Acetaminophen Psi Nomogram: A Sensitive and Specific Clinical Tool to Predict Hepatotoxicity Secondary to Acute Acetaminophen Overdose

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Background: *Acetaminophen Psi Parameter (APP) is a composite of acetaminophen (paracetamol) level and lag time before N-acetylcysteine (NAC) therapy. The APP is a significant predictor of hepatotoxicity secondary to acute acetaminophen overdose. Acetaminophen Psi Nomogram (APN) was invented as a graphic analog of the APP for use in predicting individual patient's risk of hepatotoxicity. Clinical accuracy of the APN has never been validated.*
Objective: *The authors are reporting the validity of APN in predicting hepatotoxicity secondary to acute acetaminophen overdose at Siriraj Hospital.*
Material and Method: *This present study is a retrospective review of medical records of patients with acute acetaminophen overdose at Siriraj Hospital between January 2004 and June 2009. Each case was classified by APN into an appropriate risk group. The outcome of interest was hepatotoxicity. The validity of the APN is reported as sensitivity and specificity. Secondary outcomes include serum acetaminophen concentrations, delay to NAC therapy, and APP for each APN's risk group.*
Results: *One hundred and sixty-one patients were enrolled. Higher APN risk classifications are associated with a trend towards higher acetaminophen levels, longer delayed to NAC initiation, and larger APP. Twenty five patients (15.5%) developed hepatotoxicity. The number of patients who were above the APN's risk lines, 1% and 50% were 88 (54.7%) and 17 (10.6%), respectively, with corresponding sensitivities of 100.0% (95% CI 86.6, 100.0) and 40.0% (95% CI 21.2, 61.3). APN's risk lines 50% had specificity of 94.9% (95% CI 89.7, 97.9).*
Conclusion: *Acetaminophen Psi Nomogram is a sensitive and specific tool for prediction of hepatotoxicity secondary to acute acetaminophen overdose. By application of the APN, a significant proportion of patients may not require either further follow-up after the completion of NAC therapy or prolongation of NAC therapy. Patients in high APN's risk ranges may be treated and monitored more intensively with confidence.*

Keywords: *Hepatitis, N-acetylcysteine, Paracetamol, Poisoning, Prognosis, Validity*

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Acute acetaminophen (paracetamol) overdose is a common type of poisoning that may result in hepatotoxicity. N-acetylcysteine (NAC) therapy is an antidotal treatment that prevents and treats acetaminophen-induced hepatotoxicity. Prediction of hepatotoxicity risk is crucial for individualizing treatment plans in acute acetaminophen overdose[1]. For patients classified as having low risk of hepatotoxicity, a standard regimen of NAC should be an adequate and a cost-effective plan of management[1-3]. In contrast, patients categorized as having high risk of hepatotoxicity may benefit from a prolonged course of NAC therapy[1,4]. Acetaminophen concentrations and time lapse between ingestion to the start of NAC therapy (tNAC) are the proven determinants of hepatotoxicity[4,5]. The Acetaminophen Psi Parameter (APP) is a composite method that incorporates these factors into a hepatotoxicity prediction that has been validated[6-8]. The Acetaminophen Psi Nomogram (APN) (Fig. 1) is a graphic tool derived from the APP to aid in the visualization and simplification of the APP estimation. It allows the plotting of acetaminophen concentration and tNAC on to a graph with six predetermined lines representing hepatotoxicity risk levels[8]. The APN has never been evaluated on how well it predicts the risk of hepatotoxicity and estimates the APP.

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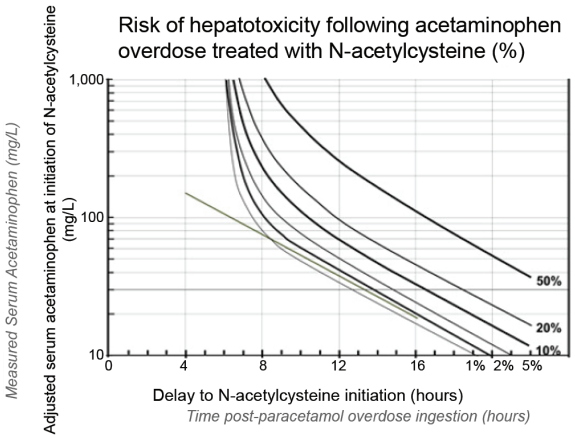

Fig. 1 Acetaminophen Psi Nomogram (reuse with written permission from the rights holder).

