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Original Article

USE OF ASPIRIN IN ACUTE CORONARY SYNDROME IN A TERTIARY CARE HOSPITAL IN KARACHI

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ABSTRACT:

Background: Large body of scientific evidence exists that use of Aspirin in acute myocardial infarction and other subsets of coronary heart disease significantly reduces morbidity and mortality. Aspirin has proved a life saving medication if taken in the early hours of myocardial infarction. This study was conducted to find out the awareness and actual use of Aspirin in patients with acute chest pain due to AMI and other acute coronary syndromes.

Design: Randomized prospective study.

Setting: National Institute of Cardiovascular Diseases (NICVD) Karachi, Pakistan.

Patients and Methods: Two hundred consecutive patients admitted to NICVD with the history of recent onset acute chest pain suggestive of myocardial ischemia/infarction. A questionnaire regarding the time of onset of chest pain, time interval of chest pain and use of Aspirin (chewed or swallowed), cause of chest pain, first consultation, use of any other remedy, risk factors, financial status, use of different types of fat, profession, family members and counseling about use of Aspirin were asked by the first author.

Results: The study included 200 patients, 150 males (75%) and 50 females (25%). 25 (12.5%) of patients, 21 (10.5%) males and 4 (2%) females were between the age of 31-40 years, 59 (29.5%), males 41 (20.5%), females 18 (9%) were in 41-50 years, while 65 (32.5%), males 50 (25%) and females 15 (7.5%) were between the age of 51-60 years. 75 (37.5%) were labourers. 191 (95.5%) belonged to lower socio-economic group with income of < Rs.10,000/- per month. Majority 129 (64.5%) were illiterate or had primary education. 141 (70.5%) of patients took Aspirin within 6 hours. 21 (10.5%) used Aspirin at home. Although 47 (23.5%) patients first consulted a GP only 11 (23.4%) were given Aspirin. 15 (7.5%) got Aspirin at local hospital and 153 (76.5%) in NICVD. 102 (51%) patients came to NICVD directly. 77 (38.5%) got thrombolytic therapy. Pepsi (or cold drink), analgesics, syrup mucain, other digestives and Bam were the other drugs and substances first used after chest pain. Stress, Hypertension, smoking, hyperlipidemia, family history, obesity and diabetes mellitus were the important risk factors. 39 (19.5%) received counseling regarding benefits of Aspirin therapy.

Conclusion: Despite compelling evidence regarding the known benefits, awareness about use of Aspirin among general physicians and community hospitals is highly unsatisfactory. Health Care Professionals need to be educated besides creating awareness among the public about the benefits of Aspirin therapy, using all available resources including the mass media.

KEY WORDS: Aspirin, Acute Myocardial Infarction, Acute Coronary Syndrome, Awareness.

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INTRODUCTION

Aspirin, which in the year 2001 completed 100 years of its use in medical practice, continues to amaze us all with the ever-increasing indications of its use. From simple pain relief to clot buster it is an amazing success story of Aspirin that can be rightly considered as one of the greatest discoveries in the field of medicine during the 19th century. It is also called wonder drug of 20th century.

Salicylates, in the form of willow bark, were used as an analgesic during the Hippocrates era. However its antipyretic effect was recognized for more than 200 years.[1] Aspirin was

introduced in the late 1890s[2] and it has been used to treat anti-inflammatory conditions. The antiplatelet activity of this agent was recognized about 70 years later.[3]

A Scottish physician, Prof. Peter Elwood, undertook the pioneering work about its use in cardiovascular disease. He published the first report on the value of Aspirin in the treatment of myocardial infarction in 1974.[4] So far over 145 randomized controlled trial on Aspirin in vascular diseases have been reported in medical press.[5] It is ironic that despite tremendous supporting data, the awareness among the healthcare professionals at large about the use of Aspirin in the prevention of life threatening conditions like IHD, MI and stroke is still very poor. This applies to the developed but more so in the developing countries.

This study was conducted to find out the use of Aspirin in acute coronary ischemic events by the patients themselves or as advised by the physician or local health care facility where they first reported after chest pain suspecting of Myocardial Infarction (MI). MI is defined according to the European guidelines for the diagnosis and management of acute coronary syndrome[6]. The mode of aspirin taken and other drugs or remedies taken by the patients themselves was also studied.

