Overview of Salicylate poisoning management in emergency department

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Abstract

Salicylate toxicity continues to be seen in the emergency department as a result of unintended consumptions or suicide efforts. A high index of suspicion is essential, with timely acknowledgment of clinical signs and symptoms of salicylate poisoning, such as ringing in the ears, hyperventilation, tachycardia, and metabolic acidosis. Early treatment can prevent organ damage and death. Principles of treatment include stabilizing the ABCs as required, limiting absorption, improving elimination, fixing metabolic problems, and offering encouraging care. No specific antidote is available for salicylates. Serial serum salicylate concentrations determination uses valuable information regarding the effectiveness of the treatment executed, assessment of these levels alone is not a substitute for clinical examination of the patient. When thinking about treatment options, the decision needs to be embellished inning accordance with the clinical status of the patient and must not depend just on a specific salicylate level. Optimum management of a salicylate poisoning depends upon whether the exposure is persistent or acute. Stomach lavage and activated charcoal work for acute ingestions however not for cases of chronic salicylism. Patients with persistent, instead of acute, consumptions of salicylates are more likely to develop toxicity, specifically of the CNS, and require intensive care.

Introduction

The term salicylate refers to any of a group of chemicals that are derived from salicylic acid. The very best known is acetylsalicylic acid (aspirin). Acetyl- salicylic acid is metabolized to salicylic acid (salicylate) after intake. The salicylates originally were derived from sailfin, the active ingredient in willow bark, which Hippocrates used 2500 years ago for dealing with pain and

fever [1,2]. Salicylates likewise take place naturally in numerous plants such as straw- berries, tomatoes, and almonds [3].

.Poisoning by aspirin is common and is under-represented in toxin center information, due to the fact that it is often not acknowledged [4-6]. If the diagnosis is made in the emergency situation department [the in-hospital mortality for unacknowledged chronic aspirin poisoning is reportedly three times higher than 7] Familiarity with the clinical presentation throughout the different phases of acute and chronic aspirin poisoning is necessary for the practice of emergency medication. The most challenging element of the clinical assessment and management of the aspirin-poisoned patient might be recognition of the subtle symptoms and signs of chronic, nonintentional aspirin overdose (table 1).

Epidemiology

Salicylate poisoning continues to be an essential overdose that often provides to emergency departments [8-10] .There were over 21,000 aspirin and non-aspirin salicylate direct exposures reported to the United States poison centers in 2004, with 43 deaths and 12,968 patients requiring healthcare facility treatment [11]. That figure is certainly an underestimate of the real occurrence of salicylate poisoning happen in the United States because toxin center data are gathered passively. One half of the reported direct exposures (10,786) were classified as intentional overdoses. The occurrence of chronic aspirin poisoning is unknown, but it is misdiagnosed regularly [12].

In recent years, product packaging methods such as child resistant packaging and decreasing the amount of medication in each plan of non-prescription analgesics have impacted the occurrence of poisoning. It is approximated that the use of child-resistant product packaging for salicylate-containing medications has led to a 34% reduction in the salicylate-related child mortality rate [13]. In England, Australia, and Ireland, analgesics are packaged and offered in percentages (ie, 4 g of acetaminophen). This has led to a 30% decline in the variety of patients needing liver hair transplant for acetaminophen-induced hepatic failure and a 22% reduction in self-destructive deaths from acetaminophen and salicylate [14]. Big aspirin overdoses were minimized by 39% usually in the countries where the limited plan formulation is required [14,15].

Pathophysiologic basis for poisoning

Salicylate is a metabolic toxin. Understanding the pathophysiology of its metabolic effects can assist to comprehend the clinical symptoms of toxicity. The metabolic derangements caused by salicylate poisoning are multifactorial, but the primary pathophysiologic mechanism in salicylate poisoning is interference with aerobic metabolism by means of uncoupling of mitochondrial oxidative phosphorylation [15a,16]. This results in the interruption of a series of enzyme-mediated mitochondrial functions and increased anaerobic metabolic process with cellular conversion of pyruvate to lactate and fast development of lactic acidosis [17,18]. The inefficiency of anaerobic metabolism leads to less energy being utilized to create ATP and release of the energy developed during the metabolic process of glucose in the electron transportation chain as heat, so salicylate poisoned patients may end up being febrile [19] .The absence of fever, however, does not rule out salicylate poisoning.

The acidosis is caused by anaerobic metabolism and the inability to buffer hydrogen ions, which is shown by the build-up of lactate. The existence of aceta salicylic acid or salicylate particles probably contributes little to the acidotic state [15a,20].