Objectives

The authors are reporting the validity of the APN in predicting hepatotoxicity secondary to acute acetaminophen overdose in a Thai population. Moreover, the authors assess how well the APN risk categories represent the APP ranges.

Material and Method

Study design and population

This is a retrospective review of patients who presented to Siriraj Hospital between January 2004 and June 2009. The inclusion criteria were patients whose ages are at least 12 years who presented with acute acetaminophen overdose (ICD-10 code 39.1). Only patients who had serum acetaminophen concentration above the "possible hepatotoxicity" on the Rumack-Matthew Nomogram and were treated with NAC were enrolled. Patients were excluded if at least one of the following is not available for review: time of ingestion, aminotransferase concentrations at presentation and follow-up at 36 to 48 hours post-ingestion. Furthermore, patients with co-ingestion with ethanol, history of chronic ethanol abuse, and baseline aminotransferase above two times upper normal limits were excluded.

The reviewers were trained to obtain acetaminophen concentrations, NAC lag time, and liver enzymes from medical records, and plot them onto the APN. All the data are recorded in the case record form and spread sheet with standardized unit. The method for plotting the APN is published in the original literature[8]. The reliability of the reviewer's data extraction were tested on 20 random sets of medical records and achieved an inter-rater agreement, assessed as kappa and correlation coefficient of at least 0.8 between each pair of reviewers. Each set of medical records were reviewed by two of the three reviewers. Investigators also obtained demographic data, dose and time of acetaminophen ingestion, history of ethanol abuse and co-ingestion, co-ingestion of other drug/substances, underlying liver disease, and patient's outcome at discharge.

Using acetaminophen concentration and tNAC, each patient was classified into seven groups by the six risk lines on the APN (Fig. 1). The corresponding risk of hepatotoxicity (RH) for each group is RH <1%, RH ≥1%, RH ≥2%, RH ≥5%, RH ≥10%, RH ≥20% and RH ≥50%, respectively. The APPs were calculated using the Psi calculator, which was developed and validated. The calculator may be downloaded from our website at the URL provided at the end of this article. The inputs required for the APP calculation are acetaminophen concentration and tNAC[6-8]. Then, Serum acetaminophen concentrations of patients were categorized into three hepatotoxicity risk groups, possible risk, probable risk and high risk by using the existing hepatotoxicity risk-line on the Modified Rumack-Matthew Nomogram as reference points[5,9]. Four-hour-equivalent acetaminophen concentrations were derived from measured acetaminophen concentration and time of blood collection, with the assumed acetaminophen elimination half-life of 4 hours. At the same time, patients are grouped by tNAC into early, slightly delayed and delayed NAC therapy. Criteria for classification of acetaminophen concentrations and tNAC are listed in Table 1. The research protocol was approved by Siriraj Institutional Review Board.

Data analyses

Data were displayed as median, interquartile range, frequency, and percentage of the risk groups and the groups with or without hepatotoxicity. At the same time, the comparisons between the groups with or without hepatotoxicity were performed using Mann-Whitney U Test and Chi-squared when appropriate. Incidence rates and relative risk ratios with 95% confidence intervals of the risk groups were calculated[10], since the data in table 2 were analyzed as a retrospective cohort study. In defining the diagnostic validity for each cut-off line on the Psi Nomogram, patients whose acetaminophen concentrations are on or above the cut-off line are considered to "test positive" and those below are "test negative". The presence of hepatotoxicity, defined as

1,000 iU/L, is the outcome of interest. Predicting validity of each risk line on the Psi Nomogram is reported as sensitivity and specificity and their 95% confidence intervals[11].

