Letter to Editor

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Risk Determination of Acetaminophen Intoxication in Cases Nomogram is not Applicable

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Abstract

The Rumack-Matthew nomogram for acetaminophen toxicity was prepared using the acetaminophen levels of untreated patients and published in 1975. In order to determine the risk, the authors aimed to determine the acetaminophen levels that cause the aminotransferase level to increase to 1,000 IU/L and above. Thus, the line presenting the values above 200 was created. In the study published by Rumack et al. in 1981, the line representing values above 150 was suggested as a safer value. On the other hand, the nomogram was designed on the known intake times of single dose, immediate-release acetaminophen preparations. This causes significant limitations in clinical practice.

Keywords: Pharmacokinetics, toxicology, acetaminophen

Özet

Parasetamol toksisitesi için Rumack-Matthew nomogramı tedavi edilmeyen hastaların asetaminofen düzeyleri kullanılarak hazırlanmış ve 1975 yılında yayınlamıştır. Risk belirlemek için yazarlar aminotransferase seviyesinin 1,000 IU/L ve üzeri değerlere yükselmesine neden olan parasetamol düzeylerini tespit etmeyi amaçlamıştır. Böylelikle 200 üzerindeki değerleri temsil eden cizgi oluşturulmuştur. Rumack ve arkadaşlarının 1981 yılında yayınladıkları çalışmada ise 150 üzerindeki değerleri temsil eden cizgi daha güvenli bir değer olarak önerildi. Öte yandan nomogram tek doz, hızlı cözünen preparatların bilinen alım süreleri üzerine dizayn edildi. Bu klinik uygulamada önemli limitasyonlara neden olmaktadır.

Keywords: Farmakokinetik, toksikoloji, asetaminofen

Dear Editor,

The Rumack-Matthew nomogram for acetaminophen toxicity was prepared using the acetaminophen levels of untreated patients and published in 1975. To determine the risk of mortality, the authors aimed to determine the acetaminophen levels that cause the aminotransferase level to increase to 1.000 IU/L and above1. Thus, the line presenting the values above 200 was created. In the study published by Rumack et al. in 1981, the line representing values above 150 was suggested as a safer value[2]. On the other hand, the nomogram was designed on the known intake times of single dose, immediate-release acetaminophenpreparations. This causes significant limitations in clinical practice.

The first limitation is the risk assessment situation when the time of ingestion is unknown, or it is wider than 24 hours. It is almost always possible to determine at least one window of time during which ingestion occurs. The earliest possible time for ingestion is used as the intake time for risk assessment. If this time window cannot be determined or wider than 24 hours; both acetaminophen and aminotransferase value should be tested. If aminotransferase is elevated, treatment with N-acetylcysteine should be initiated regardless of the acetaminophen level. In cases where the intake time is not completely known and the acetaminophen level can be determined, treatment with N-acetylcysteine should be started, considering that the patient is at risk. If the acetaminophen level is below the toxic level on admission and the aminotransferase is normal, there is no evidence of possible liver damage and N-acetylcysteine therapy is unnecessary[1].

The second limitation is the risk assessment situation after taking extended or modified-release acetaminophen. In taking extended-releaseacetaminophen-containing drugs, serum acetaminophen level can be measured and evaluated according to the nomogram, and the necessity of antidote treatment can be checked. However, the validity of this decision requires further evaluation. Intoxications with short-release and long-release combined preparations require more careful evaluation1. In the study conducted with 2596 patients ingesting slow-release acetaminophen-containing

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drugs were evaluated, it was shown that there was no risk increase between intoxication and immediate-release drug intoxication with the extended-release drug[3].

A third limitation is the risk assessment in patients with symptoms and signs of liver injury after acute intake. N-acetylcysteine therapy should be initiated promptly in patients with symptoms and signs of liver injury after acute ingestion. Aminotransferase and serum acetaminophen measurement should be done. In the presence of high aminotransferase level and serum acetaminophen level detected below the treatment line, the history should be taken again regarding the time of administration and repeated doses of very high acetaminophen. N-acetylcysteine therapy should continue until the causes of liver failure and elevated aminotransferase values are clearly identified[1,4].

Another limitation is the risk assessment after repeated intake. Usually, the rate of serious acetaminophen toxicity after repeated doses is very low5. Serious acetaminophen toxicity may occur following high doses or after prolonged high-dose intake. In normal adults, as with alcoholics, the highest dose of chronic ingestion of 4 g/day is generally safe6. Since hepatotoxicity risk is affected by patient-related factors, amount of intake and duration of intake, a safe cutoff value for hepatotoxicity has not yet been determined for repeated doses. In the presence of toxicity risk after repeated high doses of acetaminophen, screening tests including acetaminophen and aminotransferase and additional tests may be required depending on their results and clinical features.

As a conclusion, emergency medicine specialists and anesthesiologists should keep in mind that the nomogram does not meet all scenarios in paracetamol intoxication and should be prepared for scenarios where the nomogram cannot be used.

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