PATIENTS AND METHODS

Two hundred consecutive patients who presented with acute onset of chest pain and were hospitalized in the National Institute of Cardiovascular Diseases (NICVD) at Karachi were studied. There was no exclusion as regard to age or sex of the patients. A proforma was designed which contained 23 questions regarding education, profession, financial status, use of fat, time of chest pain, time and first drug/ remedy taken, first consultation. The proforma also included questions regarding aspirin whether taken on their initiative or advised to do so, whether chewed or swallowed, any counseling done. Data was also collected regarding the administration of thrombolytic therapy, first or recurrent attack, risk factors and possible cause of chest pain. The questions and the responses were handled by the first author.

RESULTS

The study included 200 patients, 150 (75%) males and 50 (25%) females. Their age distribution is given in table-I. Majority (62%) of the patients were between 31-40 years (29.5%) and 41-50 years (32.5%). Table-II shows their educational status. Majority (64.5%) were either illiterate (47%) or had primary education (17.5%), while 20% had secondary education. Queries about financial status (table-III) revealed that 46 (23%) of patients had income of less than Rs.2000/= per month, 66 (33%) had between

Table-I: Age of Patients (n = 200)

	Male		*Female*	
Years	*No. of Patients*	*Percentage*	*No. of Patients*	*Percentage*
31-40	21	10.5	4	2
41-50	41	20.5	18	9
51-60	50	25	15	7.5
61-70	20	10	8	4
> 70	18	9	5	2.5
Total	150	(75)	50	(25)

Table-II: Educaitonal Status (n = 200)

Education	*No. of Patients*	*Percentage*
Illiterate	94	47
Primary	35	17.5
Secondary	40	20
College	23	11.5
Graduation	8	4

Table-III: Financial Status (n = 200)

Financial Status (Rs)	*No. of Patients*	*Percentage*
< 2000/=	46	23
2-5000/=	66	33
5-10000/=	79	39.5
> 10000/=	9	4.5

Rs.2-5000/=, 79 (39.5%) had between Rs.5-10,000/= and 9 (4.5%) had income greater than Rs.10,000/= per month. As regard their profession 75 (37.5%) were labourers, 44 (22%) were housewives and 35 (17%) were office workers (Table-IV). Patients's total number of children ranged from 0 - 12 with a mean number of children of 5.74.

Information solicited regarding use of various types of fat showed that 90 (45%), 46 (23%) and 4 (2%) respectively used oil, Dalda Ghee and Desi Ghee exclusively while the remaining used all these interchangably (Table V). After the onset of chest pain 39 (19.5%) patients opted to take some measures in an attempt to reduce the pain. These measures were 4 (2%) patients took cold drink e.g. (Pepsi) as first drug/remedy, 13 (6.5%) used some analgesic, 9 (4.5%) used antacid syrup mucain or other digestives, 4 (8%) applied Bam, 9 (4.5%) were administered unidentified injection (table-VI). 29 (14.5%) used sub-lingual nitrate and 132 (66%) took aspirin in combination with sub-lingual nitrate either themselves or on advice of the GP/ family physician, at local healthcare facility or at the NICVD. After the onset of chest pain 47 (23%) first consulted the General Practitioner, 51 (25.5%) went to the local hospital and 102 (51%) came to the NICVD (Table-VII). 21 (10.5%) had taken aspirin at home while 11 (5.5%) were advised to take aspirin by the GP/Family Physician, 15 (7.5%) got aspirin at local hospital and majority 153 (76.5%) were given aspirin when they arrived at NICVD (Table-VIII) 141 (70.5%) of patients took aspirin within 6 hours, 48 (24%) had it within 6 – 24 hours while 11 (5.5%) got aspirin after 24 hours (Table-IX). 28 (14%) used aspirin by themselves in which 3 (10.7%) chewed the aspirin tablet and 25 (89.3%) swallowed it while 172 (86%) had taken aspirin on advise in which 135 (78%) chewed and 37 (21.5%) swallowed it (Figure 1).

Table-IV: Profession of Patients
(n = 200)

Profession	*No. of Patients*	*Percentage*
Labourers	75	37.5
House Wives	44	22
Office Workers	35	17.5
Business	18	9.0
Drivers	11	5.5
Medical personnel	7	3.5
Teachers	7	3.5
Actors	2	1.0
Imam Masjid	1	0.5

Table-V: Use of Fat
(n = 200)

Fat	*No. of Patients*	*Percentage*
Oil	90	45
Dalda Ghee	46	23
Desi Ghee	4	2
Oil + Dalda Ghee	57	28.5
Oil + Dalda Ghee + Desi Ghee	3	1.5

Table-VI: First measure taken after chest pain
(n = 200)