Results

Out of 746 patients who presented at Siriraj Hospital during the study period with acetaminophen overdose, 161 fulfilled the inclusion criteria and were enrolled in this study. Five hundred eighty five cases were excluded because of age (25 cases), acetaminophen concentrations below the treatment line (481 cases), uncertain times of ingestion (38 cases) and ethanol use or ethanol co-ingestion (41 cases). Among 161 patients in the study, 137 (85.1%) were female. The median age and interquartile range was 21 years and 18 to 26 years, respectively. Twenty-five (15.5%) patients developed hepatotoxicity with no liver failure or mortality. Subjects who developed hepatotoxicity were not significantly different in age and gender from those with no hepatotoxicity. Five patients had co-ingestions (amitriptyline, alprazolam, loratadine, and chlorpheniramine), all of whom were in the non-hepatotoxicity group. The authors performed Chi-squared tests which revealed that hepatotoxicity was significantly association with delayed NAC therapy (≥8 hours). Approximately one third of non-hepatotoxicity cases were possible, probable, and high-risk hepatotoxicity; while 92% of hepatotoxic cases were high-risk with no cases in the possible group. More than half of the non-hepatotoxicity patients were classified as early NAC therapy with a minority (9.6%) who had delayed NAC therapy. None of the hepatotoxicity patients had early NAC therapy (Table 2). Four-hour equivalent acetaminophen concentration and the Psi Parameter

Table 1. Classification of acetaminophen concentrations in to risk-level categories and classification of lag time to N-acetylcysteine therapy from the time of ingestion

Variable	Category	Meaning
[APAP]	Possible risk	[APAP] between possible and probable hepatotoxicity risk lines (150-199 mg/L at 4 hours)
	Probable risk	[APAP] between probable and high risk lines (200-299 mg/L at 4 hours)
	High risk	[APAP] above high risk line (≥300 mg/L at 4 hours)
tNAC	Early	NAC onset <8 hours
	Slightly delayed	8 hours ≤ NAC onset <16 hours
	Delayed	NAC onset ≥24 hours

[APAP] = acetaminophen concentration; tNAC = time lapse between ingestion to the start of NAC therapy

Table 2. Comparisons of parameters between the non-hepatotoxicity and hepatotoxicity groups

Parameter (units), frequency (percentage)	Non-hepatotoxicity (n = 136)	Hepatotoxicity (n = 25)	p-value
Age (years), median (IQR)	22.0 (18.0-27.0)	21.0 (19.0-24.0.6)	0.34
Gender-female, count (percent)	117 (86.0%)	20 (80.0%)	0.54
Drug co-ingestion, count (percent)	5 (100%)	0 (0)	-
Transaminase follow-up time (hours), median (IQR)	44.0 (38.0-48.0)	150.0 (136.0-180.0)	<0.001
tNAC, count (percentage among time group)			<0.001
Early	74 (54.4%)	0	
Slightly delayed	49 (36.0%)	15 (60.0%)	
Delayed	13 (9.6%)	10 (40.0%)	
Acetaminophen concentration group, count (percentage among risk group)			<0.001
Possible risk group	47 (34.6%)	0	
Probable risk group	48 (35.3%)	2 (8.0%)	
High risk group	41 (30.1%)	23 (92.0%)	
4-hour [APAP] (mg/L), median (IQR)	231.2 (185.5-320.2)	514.1 (430.0-1,189.0)	<0.001
APP (mM·hour), median (IQR)	0.001 (0.001-2.283)	7.565 (4.475-20.633)	<0.001

NAC = N-acetylcysteine; tNAC = time lapse between ingestion to the start of NAC therapy; IQR = interquartile range; 4-hour [APAP] = 4 hour equivalent acetaminophen concentration; APP = The Acetaminophen Psi Parameter

of the hepatotoxicity cases were significantly higher than the non-hepatotoxicity cases.

