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SALICYLATE POISONING – A SHORT REVIEW

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ABSTRACT

Salicylate poisoning remains a major clinical problem involving accidental ingestion in children and intentional/accidental overdose in adults. At times the diagnosis is not apparent, especially when aspirin is taken as part of a multi-drug ingestion. The presence of an unexplained acid-base abnormality may be the only clue in the individual. The objective of this review is to assist the hospital management of patients with a suspected exposure to salicylates by 1) describing the process by which evaluate an exposure to salicylates, 2) identifying the key factors in managing cases of salicylate exposure, and 3) providing clear and practical recommendations that reflect the current state of knowledge. Our review can suggests that evidence based guidelines that will guide clinicians and clinical pharmacist through the management of the patient in the casualty with acute and chronic salicylate poisoning.

INTRODUCTION

By 1829, Johann Buchner, professor of pharmacy at the University of Munich discovered a compound salicin in willow plants (Salix alba) that gave pain relief. In 1838, an Italian chemist was able convert salicin to an acid of crystallized, colorless needles, which he named salicylic acid. Since salicylic acid contains phenolic and carboxylic acid groups, it was irritating to the mouth, throat, and stomach. It was in 1899, that the Bayer Company in Germany patented the ester acetylsalicylic acid and marketed the product as “aspirin” . Their studies showed that this material was less of an irritant and the acetylsalicylic acid hydrolyzed in the small intestine to salicylic acid, which was then absorbed into the bloodstream. In 1899, a German chemist named Felix Hoffmann, who worked for a German company called Bayer, rediscovered Gerhardt's formula. Felix Hoffmann made some of the formula and gave it to his father who was suffering from the pain of arthritis, with good results. Felix Hoffmann then convinced Bayer to market the new wonder drug. Aspirin was patented on February 27, 1900. The folks at Bayer came up with the name Aspirin, it comes from the 'A" in acetyl chloride, the "spir" in spiraea ulmaria (the plant they derived the salicylic acid from) and the 'in' was a then familiar name ending for medicines. Aspirin was first sold as a powder. In 1915, the first Aspirin tablets were made. Interestingly, Aspirin ® was once a trademark belonging to Bayer. [1] There are several forms of salicylate are available for use as tablets, powders, and suppositories in the market. In addition to regular aspirin, it is also formulated as an enteric-coated tablet intended for dissolution in the small intestine. Dermal preparations of Salicylates may be absorbed and cause systemic toxicity. (Table 1.)

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EPIDEMIOLOGY

In US 2004, there were 2.4 million cases of human poisoning reported to the Poison Control Centers. Analgesics were the most frequently used products containing salicylates accounted for greater than 20,000 exposures and more than 10% of deaths occurred. In England, 10% of adult hospital admissions for deliberate

self-poisonings. Many common medical and psychiatric presentations result of undiagnosed aspirin poisoning. Thus, the data may underestimate the true incidence of aspirin poisoning. [2-5]. The objective of this review is to assist the hospital management of patients with a suspected exposure to salicylates by 1) describing the process by which evaluate an exposure to salicylates, 2) identifying the key factors in managing cases of salicylate exposure, and 3) providing clear and practical recommendations that reflect the current state of knowledge.

Table 1. Physical and Chemical Properties of Salicylic Acid [6-8]

Physical characteristics	Needles with water and monoclinic prisms with alcohol
Molecular formula	$C_7H_6O_3$
Molecular weight	138.12
Boiling point	211◦C (20 mm Hg); Sublimes at 76◦C
Melting point	158–161◦C
Solubility	Soluble in acetone, Oil of turpentine, Alcohol, Ether, Benzene; Slightly soluble in water
Octanol/Water partition coefficient (log P)	2.25
Refractive index	1.565
Density	1.443
pH of saturated aqueous solution	2.4
Flash point	315◦F
Stability	Emits acrid smoke and irritating fumes when heated to decomposition
Reactivity	Incompatible with iron salts, spirit nitrous ether, lead acetate, and iodine; colored reddish by ferric salts
Autoignition temperature	1013◦F

TOXICOKINETICS

Salicylates are rapidly and completely absorbed in the stomach, and to a slightly lesser extent from the small intestine, but distributed unevenly throughout body tissues after oral use. Delayed absorption is seen in the following conditions : Enteric coated pills, Pylorospasm, Pyloric stenosis, and benzoar formation.