Drug/substance	*No. of Patients*	*Percentage*
Pepsi (Cold drink)	4	2
Analgesics	13	6.5
Mucain etc. (Antacid)	9	4.5
Bam	4	8
Unidentified Injections	9	4.5

Table-VII: First Consultation
(n = 200)

Place	*No. of Patients*	*Percentage*
GP	47	23.5
Local Hospital	51	25.5
NICVD	102	51

Seventy-seven (38.5%) patients who reached NICVD within six hours after the onset of chest pain and had no contraindication were administered thrombolytic therapy. 39 (19.5%) of patients had counseling about aspirin therapy. Major risk factors (Table-X) included stress 132 (66%), hypertension 130 (65%), smoking 118 (59%), hyperlipidemia 64 (32%), sedentary life style 60 (30%), positive family history 59 (29.5%), obesity 53 (26.5%) and diabetes mellitus 51 (25.5%). Cause of chest pain (Table-XI) revealed chronic stable angina 4 (2%), Acute coronary syndrome 77 (38.5%), ST Elevation MI in 101 (50.5%), Non ST Elevation MI 18 (9%) and others (IHD, cardiomyopathy) 37 (17.5%).

Table-VIII: Place where Aspirin was first taken
(n = 200)

Place	*No. of Patients*	*Percentage*
Home	21	10.5
GP	11	5.5
Local Hospital	15	7.5
NICVD	153	76.5

Table-IX: Time interval between Aspirin intake and onset of chest pain
(n = 200)

Time (hour)	*No. of Patients*	*Percentage*
< 1	46	23
1 - 2	46	23
3 - 4	34	17
5 - 6	15	7.5
7 - 12	28	14
13 - 24	20	10
> 24	11	5.5

Table-X: Risk Factor
(n = 200)

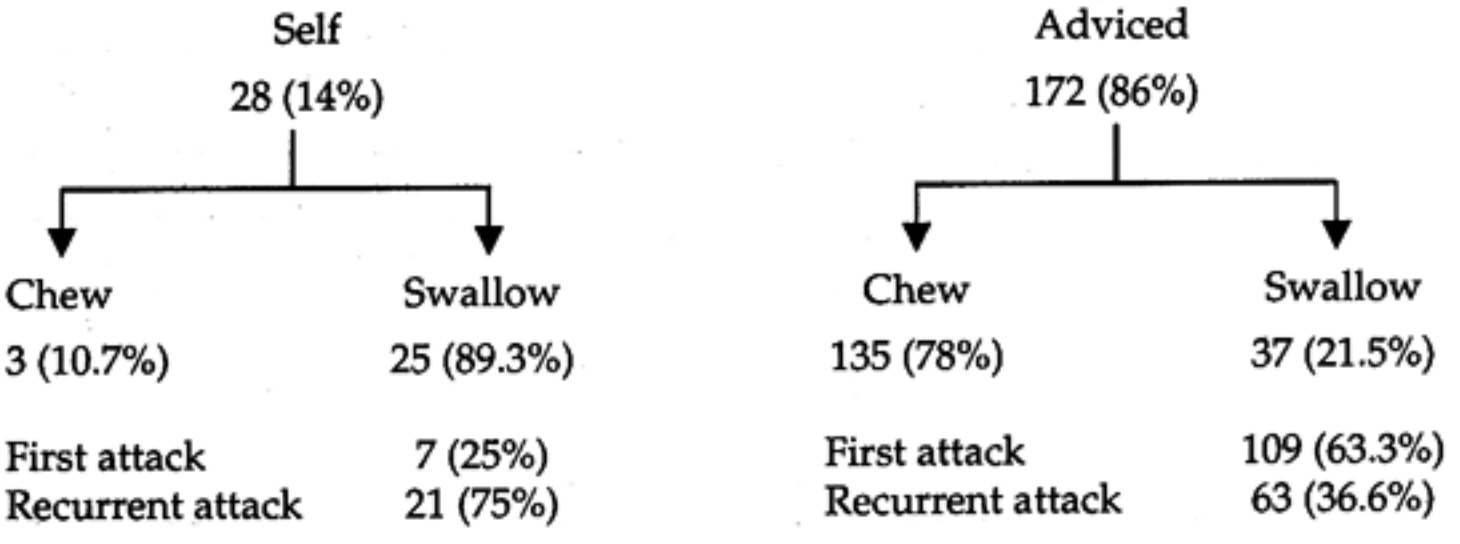
Risk Factor	*No. of Patients*	*Percentage*
Stress	132	66
Hypertension	130	65
Smoking	118	59
Hyper lipidemia	64	32
Sedentary life style	60	30
Family History	59	29.5
Obesity	53	26.5
DM	51	25.5