In the APN risk classification, almost half of the patients (45.3%; 73 out of 161 cases) were classified into a group with hepatotoxicity risk <1% (Table 3). The hallmark of this group was early start of NAC therapy, with the mixture of possible risk to high risk acetaminophen concentrations. There were clear trends towards more delayed NAC therapy, higher acetaminophen concentrations, and larger Psi Parameters in the groups with increasing hepatotoxicity risks. Hepatotoxicity risk groups above 20% consisted solely of acetaminophen concentrations in the high-risk group. There was no hepatotoxicity in the group with APN hepatotoxicity risk ≤1%, while the incidence rates and relative risk of hepatotoxicity consistently increased in higher APN risk groups. The median and interquartile range of the Psi Parameters in the APN risk group <1% are 0.0 mM·hour. The relative risk, as calculated by using the APN hepatotoxic risk <1% group as the reference for comparison, were statistically significant in all groups with hepatotoxicity risk of 1% or more.

In Table 4, cut-off lines 1%, 2%, and 5% were shown to have very high sensitivity (100% with 95% CI 86.2, 100.0), while the cut-off lines 20% and 50% had high specificities (86.0% (95% CI 79.04-91.37) and 94.9% (95% CI 89.7-97.9), respectively).

Table 3. Characteristics and outcomes of the hepatotoxic risk groups as classified by the acetaminophen psi nomogram

Risk group	<1% (n = 73)	≥1% (n = 88)	≥2% (n = 85)	≥5% (n = 69)	≥10% (n = 54)	≥20% (n = 37)	≥50% (n = 17)
Hepatotoxicity, count (%)	0	25	25	25	23	18	10
[APAP], count (%)							
Possible risk	36 (49.3)	11 (12.5)	8 (9.4)	0 (0)	0 (0)	0 (0)	0 (0)
Probable risk	29 (31.9)	2 (23.9)	2 (24.7)	14 (20.3)	4 (7.4)	0 (0)	0 (0)
High risk	8 (11.0)	56 (63.6)	5 (65.9)	55 (79.7)	50 (92.6)	37 (100)	17 (100)
4-hour [APAP] (mg/L), median (IQR)	200.8 (178.1-237.6)	170.6 (166.3-180.9)	202.5 (184.0-257.1)	271.3 (231.5-335.7)	324.0 (301.5-388.7)	469.2 (387.3-527.3)	1,189.0 (787.5-1,894.6)
tNAC, count (%)							
tNAC <8 hours	73 (100)	1 (1.1)	1 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)
8 ≤ tNAC <16 hours	0 (0)	64 (72.7)	61 (71.8)	47 (68.1)	34 (63.0)	19 (51.4)	7 (41.2)
16 ≤ tNAC hours	0 (0)	23 (26.1)	23 (27.1)	22 (31.9)	20 (37.0)	18 (48.6)	10 (58.5)
APP (mM·hour), median (IQR)	0.0 (0.0-0.0)	0.9 (0.8-0.9)	1.4 (1.1-1.5)	2.2 (2.1-2.3)	3.5 (3.7-4.0)	6.6 (5.1-7.5)	20.6 (13.3-39.6)
Relative risk (95% CI)	Reference	42.40 (2.66-684.75)	43.88 (2.72-708.46)	53.91 (3.35-868.79)	63.24 (3.93-1,018.62)	72.05 (4.46-1,163.33)	86.33 (5.30-1,405.43)

[APAP] = acetaminophen concentration; 4-hour [APAP] = 4 hour equivalent acetaminophen concentration; tNAC = time lapse between ingestion to the start of NAC therapy; 95% CI = 95% confidence interval, APP = The Acetaminophen Psi Parameter

Discussion

It is challenging to find a clinical tool that enable individualized prediction of hepatotoxicity secondary to acute acetaminophen overdose[1,12,13]. The advent of the APP addresses this particular demand by using acetaminophen concentration and time onset of NAC therapy to quantify hepatotoxicity risk. The APP is designed to reflect hepatocyte exposure to N-acetyl-p-benzoquinoneimine (NAPQI), the toxic metabolite of acetaminophen, before NAC therapy is starts[7]. When the APP is larger, either due to a higher acetaminophen concentration or a longer lag time to NAC or both, the risk of hepatotoxicity is higher[8]. However, the APP requires complicated mathematical calculations that cannot be easily done in clinical practices. A much more practical tool, the APN is a result of the initial validation of the Psi Parameter involving the Canadian population[8]. In a 2011 publication, the authors subsequently confirmed the validity of the APP in Thai population and its superiority over acetaminophen concentration and tNAC at predicting hepatotoxicity[6]. The APN consists

