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Letters

Effects of legislation restricting pack sizes of paracetamol on self poisoning

It's too early to tell yet

EDITOR—Any measure that will reduce the incidence of paracetamol poisoning is to be welcomed. Hawton et al report the impact of legislation restricting pack sizes of paracetamol and salicylate on self poisoning,[1] but there are major limitations in interpretation—for example, the period studied after the legislation came into force is too short (one year) for its impact to be fully assessed. This is particularly relevant in the assessment of patients with acute liver disease as the numbers are small and there will be baseline variability.[2] The data from the liver unit at King's College Hospital cross the line indicating an incidence rate ratio of 1, and the data from Leeds, Newcastle, and the Royal Free Hospital have incidences close to zero.[1]

The authors give data on blood paracetamol concentrations and mean number of tablets taken per paracetamol overdose, but these did not greatly change and would be the main determinant of outcome in early paracetamol poisoning.[3] Certainly, prothrombin time would not be expected to be a good marker, not least because of the availability of adequate treatment with acetylcysteine.

Over the same period Donogue et al examined 2020 cases of deliberate paracetamol poisoning; they concluded that the incidence did not change after pack size was restricted in the Republic of Ireland.[4] In addition, our data show that the pack size legislation is not complied with, at least in London, and considerably more than the restricted number of pills can be bought in pharmacies, supermarkets, and corner shops.[2]

In conclusion, restrictions on pack size are not being adhered to universally. It is too early to make any causal conclusions on their impact on either the incidence of paracetamol poisoning in general or acute liver failure in particular.

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Authors did not look at effects on all deliberate and accidental self poisoning

EDITOR—Hawton et al provide some evidence of a decrease in the severity and incidence of paracetamol and salicylate poisoning after pack sizes of these drugs were restricted.[1] They have not, however, considered the effect on deliberate self poisoning as a whole, or on self poisoning with other drugs.

Limiting access to one type of drug may simply increase the incidence of overdose with other potentially more dangerous substances. It is important to determine if poisoning with other agents increases.[2] Although the authors allude to this in their discussion, they mention only the small but significant increase in overdoses with paracetamol compounds and paracetamol with other drugs. Using self poisoning with paracetamol and salicylates alone as a measure of the effect of this legislation on self poisoning is erroneous and potentially dangerous.

Hawton et al have not considered the effect of the legislation on accidental poisoning in children. This is a critical public health issue and needs to be evaluated alongside deliberate self poisoning to assess the impact of any change in legislation. Data from poison information centres would be useful to evaluate any changes in paediatric accidental poisoning.

With only one year of data after the change of legislation available, it is of concern that the results are not significant for the larger liver transplant units alone. Furthermore, the biochemical data do not support the decrease in severity of cases, with no change in the mean highest blood paracetamol concentration. The slight decrease in mean highest prothrombin time is a poor measure of severity: about half of patients with paracetamol poisoning without hepatotoxicity will have a raised prothrombin time,[3] so it is a poor indicator of liver poisoning.

We are concerned that the authors conclude that the legislation has been relatively successful without properly assessing its effects on all deliberate and accidental self poisoning.

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Paracetamol should be packaged with its antidote

EDITOR—Paracetamol overdose is the most common cause of acute hepatic failure. Hepatocytes become sensitive to paracetamol metabolites and inflammatory mediators[1] when intracellular glutathione is depleted due to metabolism of paracetamol.[2] For this reason, many clinical conditions associated with glutathione depletion—for example, chronic alcohol abuse, multiorgan system failure, chemotherapy, and certain metabolic diseases—place patients at risk of paracetamol toxicity, even at therapeutic doses of paracetamol. In addition, patients without predisposing disease are at risk because over the counter preparations often contain paracetamol and represent sources of potential overdose.

Importantly, Hawton et al report that morbidity and mortality from paracetamol overdose decreased after legislation in the United Kingdom to restrict the package sizes of the drug.[3] As the authors note, however, restricting the package size did not completely resolve the problem.

Acetylcysteine, which provides the cysteine necessary to replenish glutathione depleted by paracetamol, is used to treat paracetamol overdose.[4] Intravenous acetylcysteine is used in some areas, but oral treatment protocols are highly effective. Treatment is most effective when started soon after paracetamol is ingested,[5] but delays are still common. We therefore suggest that toxicity caused by paracetamol overdoses, whether intentional or not, is best treated by prevention—that is, by formulating or packaging paracetamol with sufficient amounts of acetylcysteine to prevent toxicity.

Acetylcysteine preserves the antipyretic and analgesic properties of paracetamol, and its coadministration should not interfere with the effectiveness of paracetamol. As it has been used for many years at high doses with minimal toxicity, giving it at the estimated doses together with paracetamol should not pose any safety issues.

The disagreeable smell and taste of some acetylcysteine formulations, particularly those used clinically

in the United States, might be a problem, but the contaminants responsible for the bad smell and taste are not present in appropriately manufactured formulations. Our estimates indicate that including <200 mg acetylcysteine per 500 mg paracetamol would prevent toxicity. We therefore do not foresee any obstacles to the introduction of acetylcysteine-paracetamol products. The efficacy of such formulations for preventing morbidity and mortality should be evaluated.

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The authors have filed a disclosure and patent application for a combination treatment of acetaminophen with acetylcysteine.

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BMJ 2001 322: 1203. [Abstract] [Abridged text] [Full text]