a health maintenance organization covering two million people in Israel. According to the National Health Act in Israel, MHS may not bar applicants for any reason, thus all Israeli population sectors are represented in MHS.

For the purpose of the present analysis we identified 15 communities where DSW was introduced as a major source of drinking water in 2013, when the Sorek desalination facility was introduced in central Israel, and compared them to 24 communities where no such change took place, and where, hence, communities continued to consume regular ‘hard’ drinking water.

The study periods compared therefore the years 2010–2013 vs. 2014–2016.

The information published officially regarding distribution of DSW was cross checked by measuring magnesium in 53 samples of tap water from areas of both DSW and non-DSW use. The mean magnesium levels in the DSW communities was 5.4 mg/l (range 0–9.42), compared to 25.1 mg/l (11–37.5) in tap water from naturally occurring ‘hard’ water.

For the years studied, we extracted from the MHS database all serum magnesium measurements performed on MHS members residing in the selected communities. When more than one measurement was available, only the first one was included. All measurements were performed in a single MHS central laboratory.

Using the unpaired Student’s t test we compared mean serum magnesium concentrations for the period of 2010–2013 to 2014–2016 in communities consuming mostly DSW, as well as for the communities consuming natural water. In parallel, using the Chi square test, we compared for the same periods the proportions of magnesium concentrations equal or below the lower normal range of 1.6 mg/dl.

RESULTS

A total of 66,764 subjects had serum magnesium concentrations available in communities that used or did not use DSW.

The normal range of serum magnesium concentrations is 1.7–2.4 mg/dl (0.7–1 mmol/l; 1.5–2 mEq/l) (Williamson et al. 2011). In the communities that switched to DSW in 2013, the mean serum magnesium was 2.065 ± 0.19 mg/dl before desalination. Following desalination, mean levels decreased to 2.057 ± 0.19 (p < 0.0001). In these communities 1.62% of subjects exhibited serum concentrations ≤1.6 mg/dl during 2010–2013. Their proportion increased by 18.5% in 2014–2016 to 1.91% (p = 0.0057) (Table 1).

Further sub-analysis compared the proportion of low magnesium concentrations ≤1.6 mg/dl in 2010–2013 to

<table>
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<tbody>
<tr>
<td>DSW introduced</td>
<td>n = 32,973</td>
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<tr>
<td>mean 2.065 ± 0.19 mg/dl</td>
<td></td>
</tr>
<tr>
<td>≤ 1.6 mg/dl 1.62%</td>
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</tr>
<tr>
<td>DSW not introduced</td>
<td>n = 6,368</td>
</tr>
<tr>
<td>mean 2.056 ± 0.2 mg/dl</td>
<td></td>
</tr>
<tr>
<td>≤ 1.6 mg/dl 2.18%</td>
<td></td>
</tr>
<tr>
<td>DSW introduced</td>
<td>n = 22,050</td>
</tr>
<tr>
<td>mean 2.057 ± 0.19</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>DSW not introduced</td>
<td>n = 5,373</td>
</tr>
<tr>
<td>mean 2.063 ± 0.18</td>
<td>p &lt; 0.01</td>
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*Not significant.
those in 2014, and separately to those in 2015–2016, showing a gradual and consistent increase (Table 2) as more DSW was introduced. Comparing 2010–2013 to 2015–2016 showed a 24% increase in the proportion of low serum magnesium concentrations ≤1.6 mg/dl (p = 0.0019).

No such changes were recorded in the communities that continued not to consume DSW (2.056 ± 0.2 mg/dl between 2010 and 2013; and 2.065 ± 0.18 mg/dl between 2014 and 2016, not significant). In these non-desalinated communities there was a modest 9% decrease in the proportion of magnesium levels below 1.6 mg/dl (from 2.18 to 1.98%) (Table 1).

**DISCUSSION**

Although the WHO recommends careful follow up of potential changes in magnesium status after introduction of DSW, there is virtually no published data to quantify the potential health risks in humans.