Table 4. Validity of acetaminophen psi nomogram cut-off line in predicting hepatotoxicity; positive and negative tests mean the plotted risk above and below each particular line, respectively

Cut-off lines	Sensitivity (95% CI)	Specificity (95% CI)
1%	100.0 (86.2, 100.0)	53.7 (44.9, 62.3)
2%	100.0 (86.2, 100.0)	55.9 (47.1, 64.4)
5%	100.0 (86.2, 100.0)	67.7 (59.1, 75.4)
10%	92.0 (73.9, 98.8)	77.2 (69.2, 84.0)
20%	72.0 (50.6, 87.9)	86.0 (79.0, 91.4)
50%	40.0 (21.2, 61.3)	94.9 (89.7, 97.9)

95% CI = 95% confidence interval

of acetaminophen concentration (vertical axis), time from ingestion (horizontal axis), and six hepatotoxicity risk lines (Fig. 1). The APN's designated risk lines were derived from a logistic regression model of APP on hepatotoxicity, but their validities have never been tested[8]. To the authors' knowledge, this is the first validation of the APN. The overlap in study population between this current study and previously published study[6] is intentional. Since the validity of APP is proven[6], the authors attempt to take this further by graphically categorize risk groups by the APN and showing that there is an accordingly increased relative risk of hepatotoxicity. Patients with ethanol abuse and co-ingestions are excluded in order to fulfill the assumptions for the APN[8]. The difference in inclusion criteria resulted in the different number of subject that the authors enrolled in this current study from the Psi Parameter study. The rate of hepatotoxicity (15.5%) in this study is comparable with the other published rates[3-5,14,15]. The time for transaminase follow-up of at least 36 hours should be long enough to detect all the abnormal transaminase concentrations, if they do exist[16,17]. The increasing trends of tNAC and acetaminophen concentrations and increasing Psi Parameter, in higher APN risk groups imply that the APN functions well as a graphic analog of the Psi Parameter (Table 3). The parallel between the Psi Nomogram risk group and discrete interquartile ranges of the Psi Parameter, as well as the corresponding relative risks proves the APN's usefulness as a risk assessor for acute acetaminophen-induced hepatotoxicity.

The sensitivity of the APN risk lines 1, 2, and 5% of the nomogram is 100% with 95% confidence intervals of 86.2 to 100 indicates that the APN is a sensitive tool in screening out the patients who are at minimal risk of hepatotoxicity. Moreover, the APN's 50% risk line has a high specificity (94.9%) in predicting hepatotoxicity secondary to acute acetaminophen overdose.

The limitation for the use of the APN is the possibility that the time of ingestion is erroneous, which may generate a wrong classification in the APN risk group. The APN risk group with a narrow range on the plot, such as the 1-2% risk group is more prone to be misclassified. Another potential drawback of the APN is the dramatic changes in acetaminophen concentrations that may even cause changes in risk stratification by modified Rumack-Matthew Nomogram. These occurrences have been reported to cause significant hepatotoxicity in 'line crossers', patients whose initial acetaminophen concentrations were below the possible hepatotoxicity line and subsequently showed concentrations as extreme as high risk hepatotoxicity ranges. These incidences have been associated with ingestions of extra strength acetaminophen formulations, co-ingestions or ingestion of combination formulation of acetaminophen and diphenhydramine, hydrocodone and propoxyphene[9,18,19]. In this present study, the number of co-ingestion was low and the follow-up periods were adequate for detection of all hepatotoxicity cases. Since this is a retrospective study with a relatively small subject number, numbers of cases and hepatotoxicity in each risk group are small and the accuracies of estimations of risk and validity may be limited.

