Health Canada Ban on Ephedrine – A Post-ban Assessment of Effectiveness

Ishvinder S. Chattha, Medicine 2011
Reviewed by Dr. David Massel

Ephedrine is the pharmacologically active alkaloid found in extracts from the *Ephedra* genus of shrubs native to Central Asia. Its pharmacological properties have been put to use in various weight-loss products, athletic enhancers, decongestants and bronchodilators. Due to its primarily negative cardiovascular effects, an incomplete ban has been placed by Health Canada on ephedrine usage, which is now restricted to use solely in nasal decongestives and restricted to 8mg doses. Ephedrine bans have been successful in reducing ephedrine sales, however it has not been effective in changing the widespread beliefs of college students or eliminating illegal ephedrine usage. The ban also does not take into account the synergistic effect of caffeine and ephedrine. Additional research into the synergistic effects of caffeine and ephedrine should be conducted in order to address the need of a full ban in order to protect against cardiovascular complications.

Introduction

Governmental restrictions on the usage of pharmacologically active substances can be triggered by newly uncovered scientific evidence, increasing public awareness, political motivations, or a combination of these factors among others. Post-restriction data is commonly lacking in regards to effectiveness of policies, implementation, and regulation. This article assesses the post-restriction literature in regards to the 2001 Health Canada restrictions on the usage of ephedrine to determine the effectiveness of the incomplete ban.

Ephedrine is the pharmacologically active alkaloid found in extracts from the *Ephedra* genus of shrubs native to Central Asia. Ephedrine is a sympathomimetic amine, which exerts its affects primarily through interacting with α – and β-adrenergic receptors which mediate sympathetic responses. It also stimulates the release of endogenous catecholamines and inhibits their reuptake from the synapse. Ephedrine’s actions on the sympathetic nervous system have been put to use in various weight-loss products, athletic enhancers, concentration aids, decongestants and bronchodilators.

Several adverse cardiac events have been documented from ephedrine usage: the most severe including myocardial infarction, stroke, and sudden death. In 2001, after 60 adverse events were reported in Canada, Health Canada restricted the sale and dosage limit of ephedrine products. Ephedrine is now authorized for use only as a nasal decongestant and at a maximum dose of 8 mg with no more than 32 mg in a 24 hr period.

It is important to assess the changes in ephedrine usage and ephedrine-related adverse events after the restriction has been put in place in order to evaluate the effectiveness of such legislation as it is a common form of prevention. This article looks at the literature concerning ephedrine related adverse events and epidemiological data in order to assess the rationale and effectiveness of Health Canada’s incomplete ban on ephedrine products.

Pharmacological Properties

Ephedrine’s sympathomimetic effects are mediated through interactions with α – and β-adrenergic receptors. It also stimulates the release of endogenous catecholamines from neurons through increasing the number of vesicles released during each action potential and also delays their reuptake from the synapse. Ephedrine’s affinity to β-receptors is greatest for β1 followed by β2 then β3 receptors. Ephedrine produces positive ionotropic effects and chronotropic effects. It is a powerful vasoconstrictor and is arrhythmogenic.

Ephedrine readily crosses the blood-brain barrier producing central nervous system effects resembling those of amphetamines. Ephedrine has an 85% bioavailability, half life of three to six hours, and is removed through renal excretion.


**Adverse Effects**

Before ephedrine restrictions were put in place in the US, The American Association on Poison Control Centers, in 2003, reported that ephedrine related adverse events accounted for more than one-half of all reported dietary supplement related adverse reactions while ephedrine product sales accounted for less than 1% of the marketplace.\(^9\) This disproportion highlights the concerns regarding ephedrine usage.