Table-XI: Cause of Chest Pain
(n = 200)

Cause	*No. of Patients*	*Percentage*
Chronic stable angina	4	2
Acute Coronary Syndrome	77	38.5
ST Elevation MI	101	50.5
Non ST Elevation MI	18	9
Other (IHD, cardiomyopathy)	37	17.5

Figure: 1

Mode of administration of Aspirin
(n = 200)



DISCUSSION

Our study shows that only a small percentage of the patients 10.5% took aspirin on their own initiative, a further 5.5% on the advise of the family physician and another 7.5% as advised by local hospitals. This reflects a very poor awarness on the part of patients, their GPs and local hospital. It is also a fact that inspite of enormous data available about the efficacy and safety of aspirin in acute coronary ischemic events, studies elsewhere also suggest that aspirin still remains underused for the treatment of acute coronary syndromes[7,8] and for secondary prevention of recurrent events[9,10,11]. According to some reports more than 10% of patients suffering an AMI do not receive aspirin therapy despite the absence of contraindications,[7] and 20 - 50% of post infarction patients may not be taking aspirin on an ongoing basis[9,10]. These statistics are even worse in the elderly population: almost 30% of medicare patients hospitalized for unstable angina are not treated with aspirin in the short term,[8] and as many as 80% of nursing home patients with a prior history of MI may not be given aspirin[11]. A more recent report has showed that only 37% patients who have cardiovascular disease and only 13% with risk factors for cardiovascular disease use aspirin regularly.[12]

The review of the data about Aspirin shows overwhelming evidence about the benefits of this drug. The landmark trial ISIS-2 has provided strong evidence for the survival benefit offered by the use of aspirin as an antithrombotic agent in the acute treatment of myocardial infarction. In this study 17187 patients presenting within 24 hours of onset of suspected acute MI were randomized to receive intravenous Streptokinase (SK), 162.5 mg of aspirin daily for 30 days, both or neither. At the end of 5 weeks, patients receiving aspirin therapy alone had 23% reduction in vascular mortality and nearly 50% reduction in the risk of non-fatal reinfarction and non-fatal stroke, which were highly significant.[13] There was no increase in major bleeding complications with aspirin therapy and the mortality benefit was maintained after 10 years of follow-up.[14] Six large randomized trials used aspirin alone as long term treatment after an AMI.[4,15,16,17,18,19] Out of these five showed trend towards a decrease in mortality. In a meta analysis performed by the Anti-platelet Trialists Collaboration[5], therapy with Aspirin was shown to be highly effective.

Studies have also shown that subjects who took aspirin on every recommended day experienced a 51% reduction in vascular events whereas those who took aspirin on less that half the days recommended showed only a 17% reduction.[20] Moreover an MI, which occurred in a patient taking aspirin, is likely to be of the small non-Q wave variety[21] which is quite significant.

In 1998, FDA of USA advised that individuals experiencing symptoms of heart attack should immediately take Aspirin. Taken within 24 hours, it results in 23% reduction in mortality.[22]

Aspirin is well established in the primary prevention of coronary events in the high risk individuals.[23,24] and low dose aspirin 75 mg daily each reduced the incidence of major episodes by about 20% over a median period of 6.8 years.[25]

There is no significant heterogeneity in the effect of aspirin in males and females, with and without an association with diabetes, or of different ages. At the fifteenth European Aspirin Foundation Scientific Meeting[26], Gerry Fowkes, Professor of Epidemiologist and Head of Public Sciences, the University of Edinburgh proposed that the concept that aspirin may be useful in secondary but not primary prevention is misleading. Categorizing people as 'primary' or 'secondary' is to do so on past events. He opined that it is more appropriate to divide people according to their risk of future event. Male smokers who are hypertensive and hypercholesterolaemic are obviously at higher risk than those without these risk factors, and whether or not they have had a previous event is a minor part of the clinical decision to prescribe aspirin.[26]

Early aspirin (at least 325 mg soluble aspirin)

in the acute stage of myocardial infarction is now standard practice, even when the patient has already been taking 100 mg aspirin a day. However, even now some doctors' bag do not contain soluble aspirin, and only 10.5% of patients in our study had taken aspirin before reaching the hospital. The plasma half-life of aspirin is only about 30 minutes; so fresh platelets can only be acetylated by an added dose of aspirin, and not by aspirin taken that morning.[26]