Disturbance with oxidative phosphorylation by salicylate likewise will affect glucose homeostasis negatively by causing glycogen depletion, gluconeogenesis, and catabolism of proteins and complimentary fats, the end result being low serum glucose levels and main nervous system (CNS) hypoglycemia relative to serum glucose levels [15a].

Absorption and metabolism of salicylate

The pharmacokinetic profile of aspirin is distinct and describes the special attributes of clinical poisoning. The ionization continuous (pKa) of aspirin is 3, which means that at a pH of 3, around half of the readily available chemical remains in the ionized state. In an acidic environment like the stomach, more of the drug will be absorbed compared with tissues at a higher pH [21] The absorption of aspirin from the stomach can be delayed by the existence of food in the stomach and the formula of the aspirin, (eg, enteric coating of pills may develop concretions and bezoars that limit available area for absorption) [22]. Aspirin is believed to trigger spasm of the pyloric sphincter, increasing gastric transit time and lengthening the time that aspirin is in the acidic

environment of the stomach, favoring increased absorption [21] .Salicylates also are soaked up easily in the unionized kind from the small intestine [23,24].

Dermal salicylate solutions generally do not result in tissue penetration much deeper than 3 to 4 mm in animal research studies [25,26] and human volunteer experiments [27] .Methyl salicylate has less dermal absorption than either camphor or menthol, with lower mean plasma levels and much shorter elimination half-life than either substance in people [28] Considerable amounts of salicylate typically are not taken in through the skin other than in select patients, such as children and patients with jeopardized skin such as burn patients or patients who have extreme psoriasis [29-31].

In therapeutic doses, the major path of salicylate biotransformation is conjugation with glycine in the liver. A percentage of aspirin is excreted the same in the urine [15a] .In overdose, the liver's ability to metabolize the drug is overwhelmed, and the same salicylate excretion through the kidney ends up being a far more crucial removal route.

Table 1

Pitfalls in the emergency department management of salicylate–poisoned patients
Failure to recognize the presence of salicylate toxicity
Failure to appreciate the presence of continued absorption of salicylate
Misinterpreting clinical significance of serum salicylate levels, because units of measure were unclear
Reliance on one or two serum levels of salicylate that may not describe a trend of decreasing total body burden of aspirin clearly
Misinterpretation of low serum salicylate levels as nontoxic and failure to comprehend the changing acid–base status of the patient

Waiting until serum salicylate levels are determined before beginning urinary alkalinization
Accidentally adding bicarbonate to isotonic saline (creating a hypertonic solution) rather than intravenous dextrose/water solutions to alkalinize the urine

Salicylate–induced acid-base changes

Respiratory alkalosis

Due to the fact that of direct stimulatory results on the respiratory centers of the cerebral medulla, salicylate toxicity initially will produce a pure breathing alkalosis. This is identified in the blood gas by a decrease in the partial pressure of liquified CO2 accompanied by a raised pH and typical to somewhat lower levels of serum HCO3 [32]. There is some controversy as to whether pediatric aspirin poisoned patients demonstrate this phase of acid-base derangement. Pediatric patients might present later on in the course of the poisoning, or the centrally moderated active ventilatory stage of aspirin poisoning might be so subtle in children that it often is missed [33-36].

Blended acid-base disturbances

As the poisoning advances and more of the aspirin is absorbed into the serum and is incorporated into the mitochondria, uncoupling oxidative phosphorylation, lactic acid builds up in the serum, and metabolic compensatory mechanisms are initiated [16] .Hyperventilation ends up being a real compensatory mechanism in addition to the by-product of central medullary stimulation [20] This stage is defined metabolically by an ongoing reduction in the pCO2, significant decrease in measured HCO3 and possibly a de- crease in serum pH, depending upon the capability of the patient to keep the respiratory demands of the establishing acidosis and to maintain bicarbonate in the kidney [37] .A common error at this stage of the poisoning is to acknowledge that the serum pH is close to 7.4 or slightly higher than 7.4, and presume that the patient is compensating sufficiently for the acidosis

Metabolic acidosis

As the capability to compensate for the acidosis is overwhelmed, pH drops; lactic acid collects, and serum bicarbonate is taken in. Patients who reach the stage of aspirin poisoning where pH is less than 7.4 with reduced pCO2 and low serum bicarbonate are alarmingly unstable, likely to decompensate hemodynamically and will begin to demonstrate other symptoms of end-organ injury [37].

