

## UNDER USE OF ASPIRIN IN ACUTE CORONARY SYNDROMES

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From simple pain relief to clot buster, it is an amazing success story of Aspirin the miracle drug of 21st century which continues to surprise the healthcare professionals with its ever increasing indications. Aspirin's first appearance in the market in 1899 was a low key affair. It entered the world with a whisper than a bang but has now emerged as a pharmaceutical superstar.<sup>1</sup> It is estimated that so far over twenty five thousand scientific papers have been published on Aspirin. On an average a scientific paper is published on aspirin every two hours. Lancet in its editorial in 1998 called it a poor man's statin.<sup>2</sup> It was a great tribute to this drug which has completed a century in clinical practice. So far over a trillion tablets of aspirin have been consumed. In fact discovery of Aspirin is considered as one of the most amazing creations in medical history. Its analgesic and antipyretic properties were well known but the pioneering work regarding its use in cardiovascular diseases was done by a Scottish physician Peter Elwood.<sup>3</sup> Soluble aspirin was formally introduced on 20<sup>th</sup> November 1948 at London Medical Exhibition.<sup>1</sup> Over the years numerous studies have now confirmed its safety and efficacy in not only primary and secondary prevention of heart attacks but also in stroke, deep vein thrombosis, bowel, lung, breast cancer, cataract, migraine, infertility, Alzheimer's disease and herpes. The list is now increasing with the every passing day as more and more indications are being identified by the investigators.<sup>1,4-9</sup> It is by far the most extensively studied and researched drug.

ISIS-2 (Second International Infarct Survival Study)<sup>10</sup> has provided strong evidence about the benefits offered by Aspirin as an anti-thrombotic agent in the treatment of acute myocardial infarction but Aspirin still remains underused. In 1996 it was found that nearly 50% of myocardial infarction patients in United States did not take aspirin. Two years later only 45% of myocardial infarction patients at teaching hospitals in United States were given Aspirin and less than 25% within thirty minutes of admission when the drug is considered most effective.<sup>1</sup>

A study conducted in Pakistan in 2002 showed that only 10.5% of patients experiencing chest pain took aspirin on their own at home while 23.4% of them were prescribed Aspirin by their GPs. Local hospitals administered aspirin to 7.5% while 70.5% took Aspirin within six hours after reaching hospital and 76.5% of patients admitted in the NICVD were receiving Aspirin therapy.<sup>11</sup>

A more recent study showed that out of fifty two patients with chest pain that were identified only 13 patients (25%) received aspirin. Reason given for not administering aspirin to other 39 patients included chest pain was not felt to be cardiac in thirteen (33%), ten patients (26%) had already taken aspirin on that day, the medical provider was a basic level emergency medical technician who could not administer aspirin to six patients (15%), pain subsided prior to arrival of emergency medical services in three patients. The investigators concluded that the most common reason that paramedics did not administer aspirin was their belief that the chest pain was not of a cardiac nature while the other common reason being their inability to administer aspirin.<sup>12</sup>

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Now billions of people around the world are taking aspirin to ward off heart and artery disease. The FDA has approved the use of aspirin to reduce the risk of:<sup>13</sup>

- \* Heart attack in people who have stable angina, predictable chest pain due to impaired blood flow to the heart.
- \* Death in people having heart attack.
- \* Second heart attack in people who have already suffered a heart attack or have unstable angina, chest pain caused by unpredictable impairment of blood flow.
- \* Second stroke in people who have already had one ischemic stroke because of blockage in blood vessel which supplies to brain or those experiencing transient ischemic attack (TIAs).

Though the situation appears to have improved a bit but scientists still worry that the message was not getting through and many people are still dying needlessly because they are not taking the drug when they should. Realizing this situation, some conscious healthcare professionals all over the world formed Aspirin Foundations to promote the use of aspirin in its well established indications. Pakistan Aspirin Foundation was founded in 1997 with similar aims and objectives.<sup>14</sup> Since then, it has been holding continuing medical education programmes for healthcare professionals as well as educating the public in the use of aspirin. It also published a book "Aspirin- the life saving miracle drug"<sup>15</sup> in 2001 besides distributing thousands of copies of its revised, updated Consensus Report on Medical Uses of Aspirin which covers its indications, dosage and contraindications in detail.

