Assessing Acetaminophen Toxicity and Treatment with N-acetylcysteine

In an acetaminophen (APAP) overdose, there are frequent misunderstandings about the interpretation of APAP levels and the need for treatment with the antidote, n-acetylcysteine (NAC). The only way to properly assess for potential APAP toxicity is by plotting the APAP level against time since ingestion on the Rumack-Matthew nomogram. Potential toxicity cannot be assessed by the APAP level alone. Many labs give an APAP therapeutic range of 10-20 mcg/mL. However, an APAP level of 20 mcg/mL at 15.5 hours or later after an APAP ingestion is not “therapeutic,” but plots in the “possible toxicity” area of the nomogram and requires treatment with NAC.

After one APAP level plots in the toxic range on the nomogram, and treatment is initiated, there is no need to draw consecutive levels during the course of treatment. APAP levels will fall during treatment and decreasing consecutive levels does not rule out toxicity. A repeat APAP level may be indicated during treatment if the APAP formulation was either extended-release or contained a narcotic or diphenhydramine. If the time of ingestion is unknown, NAC will need to be given if any APAP is detected in the patient’s serum, regardless of falling serial levels.

An APAP level does need to be drawn at the end of any treatment course of NAC to make sure there is no APAP remaining in the serum. If any APAP remains, further treatment with NAC may be indicated, and the decision of whether or not to treat with additional NAC is decided on a case-by-case basis.

When NAC treatment is initiated early after an APAP overdose, the prognosis for these patients is excellent. IV NAC is frequently selected over oral NAC due to the shorted treatment time and the relative ease of administration. However, there are frequent errors and misunderstanding about the administration of IV NAC due to the three different doses given over three different time frames. IV NAC is given in 3 back-to-back infusions, lasting a total of 21 hours. Of note, oral NAC is equally effective in most situations.

For questions about interpretation of APAP levels or treatment with NAC, contact the Iowa Statewide Poison Control Center at 800-222-1222.

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