

Letter to the Editor

Plasma Salicylate Levels in Surgical Patients During the Postoperative Period

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Lysine acetylsalicylate, a soluble salt of acetylsalicylic acid (aspirin) for intravenous use, is frequently given as an analgesic during the postoperative period. Advantages of the intravenous form include its greater systemic availability in comparison with oral formulations of aspirin, and better tolerance, because passage through the stomach is avoided.

In the bloodstream aspirin is hydrolysed to salicylate by non-specific enzymes called esterases in the blood and liver (Williams et al 1989). Some authors have noted that surgical stress and anaesthetic agents alter the kinetics of drugs in patients during the postoperative period (Vessell & Biebuyck 1984; Wood 1991). In addition, aspirin esterase activity was found to decrease during the same period (Puche et al 1993). We designed the current study to determine concentrations of salicylate after a bolus dose of lysine acetylsalicylate, which is frequently used as an analgesic during this period.

The study group comprised eight surgical inpatients (men and women, 49 ± 13 years, 78 ± 10 kg, mean \pm s.d.) admitted to Surgical Service B of the University of Granada Hospital for cholecystectomy. None of the patients had evidence of liver or kidney disease, alcoholism, collagenosis, obesity or cholinesterase-related anomalies. Allergy to salicylates was ruled out and none of the patients had received aspirin or similar compounds for at least 15 days before the study. None of the patients had post-surgical complications. The control group consisted of six healthy volunteers (men and women, 26 ± 3 years, 73 ± 6 kg, mean \pm s.d.). All participants gave their informed consent to participate in the study, which was approved by the hospital's ethics committee. All patients were operated on under general

anaesthesia (fluothane) with assisted breathing, and were discharged between 7 and 10 days later.

A sample (1 mL) of blood was obtained for determination of basal plasma salicylate concentration and a bolus of lysine acetylsalicylate (Dolomega, Almirall-Omega; 7 mg kg^{-1}) was then given intravenously. Samples (1 mL) of blood were then taken via endovenous catheter in the contralateral arm after 5, 7.5, 10, 15, 30, 45, 60, 90, and 120 min. In patients the assay was performed 48 h after surgery, during the period of post-injury reaction (Cuthbertson 1980). All blood samples were collected between 0900 and 1300 h and were transferred to assay tubes containing 2 mM physostigmine to avoid spontaneous hydrolysis of the lysine acetylsalicylate. The tubes were centrifuged immediately and plasma (0.4 mL) was stored at -20°C until analysis. Plasma salicylate was determined in duplicate with an automatic micro-method (TDX Analyser, Abbott Instruments) and the results were expressed as mg L^{-1} . The intra- and inter-analysis variability of the method was $< 5\%$. The area under the curve (AUC) from 5–120 min was calculated with the trapezoidal and Simpson's rules. Differences were investigated with Student's *t*-test for independent samples, with a level of significance of $P < 0.05$.

It is apparent from Figure 1 that plasma salicylate levels were lower in surgical patients than in healthy controls. Differences first appeared 5 min after administration of lysine acetylsalicylate, and remained evident for a further 40 min. After 45 min plasma salicylate concentrations were similar in the two groups. The AUC from 0–120 min was $3672 \pm 728 \text{ mg L min}^{-1}$ for the control group and $770 \pm 318 \text{ mg L min}^{-1}$ for patients ($P < 0.001$).

During the first 45 min blood levels of salicylate after a single intravenous bolus dose of lysine acetylsalicylate (7 mg kg^{-1}) were clearly lower in healthy controls than in patients who underwent uncomplicated cholecystectomy. This might have been because of the decrease in plasma esterase

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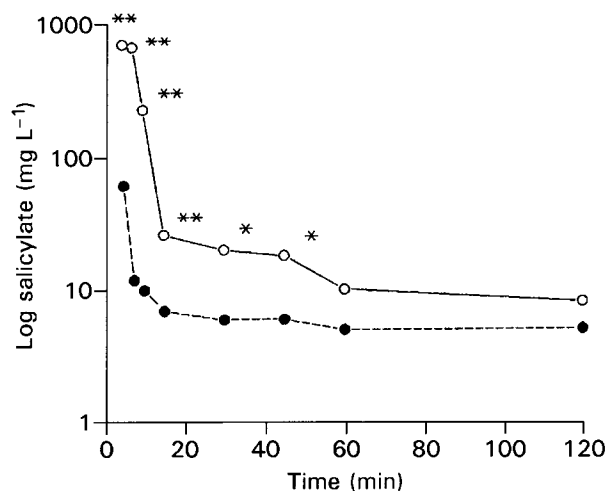


Figure 1. Plasma levels of salicylate in ○ healthy control subjects and ● surgical patients after administration of an intravenous bolus of lysine acetylsalicylate (7 mg kg^{-1}). * $P < 0.05$, ** $P < 0.001$, significantly different from controls.

activity in surgical patients during the postoperative period. In an earlier study we found postoperative decreases of as much as 20% in the activity of plasma aspirin esterase and cholinesterase, two enzymes involved in the hydrolysis of aspirin to salicylate in the bloodstream (Puche et al 1993). Another factor that might contribute to the decrease in plasma salicylate concentration and the AUC in the group of surgical patients is haemodilution as a result of water retention induced by postoperative cortisol and antidiuretic hormone secretion, and by the decrease in renal filtration and excretion. These changes form part of the post-injury reaction induced by surgery (Cuthbertson 1980).

Because of the evidence of the relationship between salicylate concentration and analgesic response (Seymour et al 1984), our findings are of interest because the postoperative decrease in salicylaemia might impair analgesia. Because salicylates are cheap and affective, further studies should be directed toward determining the optimum dose in surgical patients, because a decrease in circulating drug levels during the postoperative period might be further complicated by individual variations in response to the drug.

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