*AAUS Study:* Pakistan Aspirin Foundation conducted a study which was named Aspirin Awareness and Usage Study (AAUS) to find out about the use and awareness of Aspirin in Acute Coronary Syndromes presenting for admission at hospitals and coronary care units, pattern of prescribing aspirin and other cardiovascular drugs at discharge from hospitals, by family physicians or the patient on their own initiative. Male and female patients of all age groups suffering from coronary artery

disease, acute coronary syndrome, and unstable angina, acute myocardial infarction both STEMI and NSTEMI were included. Patients with known bleeding disorders, those suffering from peptic ulcer disease, hypersensitivity to aspirin, pregnant women after 36 weeks of gestation and those with known G6PD deficiency were excluded. To begin with twenty five centers all over the country were identified but only seventeen participated. Findings of this study were presented at a seminar organized by Pakistan Aspirin Foundation at Gujranwala and Gujrat<sup>16</sup> on May 6, 2006.

This is the first study of its kind done in Pakistan which enrolled patients admitted to tertiary cardiac care facilities in big cities as well as coronary care units at various district hospitals all over the country (Table-I).

In all 1527 Proformas were received but only 1400 were complete enough for inclusion in the final evaluation as those with incomplete information were excluded. Dr. Maqbool H. Jafary finalized the study protocol while Prof.

Table-I: Participating centers and co-investigators for AAUS study (Aspirin Awareness and Usage Study)

*Chief investigator:* Prof. Abdus Samad, Executive Director Karachi Institute of Heart Diseases, Karachi. Pakistan.

1. Prof. M Akbar Chaudhry	Fatima Jinnah Medical College Ganga Ram Hospital, Lahore.
2. Major Gen. Ashur Khan	Hearts International Hospital, Rawalpindi.
3. Dr. Sohail Tufail	Dist. Headquarters Hospital. Sialkot.
4. Dr. Fazlur Rehman	Red Crescent Hospital, Hyderabad.
5. Prof. Nazir Memon	Liaquat University Hospital, Hyderabad.
6. Dr. Akram Sultan	CCU Civil Hospital, Mirpur Khas. Sindh.
7. Prof. M. Sarwar	Doctor's Hospital, Lahore.
8. Prof. M. Ishaq	NICVD, Karachi.
9. Dr. Saeed Sangi	CCU Civil Hospital, Larkana
10. Prof. Javed Akram	KEMC/Mayo Hospital, Lahore.
11. Dr. Shafique Ahmad	CCU BV Hospital, Bahawalpur.
12. Prof. Ejaz Ahmad Vohra	Ziauddin University Hospital, Karachi.
13. Prof. Afzal Mattu	PIMS, Islamabad.
14. Major Gen. M. H. Nuri	AFIC-NIHD, Rawalpindi.
15. Prof. Mansoor Ahmad	Liaquat National Hospital, Karachi.
16. Dr. Javed Iqbal	CCU, Dist. Hqr. Hospital, Faisalabad.
17. Dr. Waqar Mufti	Ayub Med College Hospital Abbottabad.

Abdus Samad was the chief investigator. Out of this 1400, five hundred sixty eight patients (41%) were STEMI and only 226 patients (16%) were NSTEMI. Six hundred six (43%) patients were suffering from unstable angina. The patients enrolled included 68.1% males and 31.9% females. The presenting symptoms as revealed in this study were chest pain in 1299 patients (91.1%) shortness of breath 602 patients (42.3%) and syncope 187 patients (6.1%) The mean age of patients was  $52.2 \pm 10.7$  years which is almost a decade earlier than seen in the West.

The most startling disclosure in the study was that majority of the heart attack patients reach hospitals after a mean of  $13.2 \pm 6.2$  hours delay after the onset of symptoms. This means that the time for thrombolytic therapy to be of any use is already over. Only 50% of patients suffering from acute coronary syndrome were prescribed aspirin at the time of discharge from hospitals. While 71.7% patients were given Aspirin in wards only 59.9% of patients reaching the emergency room were given aspirin. About 20.8% of patients were prescribed aspirin therapy by the family physicians and only 16% took aspirin at home when they suffered from chest pain. Out of these 1400 patients, four hundred forty four (31.2%) were taking aspirin before the onset of symptoms. Findings of this study also showed that incidence of myocardial infarction has also increased in women to over 30% as against previously reported figures of 10-15%.<sup>17</sup>

*Adverse Reactions:* Only forty four patients (3.1%) had adverse reactions which included allergic reactions 0.9%, G.I. bleeding 2.1% and others 1.1% which are quite negligible proving once again the safety and efficacy of this wonder drug.

