THE EFFECT OF ASPIRIN ON REBLEEDING IN TRAUMATIC HYPHEMA*

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ASPIRIN HAS OFTEN BEEN USED AS AN ORAL ANALGESIC IN THE MANAGEMENT OF pain associated with traumatic hyphema. However, aspirin has an inhibitory effect on the blood clotting mechanism by its action on platelets. Therefore, it would be contraindicated in a disease process depending on clot formation for resolution. Newell warned about the prolonged bleeding time following ingestion of aspirin and suggested that we forgo its use in patients who were to have intraocular surgery.[1] Stuart's studies showed that aspirin inhibited collagen-induced platelet aggregation in doses of 300 mg or more per day.[2] This effect began as early as 15 minutes after the first dose of aspirin. Rebleeding is a serious hazard in traumatic hyphema. Secondary haemorrhages frequently occur after total or partial clearing of the initial hyphema. The reason for rebleeding is not known but it is possible that the clot in the initially torn vessel is lysed before permanent closure occurs. If platelet aggregation is diminished by aspirin, a new plug is not formed and the bleeding continues to fill the anterior chamber. Smith and Christensen have shown that systemic administration of aspirin in therapeutic doses substantially reduced fibrinolytic activity in the aqueous of the rabbit.[3] There is no evidence that this occurs in humans. However if it does, there is a balance between the platelet system and the fibrinolytic system and aspirin has a much greater effect on the platelet system.

To determine whether aspirin administration increased the chance of rebleeding, we undertook a retrospective study of patients treated with aspirin and those treated without.

MATERIALS AND METHODS

The records of 127 patients with traumatic hyphema admitted to The Hospital for Sick Children from January 1, 1970, to December 31, 1973,

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inclusive were reviewed. From March 1, 1974, to February 28, 1975, the use of aspirin was forbidden for patients admitted with hyphema. A further 28 patients were studied, two of which received aspirin before

TABLE I: ASPIRIN ADMINISTRATION AND THE INCIDENCE OF REBLEEDING IN TRAUMATIC HYPHEMA

Grade	Aspirin Number of Patients	No Aspirin Number of Patients
I		
Rebleed	7*	4*
No Bebleed	10	67
Total	17	71
II		
Rebleed	2	0
No Rebleed	6	19
Total	8	19
III		
Rebleed	3	0
No Rebleed	3	6
Total	6	6

*Rebleeds with aspirin 41%. Rebleeds without aspirin 6%. Significant to $p \leq 0.01$.
Total Rebleeds with aspirin in Grades I, II & III = 39%.
Total Rebleeds without aspirin in Grades I, II & III = 4%.

TABLE II: ASPIRIN ADMINISTRATION AND THE INCIDENCE OF REBLEEDING IN TRAUMATIC HYPHEMA

Grade	Aspirin Number of Patients	No Aspirin Number of Patients
I		
Rebleed	0	1
No Rebleed	0	13
Total	0	14
II		
Rebleed	0	0
No Rebleed	0	4
Total	0	4
III		
Rebleed	2	2
No Rebleed	0	6
Total	2	8

Total Rebleeds in Grade I = 7%.
Total Rebleeds with aspirin in Grades I, II & III = 100% (patients received aspirin before admission).
Total Rebleeds without aspirin in Grades I, II & III = 11.5%.

admission. The degree of hyphema was stated as Grade I, if bleeding was microscopic or filled less than one-third of the anterior chamber; Grade II, if bleeding filled one-third to one-half the anterior chamber; and Grade III, if bleeding filled more than half the anterior chamber. Patients in each grade were assigned to one of four groups: (1) Those who had received aspirin, (2) those who had not, (3) those in whom rebleeding occurred, and (4) those in whom it did not. The groups were then compared and the results analyzed by chi square, Fischer, and Tocher statistical techniques.

RESULTS

The results of these analyses for the retrospective part of the study are shown in Table I. The incidence of rebleeding in patients with Grade I hyphema was significantly increased by the administration of aspirin. The number of patients in each group with Grades II and III hyphema were too small to allow satisfactory testing by chi square. Therefore, Fischer and Tocher analyses were performed for Grade II and III hyphema. The differences were not significant. Results for the prospective part of the study are shown in Table II. Since the use of aspirin has been forbidden in patients admitted with hyphema, the trend is towards fewer rebleeds, however, as this is only for a 12 month period, the numbers are too small to be statistically significant.

DISCUSSION

Aspirin apparently tends to increase the incidence of rebleeding in traumatic hyphema. In the natural history of a hyphema the platelets aggregate to form plugs in the ends of the ruptured blood vessels. A clot then forms and eventually retracts and absorbs. Aspirin inhibits platelet aggregation and thus interferes with clotting.[4-10] Platelets adhere to one another in the presence of adenosine diphosphate. The initial aggregation is reversible, but later it becomes irreversible because endogenous adenosine diphosphate is released from the platelets themselves. Aspirin inhibits the release of endogenous adenosine diphosphate preventing platelet aggregation and plug formation thus prolonging the bleeding time.[4,5-7] As little as five grains of aspirin can produce this defect which persists for as long as four to seven days after salicylate has been cleared from the blood, a period corresponding to the life span of the platelet.[6,7]

In patients with traumatic hyphema where the previous history of aspirin ingestion is uncertain, platelet aggregation and bleeding time should be checked, and if diminished, a platelet transfusion may be considered. Salicylate levels in the blood are only detected if the patient is on large doses of aspirin. One five grain tablet would barely give a detectable level.