Metabolism follows first-order kinetics (dose dependent) to form oxidized and conjugated metabolites. Metabolism occurs chiefly are broken down into salicyluric acid, ether glucuronide , ester glucuronide, and gentisic acid. Renal clearance accounts for most of the compound's elimination and is enhanced from 2% to more than 80% as pH, and ionization, increase.

DIAGNOSIS [10]

I] Laboratory findings

a) Anion-gap acidosis
b) Hypokalaemia (acidosis may mask it)
c) Hypocalcaemia
d) Hypoglycaemia

II] Bed side tests

a) Ferric chloride test: Add a few drops of 10% ferric chloride solution to 1mL of urine. A purple colour indicates the presence of salicylates. However, it is not conclusive, since a positive result is also obtained in phenol, phenothiazines, phenylbutazone and oxyphenbutazone

b) Trinder's test

i) Reagent : Trinder's reagent is used which is obtained by mixing 40gm of mercuric chloride with 120ml of aqueous HCL solution and 40gm of hydrated ferric nitrate, followed by dilution to 1 litre with purified water.

ii) Method: The test can be done on urine, stomach contents or scene residue. Add 0.1mL of trinder's reagent to 2mL of sample and mix for 5 seconds. A strong violet colour indicates the presence of salicylates.

III) Confirmatory test

To estimate the serum salicylate level. Unfortunately, the seriousness of poisoning correlates poorly with serum levels. Previously the done nomogram was highly recommended to correlate serum salicylate level with the degree of intoxification at varying intervals after acute ingestion of aspirin. But there are severe limitations to its use and is now not generally considered to be reliable. Studies have indicated that it has poor predictive value.

FATAL DOSE [10]

Salicylic acid – 70 to 80gm
Sodium Salicylate – 15 to 20gm

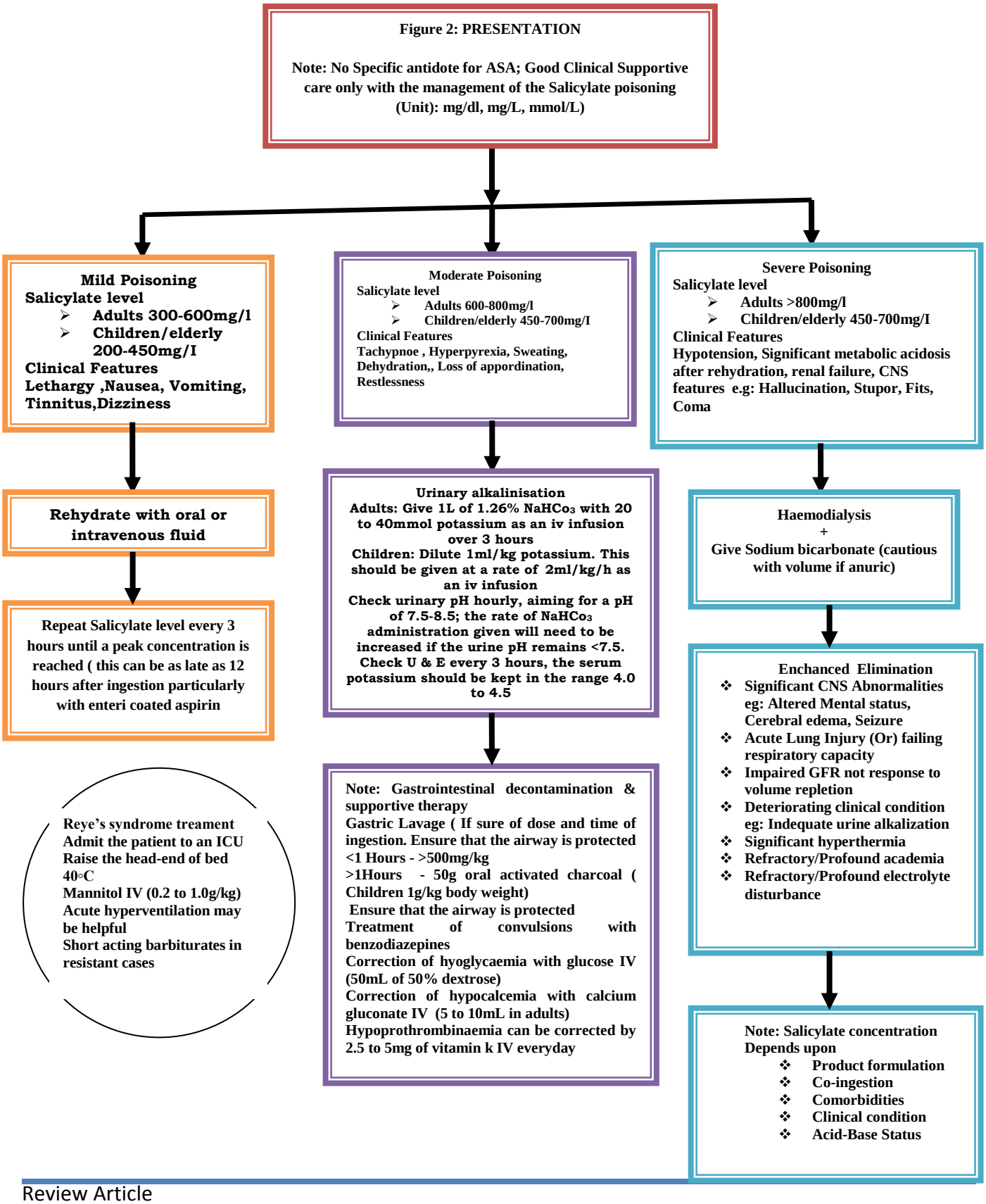
CLINICAL FEATURES [9]