*Risk Factors:* Major risk factors which contributed to acute coronary syndromes were family history of hypertension 51.8%, smoking 51.3%, hypertension 54.3%, family history of IHD 43.9% and family history of hyperlipidemias 54.3%. Other risk factors included family history of diabetes 35.6%, IHD 38.2%, diabetes mellitus 37.2% and hyperlipidemias

18%. Only 3% of the patients enrolled in the study died, 17% were referred for investigations and 13% were stable with symptoms.

The mere fact that only 50% of these patients were prescribed Aspirin therapy at the time of discharge and only 71.7% of patients in Wards got aspirin therapy is quite surprising. Most of these patients (except those where it was contra indicated) should have been given aspirin along with other prescribed drugs. Similarly most of the patients should have been given aspirin as soon as they reported in the emergency room. Again only 20.8% of family physicians prescribed aspirin therapy which shows that educational programmes for the doctors on medical uses of aspirin needs to be further intensified. Despite the fact that aspirin is a safe and effective household medication for acute coronary syndromes, its use in Pakistan is still far less than optimal goal and major time delays still occur on the part of the patients to reach hospitals after the onset of symptoms like chest pain and shortness of breath. Since over 91% of patients presented with chest pain and shortness of breath was the other major symptoms in 42.3% of patients, it is not at all difficult to diagnose these patients suffering from AMI at the family physicians level where if aspirin therapy is administered within six hours, it can save many precious lives.

The problem with poor countries, Pakistan being no exception, is that majority of their population cannot afford expensive drugs and they do not use economically priced drugs either. Moreover, the patient's psychology who thinks only expensive drugs is the best and more effective, is also responsible for under use and under-prescription of aspirin. Despite the commendable work being done by Pakistan Aspirin Foundation to create awareness and promote the use of Aspirin, it appears the message has not yet reached to the public. The healthcare professionals having been sensitized about the safety and efficacy of this wonderful drug, its optimal usage can only be ensured if the public at large is educated and convinced of its safety and efficacy so that when the

doctor prescribes aspirin, it is not taken lightly by the patients since it is an economically priced drug. In fact its low price is a major drawback, had it been an expensive drug, its acceptance by the patients would have been much better.

It is however heartening to note that as compared to the earlier study<sup>11</sup> in the present AAUS study more patients took aspirin at home immediately after suspected chest pain 16% as against 10.5%, more family physicians prescribed aspirin to such patients 23.4% as against 20.8% and more patients visiting a local hospital 59.9% as against 7.5% were prescribed aspirin. This proves the fact that the message being communicated by Pakistan Aspirin Foundation regarding use of aspirin is spreading but the pace is still slow.

This study also highlighted some other important aspects as regards conduction of scientific studies in Pakistan. Although at the investigators meetings, they were briefed in detail how to fill in the proformas but still, some of the proformas with incomplete information had to be excluded. This shows that they did not take it seriously. Some centers identified initially, later did not participate in the study since it had no incentives for them. At the same time since some healthcare facilities are in the habit of thinking too big, hence the people working their, did not show much interest to participate in this study

The findings of AAUS study has once again showed that we still need to do a lot as regards conveying the simple message among the healthcare professionals as well as public that in case of chest pain, irrespective of the fact whether it is cardiac in nature or not, single tablet of soluble aspirin or chewing of one tablet aspirin of 325mg can prove life saving. One tablet of aspirin can be given immediately at home even before the patient is taken to a family physician or a hospital. It also needs to be emphasized that every effort should be made to ensure that patients with chest pain reach the nearest healthcare facility as early as possible. Every patient with suspected chest pain on reaching emergency room should be

given aspirin therapy immediately. All acute coronary syndrome patients on discharge should be prescribed aspirin unless a clear cut contraindication exists. Long term use of low dose aspirin therapy is extremely safe, effective and could go a long way in reducing morbidity and mortality.

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