Clinical presentation

Classic salicylism

The triad of salicylate poisoning includes hyperventilation, ringing in the ears, and gastrointestinal (GI) inflammation [38,39]. Physicians should remain conscious that patients may hyperventilate with a regular respiratory rate by increasing tidal volume (hyperpnea) and need to make it a routine to observe breathing patterns carefully. Ototoxicity is a well-described phenomenon with salicylism, and it is thought to be secondary to interference with chloride channels in the cochlear hair cells that send sound waves [40,41] .The ototoxicity is most visible in the variety of serum salicylate from 20 to 40 mg/dL [40,42] Aspirin, specifically enteric-coated solutions, are known to develop concretions and bezoars in the stomach and act as a direct GI irritant resulting in nausea, throwing up, and abdominal pain [22,43,44]

Early discussion

Patients who provide early in the course of salicylate poisoning might have modest symptoms, and the hyperventilation might be misinterpreted for emotional excitation or anxiety. GI inflammation may or might not be present, and tinnitus or other symptoms of ototoxicity may be ignored unless the physician specifically checks for them with direct questioning or confrontational hearing screening. Important signs might show psychological agitation and CNS stimulation with tachycardia, increased work of breathing (increased minute ventilation), and overall free up-regulation. Early in the course of acute poisoning, fever usually will be missing [39] Clinical symptoms will vary if the patient consumed more than one drug, or the ingested aspirin formulation consisted of a CNS depressant, which may blunt the anticipated hyperventilation and respiratory alkalosis [45]

Laboratory values early in the course of aspirin poisoning will be mostly normal or will reflect the direct stimulatory impact of salicylate on the cerebral respiratory. Serum aspirin levels might rise decently (20 to 40 mg/dL), and blood gas analysis might demonstrate pure respiratory alkalosis with raised pH and low pCO2 with near-normal or regular HCO3 [39] .The decision to determine serum salicylate concentrations is not difficult. Although serum salicylate levels might not be needed to evaluate every asymptomatic overdose, liberal use of the laboratory to make the diagnosis and follow resuscitative efforts is recommended [46-48].

Late presentation

As salicylate enters the mitochondria, significant modifications in vital indications and clinical stability take place. Serum salicylate levels alone are not adequate to accurately evaluate and follow seriously poisoned patients [49] .Serum salicylate levels do not reflect the total body burden of salicylate, and so to evaluate the quickly changing acid base status of an aspirin poisoned patient, serial salicylate levels ought to be accompanied by serial blood gas analysis [5] Patients who present in the late phases of salicylate toxicity often are misdiagnosed as sepsis [50], myocardial infarction [51], or as upset or otherwise psychiatrically disrupted [43,52,53].

Death from salicylism

The progression to death from salicylate poisoning is especially tumultuous. The poisonous effects of the salicylate particle on mitochondrial function and subsequent basement membrane leakage overwhelm the countervailing capacity of the organism. This leads to significant metabolic acidosis with advancement of cerebral and lung edema. Myocardial depression and hypotension secondary to the acidosis and volume deficit happen, and CNS anxiety with seizures secondary to hypoxia, hypoglycemia, and direct CNS toxicity typically precedes cardiopulmonary arrest [54].

In one study, almost half (45%) of the patients who passed away from salicylate poisoning got to the emergency department deteriorated and alert while there [55]. In another research study, 39% of the patients who had severe salicylate poisoning requiring ICU management showed up alert

with minimal symptoms [56] .Mean postmortem salicylate serum levels on 16 patients who presented dead on arrival after aspirin overdose were 51 mg/dL (variety 17 to 101 mg/dL) [55] Postmortem examination of salicylate-poisoned patients demonstrated a number of distinct findings consisting of myocardial necrosis suggestive of harmful myocarditis [57], lung blockage, hemorrhagic gastritis with unabsorbed salicylate and GI ulceration, cerebral edema, and paratonia (extreme muscle rigidness) [55,56].

Emergency situation department examination of the salicylate-poisoned patient

Done nomogram

The aspirin nomogram, commonly referred to as the Done nomogram, after its developer Done [58,59], was first released in 1960. Data from pediatric patients who ingested a one-time dosage of aspirin were plotted gradually to create an instrument to predict toxicity. A number of crucial limitations exist with regards to the advancement of the Done nomogram that restrict its generalizability, consisting of that patients who had polydrug consumption were consisted of in the analysis, making the clinical correlation hard to translate. In addition, the nomogram assumed an elimination .When serum levels go beyond the elimination enzyme systems [half-life of 20 hours in all patients and did not permit for the modification from first-order to zero-order removal kinetics that happens 60] Although ingenious and often precise for the intended (pediatric) population, the Done nomogram has been shown to have really minimal applicability and effectiveness for the majority of aspirin-poisoned patients, and its regular use is discouraged [49].