The most common reported adverse event associated with ephedrine usage is hypertension and tachycardia.\(^10\) Ephedrine use has also been associated with both ischemic and hemorrhagic stroke, cardiac arrhythmias including ventricular tachycardia, coronary vasospasm, acute myocardial infarction, tachycardia-induced cardiomyopathy, and sudden death.\(^11\)

**Effectiveness of Incomplete Ban**

Ephedrine products have seen increasing use in the past two decades for the unapproved purposes of weight loss and improved athletic performance. Ephedrine increases the rate of weight loss by 0.6 kg per month in comparison to placebo. When combined with caffeine, the rate increased to 1.0 kg per month greater loss than with placebo.\(^12\) In the athletic arena, ephedrine and caffeine alone do not have significant effects on oxygen consumption, carbon dioxide production, or time to exhaustion in comparison to placebo. However, when taken in combination, ephedrine and caffeine have shown to produce up to a 20% to 30% increase in athletic performance as seen through improvements in run times and strength-training.\(^13\)

Although Health Canada has limited the dosage of ephedrine, when taken in combination with caffeine, a low dose can produce effects mimicking those of moderate (30-40 mg) to high dosages (70-80 mg) of ephedrine.\(^14\) This is of particular importance as ephedrine combined with caffeine produces greater weight loss and improved athletic performance, the primary reason for use among females and males, respectively.\(^15\)

The protective action of the 8 mg per dose, 32 mg/day maximum dosage has been found to have limited value as The Association of Food and Drug Officials (AFDO) states that serious adverse effects to ephedrine products may occur at dosages of 24 mg per day.\(^16\) Life-threatening adverse reactions have been reported to occur with doses of 1 to 5 mg.\(^17\) AFDO is also concerned that setting a dosage limit may falsely imply that a safe dose exists.

Several States in the US have issued a complete ban on ephedrine products. This legislation resulted in a significant reduction in methamphetamine usage (produced by ephedrine through chemical reduction) as well as methamphetamine related hospital admissions.\(^18\) Ephedrine sales through retail outlets have also dropped since the ban.\(^19\) In 1997, National Collegiate Athletic Association (NCAA) issued a ban on all ephedrine containing substances. Despite these bans, studies have shown an increasing trend in ephedrine usage amongst college athletes. In 2001, a study of NCAA athletes showed ephedrine usage at 3.9%.\(^20\) Usage has been rising since 1991, and continued to rise even after the ban was put into place.\(^21\) A 2006 study by Bents and Marsh (22) showed that among members of an NCAA hockey team, 59.0% reported that the ephedrine ban would make them less likely to use the substance, while 40.3% reported that they would use banned substances to play at higher level.

Despite the restrictions placed on the usage of ephedrine, ephedrine products are easily obtainable through products sold as nasal decongestants or via the internet.\(^23\) Federal authorities are getting involved as ephedrine can be chemically reduced to produce methamphetamines. During 2006, the most frequently smuggled precursors from other countries into Canada was ephedrine. Approximately 33.8 million tons of imported ephedrine is being used by manufacturers each year to create non-methamphetamine products for sale in Canada.\(^24\)

**Conclusion**

With the negative cardiovascular effects of ephedrine use, there is a clear methodology behind the ban of ephedrine substances. Although Canadian data do not currently exist, US data pre- and post-ban has shown that although the legislation has not completely
eliminated non-approved usage, it has decreased its overall incidence however not among select populations such as college athletes. As survey results have shown, ephedrine usage most commonly begins during high school. Further reductions in use may be attainable through education of the adverse effects, being implemented at the high school and college levels, targeting those especially at risk for ephedrine usage: athletes and weight conscious individuals.

The cardiovascular complications of ephedrine use in combination with caffeine, requires further scientific research as few studies exist on this topic. If a synergistic effect on producing cardiovascular complications is repeatedly found such as those shown by Persky et al. (26), the 8 mg per dose guideline should be reconsidered.

Cardiovascular events are being reported at dosages lower than 8 mg. The benefits of using ephedrine in pharmaceutical products need to be weighed against the risks associated with its use, both pharmacological and non-pharmacological, as over the counter medications are a source of ephedrine use for non-approved purposes.

References
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