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Electronic cigarettes and nicotine poisoning

2. JUNE 2014 BY [BERND MAYER](#) — 4 COMMENTS



In view of the established toxic effects of nicotine, the widespread availability of

nicotine containing liquids used to refill electronic cigarettes may pose a certain health risk, and even fatal outcomes of nicotine poisoning have been predicted by some public health advocates.

Here I won't talk about deliberate misuse by e.g. intravenous injection of nicotine containing solutions in suicide or homicide attempts but focus on incidents that may occur in normal use. This includes overdosing nicotine by excessive consumption of liquids with high nicotine content, inadvertent swallowing of liquid, and spilling liquid on the skin.

Symptoms of nicotine poisoning

The first symptoms are headache and dizziness, followed by nausea, vomiting and diarrhea, which appear upon severe overdosing, i.e. if the first symptoms are ignored. However, initial adverse effects will prompt vapers to stop and/or reduce the nicotine concentration of their liquids immediately. Thus, harmful or even fatal nicotine poisoning will not occur in normal use of electronic cigarettes.

Lethal dose

An estimate of the nicotine dose that is lethal to humans is required to judge the possibility of fatal outcomes by accidental swallowing or spilling of liquids. However, nicotine sensitivity varies considerably among species, and obviously LD50 values cannot be determined for humans.

Therefore, the lethal dose has to be deduced from nicotine blood levels of documented cases of fatal or near-fatal cases of nicotine poisoning that are extremely rare. Evaluation of such cases recorded in the last 100 years or so suggests that 0.1-0.2 g of systemic nicotine be lethal for adults.

Poisoning by oral intake (swallowing) of nicotine containing liquid

Considering the oral bioavailability of nicotine (20%, see my [post on nicotine basics](#)), 0.1-0.2 g systemic nicotine (applied by i.v. injection) corresponds to 0.5-1.0 g oral. I have suggested this value, which is 10- to 20-fold higher than the 50-mg dose that has been widely accepted for more than a century, in a recent publication [1]

Accordingly, drinking 25-50 ml of a liquid containing 20 mg of nicotine per ml could theoretically be lethal for an adult. However, the required volume would in fact be much higher, because vomiting and diarrhea will markedly reduce the amount of

nicotine that becomes systemically available. Thus, even in the highly unlikely case of somebody swallowing a medium size bottle of liquid, the outcome will probably not be fatal.

Obviously, the lethal dose for children is lower according to body weight, and childproof closure of liquid bottles is essential.

Poisoning by spilling liquid on the skin (dermal resorption)

The fraction of nicotine getting into the blood stream upon application on the skin is 70 – 100%, because the first pass effect limiting oral resorption is avoided (see the **post on nicotine basics**). Thus, the lethal dose of dermally applied nicotine would theoretically approach the dose estimated for intravenous injection (0.1-0.2 g), but the rate (kinetics) of resorption is an important parameter that has to be considered.

Rapid metabolism and distribution of nicotine from the blood into other tissues prevent the build-up of critical blood levels if nicotine is resorbed slowly. Therefore, smokers tolerate the inhalation of nicotine doses over the day that would be lethal when given as a bolus. The kinetics of resorption is highly relevant for dermal exposure to nicotine, because the skin functions as a reservoir for slow release of nicotine into the bloodstream [2].

Detailed investigation of this issue using human skin as *in vitro* model [3] has revealed that resorption of nicotine is slow and dependent on the solvent (e.g. about 100-fold faster in water than in ethanol). In contrast to Fick's law, the rate of resorption is maximal at medium concentrations (about 40%) and decreases at higher concentrations. Accordingly, the pure nicotine base is taken up extremely slowly. Based on the determined rate of 82 $\mu\text{g}/\text{cm}^2 \times \text{h}$ one can calculate that application of pure nicotine to a skin area of 10 cm^2 results in uptake of as little as 0.8 mg of nicotine per hour. Thus, short-term exposure of the skin to pure nicotine will not cause considerable adverse effects.

Exposure of 10 cm^2 skin to a liquid containing 20% of nicotine (200 mg/ml) in ethanol would result in uptake of 0.1 mg nicotine per hour. At lower concentrations, which are typically used in the preparation of liquids for electronic cigarettes, dermal resorption of nicotine is negligible.

Summary

Nicotine containing liquids will not exert considerable adverse effects upon inhalation, spilling liquid on the skin, or accidental swallowing a few drops. Deliberate abuse or accessibility of the liquids to children are associated with a health risk as are many other items of daily life.

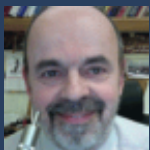
[1] <http://link.springer.com/article/10.1007%2Fs00204-013-1127-0>

[2] <http://www.ncbi.nlm.nih.gov/pubmed/3595064>

[3] <http://annhyg.oxfordjournals.org/content/43/6/405.full.pdf>

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About Bernd Mayer

Dedicated to science, critical thinking, and scientific education of young people. Fighting pseudoscience and all kind of esoteric junk.

Comments



Jonathan Bagley says

6. June 2014 at 15:41

Hello Bernd. Just now discovered your blog via https://twitter.com/Dick_Puddlecoate, and am finding the articles very interesting. I too read the paper on dermal nicotine absorption and wondered whether PG is more similar to alcohol or water regarding speed of nicotine absorption. Do you know the answer to this? Once again, thanks for the research and I'm adding your blog to my daily reading.

Reply



Bernd Mayer says

6. June 2014 at 16:57

Good point that I have swept under the carpet because I don't have a clear answer. Based on the chemistry I would predict that PG and VG resemble ethanol rather than water. However, I would not bet my house for that, because the behavior of nicotine on the skin is rather weird in several aspects according to that study.

Regardless, even if resorption in PG were similarly fast as in water, this would still be too slow to cause serious harm. Consider that nicotine disappears fast from the circulation due to tissue distribution and metabolism. Thus, if somebody would carefully keep the spilled liquid on the skin for a couple of hours (a rather unlikely scenario, I guess), this would result in a steady-state blood level determined by the rate of resorption. In other words, nicotine doesn't accumulate in the blood.

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Doctor doctor, give me the news - Facts Do Matter says:

31. March 2015 at 15:57

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29. May 2016 at 16:44

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Dedicated to science, critical thinking,
and scientific education of young
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- Bernd Mayer

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