The effect of noise on serum and urinary magnesium and catecholamines in humans

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We have studied whether a short-term exposure to loud noise was able to modify urinary catecholamine excretion and serum concentration and urinary excretion of magnesium and other related electrolytes. In 25 healthy volunteers, blood and urine concentrations of magnesium, calcium, phosphorus and creatinine, and urinary catecholamines were measured before and after exposure to noise in an industrial plant. Samples were collected at 08:00 h on the day of the experiment and soon after noise exposure (at 20:00 h). Two further urine samples were collected the following day and 2 days after the experiment, always at 08:00 h in the morning. The sound energy average level was 98 dB(A), but peak levels reached 108 dB(A). Urinary catecholamines were determined by high-performance liquid chromatography. Serum magnesium and calcium were significantly increased after exposure to noise, whereas phosphorus displayed a similar but non-significant trend (P = 0.065). Multivariate analysis of variance (ANOVA) showed significant differences both among subjects (P < 0.001) and after exposure (P < 0.001). Adrenaline, noradrenaline and dopamine values were not significantly different after exposure to noise (P > 0.05). Urinary magnesium levels were significantly different across time (P = 0.017). Urinary calcium levels were not significantly different across time (P = 0.36). Urinary phosphate values were increased after exposure to noise (P = 0.007); urinary creatinine was not changed after exposure (P > 0.05). Our study shows that noise induces significant increases of serum calcium and magnesium, with a borderline increase of serum phosphorus; this in turn is reflected in a significantly increased urinary excretion of magnesium and phosphate after exposure, which lasts for the following 2 days. Urinary calcium and creatinine were not modified by noise. The difference in catecholamine values did not reach statistical significance. Thus, we failed to substantiate a significant correlation between catecholamine secretion and magnesium metabolism, as others had suggested.

Key words: Calcium; catecholamines; magnesium; occupational hearing loss.

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Introduction

Noise-induced permanent threshold shift (NIPTS) is considered to be one of the most frequent occupational health hazards in both industrial and military environments. For the 90th percentile of the exposed population [1], the risk for presumed NIPTS increases exponentially for noise levels beyond 85 dB(A) and over prolonged periods. NIPTS manifests irreversible subtle changes in the sensory cells and other structures in the organ of Corti in the cochlea. Stereocilia of the hair cells, and primarily of the outer hair cells, become fused and/or disappear, and may subsequently disintegrate along with supporting cells; ultimately, even nerve fibres innervating the hair cells may disappear [2].
The mechanisms whereby loud noise damages the inner ear are still obscure in many respects. According to one hypothesis, noise causes a reduction of cochlear blood flow, with secondary hypoxia. Indirect methods to test this hypothesis have given different results. The metabolism of the inner ear will increase after moderate noise exposure, but decrease again after exposure to intense noise. This implies that moderate noise causes stimulation of the blood flow to the inner ear, whereas intense noise diminishes it. Histological studies [4–7], however, indicate that the acute response to intense noise [3] is a diminished flow. Canlon and Fransson [8] showed that mid-frequency sound conditioning of guinea pigs [78 dB sound pressure levels (SPL) for 13 days] protects them against a noise trauma (100 dB SPL for 24 h) and that the protective effect is maintained for at least 1 week.

Different hypotheses to justify a functional exhaustion of the ciliate cells have been formulated [9, 10]; these are based on modifications of either a mechanical or a metabolic nature, or on alterations of the cell ionic status after extended exposure to noise.

Individual susceptibility to noise seems to play an important factor determining the eventual NIPTS [11]. In this respect, biochemical mechanisms, including the pre-exposure levels of magnesium, were suggested as affecting the susceptibility to NIPTS [12].

Magnesium is an essential factor in regulating cellular membrane permeability, neuromuscular excitability, and energy production and consumption [13]. Mechanoelectrical transmission itself consumes energy [14]. Any condition that increases this energy consumption or reduces the energy supply increases the risk that the function of the hair cells may be limited temporarily or permanently [15]. In noise exposure where a high energy consumption of the hair cells is required, magnesium deficiency may increase the potential for NIPTS.