Table 2

Indications for hemodialysis in salicylated poisoned patients
Severe acidosis or hypotension refractory to optimal supportive care (regardless of absolute serum aspirin concentration)
Evidence of end-organ injury (ie, seizures, rhabdomyolysis, pulmonary edema)

Renal failure
High serum aspirin concentration (>100 mg/dL) despite relatively stable metabolic picture
Consider for patients who require endotracheal intubation unless that indication for mechanical ventilation is respiratory depression secondary to a coingestant.

Laboratory evaluation

Physicians needs to make liberal use of blood tests in the assessment of possibly aspirin-poisoned patients. Different clinical labs might report salicylate levels in various units of step (mg/dL versus mmol/L). Clinicians need to maintain consistent use of the particular systems of procedure to avoid confusion. Seriously aspirin-poisoned patients might show symptoms that enable an astute professional to carry out relative serial examinations and assess developing toxicity. Accurate acknowledgment of getting worse signs of toxicity, nevertheless, is an inexact science with unpredictable sensitivity and specificity, especially in the event of poly pharmaceutical intake or pediatric patients [45,61-63].Serum salicylate levels frequently do not show the se- verity of the poisoning. Depending on the time because consumption, presence of food in the stomach, coingestants, and presence of concretions, to name a few variables, symptoms may or may not correlate with serum salicylate levels. Symptomatic patients presumed of aspirin intake or salicylate poisoning need to have serial aspirin levels and blood gas analysis carried out till a clear pattern towards reducing (not plateau or decently increasing) levels and metabolic stability as explained by the blood gas exists.

Radiographic assessment of the aspirin poisoned patient is seldom useful, except for seriously ill patients who may have pulmonary edema or patients who have actually changed mental status that might need CT scanning of the head to remove the possibility of an alternative cause for an altered level of awareness. Big bezoars of ingested enteric-coated aspirin tablets might or might not be visible on a radiograph, and the lack of opacity on an abdominal radiograph is not sufficient to rule out the existence of a large quantity of salicylate in the gut [64].

Treatment of the salicylate-poisoned patient

Resuscitation

Depending upon the acuity of the poisoning and the existence of end-organ injury and hemodynamic instability, patients might need early, aggressive resuscitation and treatment. Since of fluid losses caused by increased respiration, fever, and metabolic activity [the majority of patients who have substantial aspirin overdose will be rather volume deficient 15a] Volume resus- citation with alkalinized intravenous fluids is sensible and recommended and ought to be initiated early in the course of the patient's treatment so that important time is not lost waiting on lab verification of elevated salicylate levels [65] .Begin by placing an adequate volume of sodium bicarbonate (3 ampules NaHCO3 with 44 mEq Naþ/ ampule) into a liter of a glucose-containing hypotonic service, such as 5% dextrose and water and infusing at 2 to 3 mL/kg per hour to promote brisk urine output. A total of 40 mEq of KCl per liter should be added to avoid hypokalemia.

Salicylate-poisoned patients who need innovative airway management are particularly difficult. Salicylate-intoxicated patients who have actually depressed mental status from the salicylate-induced cerebral hypoglycemia or acidosis or coingestants who require endotracheal intubation and mechanical ventilation present a clinical no-win situation for emergency situation physicians, since favorable pressure ventilation merely can not keep the respiratory rate and metabolic needs of seriously salicylate-poisoned patients. Hemodynamic instability and worsening of acid-base status will almost absolutely be the repercussion [66].Patients who require endotracheal intubation for airway defense and maintenance usually ought to be hemodialyzed concurrently to get rid of salicylate and the accumulated organic acids. Cautious attention to keeping a favorable acid--base status through the sensible control of ventilator settings should take place so as not to enable hypoventilation and the build-up of CO2.

Gastric decontamination

The unique characteristics of aspirin in the stomach make gastric decontamination especially troublesome. Gastric inflammation, induction of queasiness, and decreased psychological

alertness all combine to put the salicylate-poisoned patient at considerable danger for throwing up and goal from any effort at GI decontamination. Clinicians need to weigh the extremely genuine threat of goal versus the possible take advantage of any approach of gastric decontamination.

Triggered charcoal has actually been shown to be effective in decreasing the area under the curve for absorbed aspirin, and it is the most widely used method of stomach decontamination for salicylate-poisoned patients [67,68] .Multidose activated charcoal likewise has been revealed to minimize ab- sorption of aspirin and leads to reduced serum levels, but this has actually not equated into an enhanced morbidity or death rate [69]. Considered that multiple doses of activated charcoal are rather safe and normally well tolerated and seem to result in lower total body problem of aspirin, it is reasonable to suggest 25 g of activated charcoal without sorbitol offered orally every 3 hours while the patient is being kept an eye on with serial aspirin and blood gas measurements. Prior to each 25 g dose of triggered charcoal, bowel noises ought to be inspected, and if absent, the activated charcoal should not be kept.