System effects	Exposure	
	Acute	**Chronic**
Gastro intestinal	Vomiting, Abdominal Pain,	Ulceration, Pylorospasm and decreased GI tract motility can occur with large doses, Hemorrhage and inflammation
Lung	Pulmonary edema alkalosis, Hyperventilation due to respiratory	Dyspnoea, Nausea,
CNS	Depression, delirium, Lethargic, No papillary reaction**.**	Cerebral edema, Confusion, Comatose,no pupilary reaction, Agitation, Disorientation, Slurred Speech, Hallucinations, Convulsion and Hyperthermia
Liver	Hepatic failure	Reye syndrome: hypoglycemia, elevated levels of liver enzymes, fatty infiltration of liver, and coma
Hemostatic	Decreased clotting time (Hypoprothrombinemia and platelet dysfunction are the most common effects)	Increased bleeding time
Renal	Urinary ketones, Acute renal failure	Diabetes ketoacidosis
Musculoskeletal effects	Rhabdomyolysis can occur because of dissipation of heat and energy resulting from oxidative phosphorylation uncoupling	Rhabdomyolysis- the destruction or degeneration of skeletal muscle tissue that is accompanied by the release of muscle cell contents (as myoglobin and potassium) into the bloodstream resulting in hypovolemia, hyperkalemia, and sometimes acute renal failure

PATHOLOGY AND MECHANISM OF ASA TOXICITY [11]

Mechanism of toxicity	Pathological Consequences	Metabolic Compensation	Signs and Symptoms
Elevated ASA serum concentration (acidic Substance)	Decreases serum pH	Contributes to metabolic acidosis: alters platelet function	Increase bleeding time
Stimulation of medullary respiratory center	Hyperventilation	Decreases plasma PCO_2 with respiratory alkalosis	Tachypnea, pulmonary edema, tachycardia, dehydration
Renal compensation for respiratory alkalosis	Kidneys excrete more bicarbonate ions: retain more hydrogen ions	Contributes to compensatory metabolic acidosis: CNS toxicity	Irritability, restlessness, tinnitus, dehydration, seizures,coma
Inhibition of Kreb's cycle enzymes	Accumulation of organic acids (oxaloacetate)	Contributes to metabolic acidosis and lactic acidosis	Gastric irritation, nausea ,vomiting
Oxidative uncoupling of electron transport chain	Prevents combination of phosphate with ADP Increases peripheral demand for glucose	Decrease formation of ATP, enchanced glycolysis, lactic acid, Pyruvic acid: contributes to metabolic acidosis Stimulates lipidmetabolism, releases fatty acids, contributes tometabolic acidosis	Hyperthermia, tachycardia, dehydration, cardiovascular collapse, hypoglycemia

FIGURE 1. MANAGEMENT OF SALICYLATE TOXICITY [12]



CONCLUSION

Our review can suggests that evidence based guidelines that will guide clinicians and clinical pharmacist through the management of the patient to the casualty with acute and chronic exposure of salicylate poisoning.

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