The association of increased NIPTS with low levels of perilymph and serum magnesium concentrations has been demonstrated in animal experiments [16]. In rodents fed with a high dietary magnesium intake and subjected to high-impulse noise, NIPTS was reduced [17]. In a retrospective study in humans, subjective thresholds across frequencies of 3, 4 and 5 kHz were negatively correlated to serum magnesium [18]. This finding was the first indication that magnesium status in humans may be one of the factors determining variations in sensitivity to noise-induced hearing loss. Following animal experiments where a correlation was observed between serum magnesium level and NIPTS, some authors [19] have tested the prophylactic effect of magnesium in human subjects exposed to hazardous noise [420 shots fired by each subject in 6 days; the average peak level for every shot was 164 dB(A), but ear plugs reduced the peak noise level to an average of 25 dB(A)]. NIPTS was negatively correlated to the magnesium content of red blood cells, and the authors concluded that long-term additional intake of a small dose of oral magnesium was not accompanied by any notable side-effect.

Since Galland [20] has suggested that the adrenergic effects of psychological stress induce a shift of magnesium from the intracellular to the extracellular space, increasing urinary excretion and eventually depleting body stores, we have endeavoured to verify whether a short-term exposure to loud noise was able to modify the serum concentration and urinary excretion of magnesium and other electrolytes, and whether urinary catecholamine concentrations displayed corresponding changes.

**Materials and methods**

**Design**

Our experiment consisted of assaying blood and urine concentrations of magnesium, calcium, phosphorus and creatinine before and after exposure to 4 h of noise in an industrial plant. Furthermore, urinary catecholamines (adrenaline, noradrenaline and dopamine) were assayed before and after exposure.

**Subjects**

Twenty-five healthy male volunteers, not exposed to a high level of noise at work or leisure, were recruited for the study, and informed about the aims and methods of the study; all underwent a detailed audiological examination performed by an experienced audiologist, as well as an extensive array of haematology and blood biochemistry tests, before the study commenced. Air and bone conduction thresholds were determined using an Amplaid A 171 audiometer, conforming to ISO specification. Requirements for participation were normal blood biochemistry measurements and an intact auditory threshold (<20 dB hearing threshold level) in the frequency range of 1–8 kHz. Sixteen subjects met the criteria, aged from 26 to 41 years. One week before and on all days during the study, dietary consumption of magnesium was controlled; to this end, a series of foods with significant magnesium content were explicitly forbidden. In the same period, significant non-occupational exposure to noise (music, dance, motors, etc.) was also forbidden. After the tests, subjects were instructed to avoid exposure to further noise for the following 2 days.

**Blood and urine samples**

Blood and urine samples were collected at 08:00 h on the day of the experiment, and soon after the noise exposure (at ~20:00 h). Two further urine samples were collected the following day and 2 days after the experiment, always at 08:00 h. The urine samples were collected in different jars containing 0.7 g of citric acid. All samples were frozen.
at –20°C until analysis. Catecholamines were assayed in the first three urine samples.

Exposure to noise

All subjects were exposed to noise in an industrial plant for ~4 h (from 16:00 to 20:00 h); subjects were invited to remain in a room situated next to different sources of noise of a semi-continuous type. The average sound energy level, measured with a phonometer (Bruel & Kjær type 2231) was 98 dB(A), but during the exposure peak levels reached 108 dB(A). A dosimeter (Larson Davis Noise-Badge 705) was also used to verify that exposure was similar among the subjects. During the exposure, subjects were allowed to drink only water in moderate amounts.

Assays

Serum and urinary electrolytes were assayed spectrophotometrically using the same standard laboratory multi-analyser (Hitachi with Vitros 700 Clinical Diagnostic) [21].

The detection limits were: 1.00 mg/dl for calcium (serum and urine); 0.05 mg/dl for creatinine (serum and urine); 0.20 mg/dl (serum) and 1.20 mg/dl (urine) for magnesium; and 0.50 mg/dl (serum) and 5.50 mg/dl (urine) for phosphorus.