Whole-bowel irrigation is not recommended in aspirin-poisoned patients, since there are little data to support its use in salicylate poisoning.

What information do exist do not demonstrate an improved outcome [70,71] Whole-bowel irrigation with balanced electrolyte services decreases gut transit time however might increase overall area available for absorption and perhaps cause increased serum levels of aspirin. It is generally inadequately tolerated and challenging to perform [70,71].

Stomach lavage mostly has been deserted in the management of poisoned patients with the possible exception of overdose with a lethal drug and early discussion of the patient in the course of the poisoning [72-74] Serious aspirin poisoning is certainly a life danger and given the distinct potential of enteric-coated aspirin to form concretions and remain in the stomach due to pylorospasm [22], it is reasonable to think about gastric lavage with a large-bore endogastric tube (36 French or larger) if substantial salicylate poisoning is presumed, and there is no possibility of air passage com- promise [74-76]

Enhanced elimination

Restoring intravascular volume and alkalinization of the serum and urine is a crucial first-line treatment for aceta salicylic acid toxicity. Bi-carbonate diuresis is the mainstay and first-line treatment for aspirin toxicity, and it should be started early in every case of moderate salicylate poisoning [65] .The (pKa) is a logarithmic function, so a small change in urine pH will have a disproportionately bigger impact on salicylate clearance, so in theory elimination of salicylic acid is increased considerably in alkaline urine [77] .The most practical technique of producing an isotonic alkaline option in the emergency department is to add sodium bicarbonate to 5% dextrose in water. In general, one 50 mL ampule of 40% sodium bicarbonate must include 43 mEq of salt. By putting 3 ampules (150 mL overall volume) of sodium bicarbonate into one liter of D5W, the resulting service should have 132 mEq of sodium, which is basically 0.9% (regular) saline [15a] An overall of 40 mEq of KCl per liter should be contributed to avoid hypokalemia. This option ought to be instilled quickly at a rate of at least 2 to 3 mL/kg/hour to preserve a brisk urine output of 1 to 2 mL/kg/hr. The boosted excretion of salicylate requires not simply raising the pH of the urine, but likewise increasing the glomerular filtering rate [65].

The development of cerebral or lung edema following salicylate poisoning is an essential consideration, however a concern for possibly triggering these complications should not lead to insufficient or ineffective urinary alkalinization or intravascular volume remediation. Patients who establish intensifying respiratory function with increased work of breathing and hypoxia consistent with pulmonary edema or who establish modified or reduced mental status consistent with cerebral edema should have their hydration and urinary alkalinization disrupted and be examined right away for conclusive treatment (hemodialysis).

Potassium replacement long has actually been an essential element of urinary alkalinization despite a paucity of clinical proof to support the regular practice [15a] .Chronic potassium deficiency causes increased reabsorption of bicarbonate in the proximal renal tubules and trouble attaining an alkaline urine. The impacts of acute potassium exhaustion on urinary excretion of bicarbonate are uncertain [78]. It seems affordable to infuse potassium and NaHCO3 concurrently, especially in patients who are already hypokalemic. Urinary alkalinization should be postponed while efforts are made to change the serum potassium [15a].

Hemodialysis is the conclusive treatment to prevent and treat salicylate- induced end-organ injury [79]. Indicators for dialysis are listed in **table 2**. Hemodialysis will eliminate aspirin in the serum and lactate efficiently [80] Patients may have metabolized their aspirin and have actually a low determined serum concentration of salicylate, however they still may gain from hemodialysis to eliminate the byproducts of mitochondrial poisoning. Charcoal hemoperfusion is not practical in a lot of scenarios [81], and hemodialysis has ended up being the preferred method of boosted elimination of excess serum salicylate.

• Conclusion

Aspirin brings both substantial negative impacts in therapeutic doses and a substantial danger in overdose, for which there is no antidote. Its risk-benefit profile is most likely the poorest of all analgesics currently available over the counter; this is shown in existing trends in analgesic usage and overdose figures [8] .Emergency situation doctors must have a healthy respect for the erratic and unforeseeable absorption and removal kinetics of aspirin, the disastrous physiologic results of aspirin overdose and the subtle manifestations, discussion, and increased death of persistent aspirin toxicity. Assessment with the regional poison nerve center is advised to assist with the management and follow-up of all poisoned patients.

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