The occurrence of myocardial infarction peaks between about 4:00 and 10:00 hours coinciding with an increased sensitivity of platelets to aggregating agents.[27] If is also of interest that in the US Physicians Trial it was found that the reduction in myocardial infarction by aspirin was significantly greater during the early morning (59%) than during the rest of the day (34%)[20]. Mortality during and immediately affer infarction is high and rapidly decreases with time. The earlier aspirin is given, the greater the savings in death and disability are likely to be. Furthermore in view of the fact that almost half of all deaths due to myocardial infarction occur before professional help arrives, the patients should be encouraged to take aspirin immediately on appearance of symptoms.[26]

In the present study 150 (75%) of patients were males and 50 (25%) were females, similar to an earlier study[28] in which 81.1% of patients were male and 18.8% were females. This also confirms that Acute Myocardial Infarction (AMI) is more common in men as compared to women. While 12.5% of patient in the present study were between the ages of 31-40 years, earlier study[28] showed similar pattern where in 11% of patient were between 20-39 years of age. This also confirms that AMI is now seen at a much younger age in 30's in Pakistan, which indeed is alarming. In the earlier study[28] 99.04% patients who reached NICVD got aspirin whereas in the present study also almost everyone with chest pain reaching NICVD got Aspirin. This shows that aspirin therapy is standard practice for all patients reporting in Emergency Room at NICVD. However out of 47 (23.5%) patients who first consulted a GP, only 11 (23.4%) were given aspirin. Fifty-one (25.5%) of patients visited a local healthcare facility of which again only 15 (7.5%) were given aspirin while 21 (10.5%) patients took aspirin at home. Twenty-eight (14%) patients took aspirin at their own, of which only 3 patients chewed the aspirin tablet while 25 swallowed it (Figure-1). This shows that awareness about the usefulness and life-saving properties of aspirin in AMI is not satisfactory between the GP and family Physicians as well as in general public. That is why only a fraction of patients who consulted them soon after acute chest pain were advised to take aspirin.

Another significant finding is this study was that 172 (86%) of patients who were advised to take aspirin, 63 (36.6%) had recurrent attack (Figure-1), since they were not counseled properly about aspirin therapy.

While in the earlier study[28] 17.03% of patients got thrombolytic therapy (Streptokinase), in the present study 38.5% of patients were administered thrombolytic therapy which is a significant improvement during the last few years.

In the present study 102 (51%) of patients after the onset of acute chest pain felt that perhaps it was cardiac in nature, hence they reached directly at the NICVD (Table VII) where they got aspirin immediately. This also shows that due to increased awareness about heart disease among the urban population almost 50% of patients after the onset of acute chest pain rushed to the Emergency Room (ER) of NICVD.

Yet another interesting finding of this study was that 75% of patients were using oil of which 45% were using oil exclusively. Still about 50% of patients use vegetable ghee or banaspati in addition to use of oil (Table-V).

Only 39 (19.5%) of patients had some counseling either in the hospital or through the GPs or by other means about the use of aspirin, which is highly unsatisfactory. It is generally felt that used in a large number of diseases, aspirin has become the victim of its own success. The cost benefit of aspirin prophylaxis is so well established and so attractive that further placebo-controlled trials in vascular disease are neither acceptable nor necessary. However, concern has been expressed that despite convincing

evidence of its effectiveness, the knowledge of benefits of aspirin and its use by doctors is much less than desired. As such every thing possible needs to be done to promote aspirin prophylaxis in appropriate subjects and to achieve a high level of compliance in tablet taking.[29]

In Pakistan, Pakistan Aspirin Foundation established in 1997 has been working hard to promote the medical uses of aspirin in various indications. During the last 4 years, seminars on medical uses of aspirin were organized in many cities all over Pakistan. It also published a Consensus Report on Medical Uses of Aspirin, which was revised and updated in December 2001.[30] Its copies have been distributed freely among the health care professionals. Yet another important accomplishment of Pakistan Aspirin Foundation has been the publication of a book recently.[31] Aspirin considered to be a statin for the poor, particularly offers tremendous benefits in developing countries since it is not only economically priced but also easily available everywhere.

CONCLUSION

Despite its well established role, safety and efficacy in acute coronary ischemic events in general and life saving properties in AMI, aspirin remains still underused in most of developing countries, although situation is not much better in the developed world either. There is need to use all possible means to promote the use of aspirin in its well-established indications including AMI where taken immediately after the onset of chest pain, it can save precious lives. There is also need to have standard treatment protocol for most common diseases including management of AMI, which should be vigorously promoted and practiced in all health care facilities besides educating the GPs and family physicians.

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