SUMMARY

Because rebleeding in hyphema carries a serious risk of permanent damage to the eyes, aspirin should not be used as an analgesic. Tempra, Tylenol, Demerol, and codeine are more suitable analgesics for this condition.

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DISCUSSION

Dr Frank W. Newell. Drs. Crawford, Lewandowski, and Chan provide interesting evidence that interference with platelet adhesiveness with the use of aspirin is associated with a much higher incidence of rebleeding than is seen in patients who do not receive aspirin. They studied a group of 127 patients with hyphema of all degrees of severity varying from a microscopic amount of blood to hyphema filling more than one-half of the anterior chamber. Thirty-one of these patients received aspirin and twelve had rebleeding into the

anterior chamber. Ninety-six did not receive aspirin and rebleeding was observed in four patients. I believe the data adequate to conclude that aspirin should not be used to control pain in traumatic hyphema. Smith and Christensen showed significantly (89%) increased prolongation of the time required for lysis of a fibrin clot in the anterior chamber in aspirin treated animals. Balancing this is the recent report (*Am J Ophthalmol* 79:817-819, 1975) indicating that aspirin prevents breakdown of the blood aqueous barrier that normally occurs with opening the anterior chamber.

Platelet adhesiveness may be affected by oral administration of as little as 5 or 10 grains of aspirin in an adult and the result may persist for several days. This action may be desirable in individuals who do not have traumatic hyphema for the risk of myocardial infarction is about a fifth among those taking aspirin compared to those who do not. Additionally, it may have a favorable influence on diabetic retinopathy.

Aspirin may well be the most widely used drug in the world. Some 20 million pounds were used in the United States in 1972 — some 150 grains per person per year. An incomplete listing indicates that over 200 commercial compounds contain aspirin as one of its ingredients. The compound has widespread pharmacologic effects and an old joke holds that if introduced today as a new drug our current knowledge of its actions would not permit Food and Drug Administration approval. Its usual pharmacologic actions include antipyresis, analgesia, increased labyrinthine pressure, respiratory alkalosis followed by metabolic acidosis, vasodilation, gastric ulceration, decreased platelet adhesiveness, inhibition of prostaglandin synthesis, and increased effectiveness of epinephrine, corticosteroids, and thyroid hormones.

These widespread pharmacologic effects indicate some of the precautions necessary in prescribing aspirin and other salicylates. They should not be used in patients receiving oral anticoagulants or patients with gout receiving urisonics. There is an increased incidence of salicylate-induced bleeding in ethyl alcohol users. There is increased para-amino salicylic acid toxicity and an increased hypoglycemic effect of oral antidiabetic agents. Toxic salicylate effects may occur in patients who use large amounts of vitamin C and salicylic acid — two common drugs available without prescription. Corticosteroids increase the kidney excretion of salicylates and a dosage of salicylates tolerated while receiving corticosteroids may cause toxicity when the corticosteroids are discontinued. Additionally, salicylates are contraindicated with heparin and methotrexate. Finally, salicylates interfere with a variety of laboratory results: decreased protein bound iodine, decreased triiodothyronine uptake, and decreased urinary excretion of phenosulonphthalien. False positive tests also may occur: uric acid, 5-hydroxyindolacetic acid (5-HIAA) and urinary vanilmandelic acid (VMA).

I appreciate Dr. Crawford's scholarship and clinical awareness in bringing our attention to this important problem and appreciate, too, his courtesy in providing me with a copy of this paper so well in advance of the meeting.

Thank you.

DR DAVID SHOCH. I would like to congratulate Doctor Crawford on his study. There are so few studies done to evaluate the numbers of drugs that we use on the basis of hearsay, anecdotal evidence, etc. In this light I should like to tell you of a drug avoidance program we started about a year ago. At that time we had a patient for cataract surgery who was oversedated. She snored a little bit, and then at a crucial moment in the surgery sat up. All went well eventually but it was very disturbing to the surgeon and to the assistant to say the least. We decided that we really did not understand why people were given preoperative sedation for surgery under local anesthesia when all of us performed various kinds of out-patient surgery with no premedication at all. So about a year ago we stopped giving any premedication at all to patients who were to have surgery under local anesthesia. This was either the night before or the morning of surgery. The patients are told that they would receive no premedication but if they felt apprehensive in the operating room they would get a tranquilizer intravenously. In this past year one apprehensive patient asked for sedation and we gave him one mg of diazepam intravenously in surgery. No other patients have received any medication, and we have had not a single untoward incident in the operating room or during the usual postoperative hospital stay of 48 hours. I make a plea that one think perhaps about some of the drugs we use without sufficient evidence. I think papers like Doctor Crawford's will help us a great deal to restrict the use of drugs without a specific indication for them. Thank you.

DR JOHN CRAWFORD. I would like to thank the discussers. Doctor Newell's discussion added a lot and he outlined how many other drugs contain aspirin. Doctor Shoch also brought up a point that I didn't mention and that is that dentists give aspirin to patients after dental extractions. Otolaryngologists also use aspirin after tonsillectomy. This may be in the form of Aspergum. I feel as Doctor Shoch does that we must be cautious of drug side effects. Thank you very much.