Accuracy was verified by comparison of serum and urine specimens analysed using the Vitros 700 System with those analysed using the atomic absorption reference methods (for magnesium, calcium and phosphorus) and the high-performance liquid chromatography (HPLC) reference method for creatinine. In all cases, slopes were ≥0.99 and correlation coefficients were ≥0.995. For all methods, precision was evaluated with quality control materials on the Vitros 700 Chemistry Systems following NCCLS Protocol EP5-T2 [22].

Urinary catecholamines were determined by HPLC with fluorescence detection using the method of Boos et al. [23]. The detection limits were 100 ng/l for adrenaline, noradrenaline and dopamine. Urinary values of catecholamines and electrolytes were divided by urinary creatinine [24] before statistical analysis.

Statistical analysis

Data are displayed as means ± SD; significance was tested using analysis of variance (ANOVA) for repeated measures, or simple factorial ANOVA with Tukey’s test (at the 0.05 level) for separation of the means, or multivariate ANOVA as required by data structure. For calculations, the following statistical programs for personal computers were used: SPSS-PC for Windows version 6.0 and StatGraphics 2.6 for DOS.

Results

Serum electrolytes

Serum electrolyte concentrations before and after noise exposure are reported in Table 1, together with significance levels.

Serum magnesium and calcium were significantly increased after exposure to noise (Figure 1), whereas phosphorus displayed a similar but non-significant trend ($P = 0.065$).

Multivariate ANOVA for serum electrolytes and creatinine showed significant differences both among subjects ($P < 0.001$ by Hotelling’s test) and after exposure ($P < 0.001$ by Hotelling’s test).

Urinary values

Urinary values of electrolytes and catecholamines (corrected for creatinine) and creatinine are reported in Table 2; for practical reasons, samples are numbered as follows: sample 1 = before exposure (at 08:00 h); sample 2 = immediately after exposure (at 20:00 h); sample 3 = 1 day after exposure (at 08:00 h); sample 4 = 2 days after exposure (at 08:00 h).

Adrenaline, noradrenaline and dopamine values were not significantly different after exposure to noise ($P > 0.05$ by factorial ANOVA; Figure 2).

Urinary magnesium levels were significantly different between subjects ($P < 0.001$) and across time ($P = 0.017$; Figure 2). Urinary calcium levels were not significantly different across time ($P = 0.36$; Figure 3). Urinary phosphate values were significantly different between subjects ($P < 0.001$) and were increased after exposure.

Table 1. Serum concentrations of electrolytes before and after exposure

<table>
<thead>
<tr>
<th></th>
<th>Pre-exposure</th>
<th>Post-exposure</th>
<th>Significance ($P =$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>95% CI</td>
<td>Mean</td>
</tr>
<tr>
<td>Magnesium (mg/dl)</td>
<td>2.13</td>
<td>2.05–2.20</td>
<td>2.23</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td>3.49</td>
<td>3.22–3.75</td>
<td>3.80</td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td>9.86</td>
<td>9.72–10.00</td>
<td>10.27</td>
</tr>
<tr>
<td>Creatinine (mg/100 ml)</td>
<td>0.88</td>
<td>0.82–0.93</td>
<td>0.88</td>
</tr>
</tbody>
</table>
(P < 0.007; Figure 3); urinary creatinine was not changed after exposure to noise (P > 0.05).

Discussion

The involvement of magnesium in the response to stress in animals and humans has been suggested by many studies. Animals maintained on a normal magnesium-containing diet and subjected to noise stress exhibit a slight but significant reduction in microvascular lumen size; these measurements also revealed a progressive quantitative reduction as the degree of magnesium deficiency (assessed by serum concentration) increased [25]. It is possible that even a transient magnesium depletion might modulate vascular tone and/or an increased sensitivity to vasoconstrictive stimuli.

Our study shows that noise induces significant increases of serum calcium and magnesium, with a borderline increase of serum phosphorus; this in turn is reflected in a significantly increased urinary excretion of magnesium and phosphate after exposure, which lasts for the following 2 days. Urinary calcium and creatinine were not modified by noise.