With these limitations in mind, the APN is recommended for use in patients whose NAC therapy is started based on risk assessment by the Rumack-Matthew Nomogram. The APN maximizes the utilization of available data in refining risk assessment and allows the individualization of therapy by applying the acetaminophen concentration with the NAC treatment onset to predict individualized hepatotoxicity risk. The authors suggest that the APN risk line 1% is selected for clinical practice as a sensitive risk assessment line. Such selection, by sacrificing the sensitive risk lines 2% and 5%, allows a safety margin for misclassification in APN hepatotoxicity risk due to errors in reported time of ingestion. The APN is ideally applied in cases where regular acetaminophen tablet is the only substance involved, to avoid the possibility of 'line crossers'. The application of this sensitive APN 1% cut-off line will allow physicians to exclude cases with low risk of hepatotoxicity from further evaluation and treatment after completion of the initial NAC therapy course

even in face of very high initial acetaminophen concentrations[1,12]. In our series, the number of cases that may be excluded by APN 1% cut-off line is approximately 45%. In addition, the APN risk line of 50%, which has high specificity for hepatotoxicity, can be used to justify further follow-up and NAC therapy for patients who fall in to this category. Application of the APN will be beneficial for primary practitioners in developing countries or in rural hospitals, where the laboratory support is not readily available or the turn-around makes it unfeasible to use laboratory follow-up in all overdose cases. Finally, a large sample size, prospective study is required to validate the APN with more certainty.

Conclusion

The Acetaminophen Psi Nomogram is a viable alternative to The Acetaminophen Psi Parameter for assessing of hepatotoxicity risk based on timed-acetaminophen concentration and lag time to NAC therapy. The present study shows that the Psi Nomogram is a simple, sensitive, and specific clinical tool in predicting the risk of hepatotoxicity secondary to acute acetaminophen overdose.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

What is already known on this topic?

Acute acetaminophen may cause hepatotoxicity and liver failure, which can be prevented and treated with N-acetylcysteine (NAC). Hepatotoxicity risk increases with higher acetaminophen concentration and longer delay of NAC treatment. Prediction of hepatotoxicity enables physician to customize treatment regimen for the patient to maximize safety and economical utilization of resources. Acetaminophen Psi Parameter (APP) has been proven to quantify risk of hepatotoxicity on the basis of acetaminophen concentration and delay to NAC onset. However, calculation of APP is too complicated to be used in routine clinical practice.

What this study adds?

Acetaminophen Psi Nomogram (APN) is created from a logistic regression model of psi parameter on hepatotoxicity as a simpler tool for risk assessment. The authors present the first validation of the APN. Higher APN risk lines are associated with higher acetaminophen levels, later onset of NAC therapy, larger APP, and higher incidence of hepatotoxicity. The APN's 1% risk line has high sensitivity and the 50% risk line yields high specificity. Approximately 45% of acute acetaminophen overdose patients can be excluded from further follow-up and treatment after the initial NAC therapy using the sensitive APN line.

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Website for downloading Acetaminophen Psi Parameter (APP) calculator

http://www.si.mahidol.ac.th/th/department/preventive/eng/dept_news_detail.asp?n_id=23&dept_id=17

Potential conflicts of interest

None.

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อะเซตามิโนเฟนไซโนโมแกรม: เครื่องมือทางคลินิกที่ไวและจำเพาะในการทำนายภาวะพิษต่อตับจากอะเซตามิโนเฟนเกินขนาดแบบเฉียบพลัน