In a recent study from Spain, the fraction of daily magnesium intake provided by water consumption in adults was estimated at 7.5–17% assuming magnesium tap water concentration of 15–50 mg/l (Maraveri et al. 2015).

There is presently a large body of evidence showing that hypomagnesaemia is associated with increased cardiovascular morbidity and mortality (Eisenberg 1992; Kolte et al. 2014). Two systematic reviews have found an inverse relationship between tap water magnesium and rates of cardiovascular morbidity and mortality (Catling et al. 2008; Jiang et al. 2016).

However, up to the present time, no direct measure of the effect of seawater desalination on serum magnesium has been reported. In 2013 Spungen and colleagues assessed the proportion of individuals consuming DSW vs those drinking ‘hard’ water through interviews using a food frequency questionnaire. They have shown that in a community that consumed DSW 30.6% of dwellers consumed magnesium at levels below the Estimated Average Requirement, as compared to 16.7% in a community not consuming DSW (p < 0.05) (Spungen et al. 2013).

In the Surat district of India, Kanadhia and colleagues have shown that serum magnesium was significantly lower in the population consuming filtered water as compared to those consuming non-filtered water (Kanadhia et al. 2014).

Hypomagnesaemia has been estimated to have a prevalence range between 2.5 and 15% in the general population (Ayuk & Gittoes 2011). Our population-based study, including over 66,000 subjects, is the first to examine the temporal relationship between the introduction of DSW and serum magnesium levels. Because natural water accounts for 7.5–17% of magnesium needs, one cannot automatically assume that DSW will affect magnesium status, as the body may compensate with higher magnesium absorption from food. The detected 24% increase in magnesium levels below the normal range is potentially relevant, as more individuals then fall in ranges associated with cardiac morbidity and mortality. To put it into practical context, the city of Tel Aviv and adjacent townships, which constitute the largest metropolitan area in Israel, now receive mainly DSW with negligible magnesium levels. A recent study from Israel has shown that 30-day all-cause-mortality from acute myocardial infarction was more than double in patients from DSW regions compared with those from non-DSW regions (Shlezinger et al. 2016). However, this study did not follow magnesium levels in most patients. Importantly, the increase in the proportion of low magnesium levels was gradual, corresponding to more and more DSW replacing natural fresh water. Critically no similar changes were shown in communities where DSW was not introduced. It is conceivable that individuals who already have a tendency toward lower magnesium levels, such as those using diuretics (Kuller et al. 1985), individuals with alcohol addiction and withdrawal (Shane & Flink 1991-1992), and those with malabsorption syndromes (Caruso et al. 2013) to mention a few, may be at a higher risk of further lowering their serum magnesium when using DSW.

**Table 2** | Changes over time in the proportion of magnesium concentrations ≤1.6 mg/dl in communities where DSW was introduced in 2013

<table>
<thead>
<tr>
<th>Time period</th>
<th>Proportion of Mg ≤ 1.6 mg/dl</th>
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<tbody>
<tr>
<td>2010–2013</td>
<td><strong>1.62%</strong></td>
</tr>
<tr>
<td>2014–2016</td>
<td>1.81%*</td>
</tr>
<tr>
<td>2015–2016</td>
<td><strong>2.01%</strong></td>
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</tbody>
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*p < 0.0019.

**p < 0.0007.
CONCLUSIONS

Our study suggests that the introduction of DSW is associated with an increased proportion of subjects with lower than normal magnesium levels. Due to the emerging evidence of increased cardiac morbidity and mortality associated with hypomagnesaemia, it is important to consider re-introduction of magnesium into DSW. Until such changes are fully considered, it is critical to plan appropriate magnesium supplementation and population education.

REFERENCES

Ayuk, J. & Gittoes, N. J. 2011 How should hypomagnesaemia be investigated and treated? Clinical Endocrinology (Oxf.) 75 (6), 743–746.


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