We expected that audiogenic stress might induce an adrenergic response, which in turn would be the cause of a shift of magnesium from the intracellular to the extracellular compartment and a consequent increase of serum magnesium and its excretion in urine; however, the difference in catecholamine values, although there was a tendency to increase in the urine sample taken immediately after exposure, did not reach statistical significance. Thus, we failed to substantiate a significant correlation between secretion of catecholamines and magnesium metabolism, as others had suggested [20].

Several aspects need consideration. Extra- and intracellular magnesium levels have been shown to be genetically controlled in humans [26], and genetic differences in magnesium utilization may account for differences in vulnerability to magnesium deficiency and differences in body responses to stress [27]. Moreover, the psychological characteristics of personality play an important role in the stress response; it has been observed [28] that after stress, type A subjects (when compared with type B individuals) show an important increase of urinary catecholamines and serum free fatty acids, a slight increase in plasma magnesium, and a small but significant decrease in red blood cell magnesium. These results suggest that type A subjects are more sensitive to stress than are type B people and more readily lose their intracellular magnesium, the rise in plasma magnesium

![Figure 1. Concentrations of serum calcium, phosphate and magnesium before and after noise exposure.](image)

Table 2. Urinary values before and after noise exposure

<table>
<thead>
<tr>
<th>Sample no.</th>
<th>1 (before)</th>
<th>2 (immediately after)</th>
<th>3 (1 day after)</th>
<th>4 (2 days after)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>95% CI</td>
<td>Mean</td>
<td>95% CI</td>
</tr>
<tr>
<td>Adrenaline(^a) (ng/l)</td>
<td>0.069</td>
<td>0.05–0.09</td>
<td>0.098</td>
<td>0.05–0.015</td>
</tr>
<tr>
<td>Noradrenaline(^a) (ng/l)</td>
<td>0.510</td>
<td>0.40–0.62</td>
<td>0.614</td>
<td>0.47–0.75</td>
</tr>
<tr>
<td>Dopamine(^a) (ng/l)</td>
<td>2.004</td>
<td>1.70–2.31</td>
<td>2.447</td>
<td>1.69–3.21</td>
</tr>
<tr>
<td>Magnesium (mg/dl)</td>
<td>5.28</td>
<td>4.07–6.51</td>
<td>5.25</td>
<td>3.36–7.14</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td>50.69</td>
<td>34.65–66.33</td>
<td>50.71</td>
<td>29.34–72.07</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>133.71</td>
<td>109.09–158.34</td>
<td>105.09</td>
<td>70.78–141.52</td>
</tr>
</tbody>
</table>

\(^a\)Corrected for creatinine.
being a transient one, probably consecutive to the cellular loss. Furthermore, it is important to note that neuroendocrine responses to stress vary according to both the type and intensity of stress, and catecholamine and corticosteroid responses are dissociated in some forms of mild stress [29–32]. Finally, other authors have not seen increased catecholamine secretion after exposure to acute noise [33]. So we think that it is possible that our findings may be explained by a role played by the individual response to stress.

It is, moreover, theoretically possible that an episodic secretion of catecholamines, although of insufficient magnitude to increase the urinary integrated concentration significantly, might determine a magnesium shift from the intracellular to the extracellular compartment. In order to assess this, evaluation of plasma catecholamine samples could shed more light on this difficult problem; however, technical difficulties and theoretical problems (such as the difficult standardization of catecholamine samples taken in orthostatism) make this approach less than ideal.

Alterations in plasma and urinary magnesium, calcium and phosphate might thus be induced by other hormonal or non-hormonal mediators, such as cortisol or prolactin, which were not measured in our study.

A limitation of our study is the absence of a control group. Although it is true that our findings could be due to a circadian rhythm of magnesium levels in either blood or urine, there are reports in the literature that no circadian rhythm exists in urinary magnesium excretion [34]. As regards serum levels of magnesium, although a paper [35] does report some diurnal variations, these are minor and of uncertain biological significance, and have not been found by other authors [36].

Our study confirms that acute noise stress is able to induce an increase of circulating magnesium, and a subsequently increased excretion of this cation in urine, which suggests that chronic exposure to noise could facilitate depletion of the whole-body magnesium content.

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References