สัมมน โฉมฉาย, นงนุช หล่อวัฒนตระกูล, จุฬธิดา โฉมฉาย

ภูมิหลัง: *อะเซตามิโนเฟนไซพารามิเตอร์เป็นค่าที่ได้จากความเข้มข้นของอะเซตามิโนเฟน (พาราเซตามอล) ในซีรัม และระยะเวลาก่อนการเริ่มการรักษาด้วยยาอะเซทิลซิสเทอีน ค่าอะเซตามิโนเฟนไซพารามิเตอร์สามารถใช้ทำนายการเกิดพิษต่อตับจากภาวะพาราเซตามอลเกินขนาดเฉียบพลัน อะเซตามิโนเฟนไซโนโมแกรมเป็นแผนภาพที่ถูกสร้างขึ้นเพื่อใช้ประมาณค่าอะเซตามิโนเฟนไซพารามิเตอร์ และใช้ในการทำนายความเสี่ยงในการเกิดภาวะพิษต่อตับในผู้ป่วยแต่ละราย ความแม่นยำทางคลินิกของอะเซตามิโนเฟนไซโนโมแกรมยังไม่เคยถูกประเมินมาก่อน*

วัตถุประสงค์: *ผู้นิพนธ์รายงานความเที่ยงตรงของอะเซตามิโนเฟนไซโนโมแกรมในการทำนายการเกิดพิษต่อตับจากภาวะพาราเซตามอลเกินขนาดเฉียบพลันที่โรงพยาบาลศิริราช*

วัสดุและวิธีการ: *การศึกษานี้เป็นการสืบค้นเวชระเบียนผู้ป่วยแบบย้อนหลังในผู้ป่วยจากภาวะพาราเซตามอลเกินขนาดเฉียบพลันที่โรงพยาบาลศิริราช ในช่วงเดือนมกราคม พ.ศ. 2547 ถึง เดือนมิถุนายน พ.ศ. 2552 ผู้ป่วยแต่ละรายถูกจำแนกโดยไซโนโมแกรมเป็นกลุ่มความเสี่ยง ผลลัพธ์ของการศึกษาได้แก่ภาวะพิษต่อตับ ความเที่ยงตรงของอะเซตามิโนเฟนไซโนโมแกรมถูกรายงานในรูปความไวและความจำเพาะ ผลลัพธ์รองของการศึกษาได้แก่ ระดับอะเซตามิโนเฟนในซีรัม ระยะเวลาก่อนการรักษาด้วยยาอะเซทิลซิสเทอีน และค่าไซพารามิเตอร์ของแต่ละกลุ่มความเสี่ยงจากไซโนโมแกรม*

ผลการศึกษา: *การศึกษานี้มีผู้ป่วย 161 ราย กลุ่มความเสี่ยงที่สูงขึ้นจากไซโนโมแกรมมีแนวโน้มที่จะพบร่วมกับความเข้มข้นของพาราเซตามอลสูงขึ้น การเริ่มรักษาด้วยยาอะเซทิลซิสเทอีนช้าลง และค่าไซพารามิเตอร์ที่มากขึ้น ผู้ป่วย 25 ราย (15.%) เกิดภาวะพิษต่อตับ เส้นความเสี่ยง 1% และ 50% บนไซโนโมแกรม มีผู้ป่วยจำนวน 88 (54.7%) และ 17 (10.6%) อยู่เหนือเส้นทำให้ได้ความไวเท่ากับ 100.0% (95% CI 86.6, 100.0) และ 40.0% (95% CI 21.2, 61.3) ตามลำดับ เส้นความเสี่ยง 50% มีความจำเพาะ 95% (95% CI 89.7, 97.9)*

สรุป: *อะเซตามิโนเฟนไซโนโมแกรมเป็นเครื่องมือทางคลินิกที่มีความไวและความจำเพาะสูงในการทำนายภาวะพิษต่อตับจากพาราเซตามอลเกินขนาดเฉียบพลัน การประยุกต์ใช้ไซโนโมแกรมจะช่วยให้ผู้ป่วยจำนวนหนึ่งไม่ต้องได้รับการติดตามตรวจและรักษาด้วยยาอะเซทิลซิสเทอีนต่อหลังจากที่ผู้ป่วยได้รับการรักษาด้วยยาอะเซทิลซิสเทอีนไปแล้ว ผู้ป่วยที่อยู่ในช่วงความเสี่ยงสูงจากไซโนโมแกรมจะได้รับการติดตามตรวจและรักษาต่อด้วยความมั่นใจ*