

LETTER TO THE EDITOR

A METHOD TO EVALUATE ASPIRIN ANALGESIA IN MAN

Sir,

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Pain is a very complex phenomenon subject to many determinants. Numerous methods have been described to assess the threshold for pain in man and the effect of drug on it. Each method has its drawbacks.

Experimental pain can be produced in human being by different methods, mechanical, chemical, electrical and ischaemic. The intraperitoneal injection of bradykinin (2) in human subjects is a drastic procedure for routine screening purposes. The exposed blister base is quite suitable for detecting pain producing substances but is less useful for the screening of potent analgesic drugs (2). The thermal method is applicable only to centrally acting analgesics. The more powerful an analgesic, longer the time interval before pain is felt. Mechanical methods are of no value for the screening of analgesics that antagonize pain producing substances. The electrical stimulation to tooth pulp or through metallic filling is suitable for both peripherally and centrally acting analgesics. This method may frighten the individual and produce stress. The submaximum effect-tourniquet technique for inducing experimental pain has been tried only for narcotic analgesics (3).

A need was felt for screening non-narcotic analgesics which are useful in moderate type of pain originating from somatic tissues. The present method demonstrates the effect of non-narcotic analgesics on pain threshold in volunteers. Over years it has yielded consistent and satisfactory results when compared with placebo. A typical double blind study conducted in 25 female volunteers using technique is described below.

Twenty five female volunteers in age group 17-23 years agreed to participate in the trial. They were informed about the experimental procedure and type of pricking pain they would feel and to signal by raising the index finger at the onset of pain. The experiments were conducted between 9-12 a.m. after they had taken light breakfast around 8.00 a.m. Precaution was observed that they did not take any drug for 4 days before the experiment. Menstrual history and state of the menstrual cycle at the time of conducting the experiments were recorded. The pain threshold to the mechanical stimulus was determined by using a metallic cap of aerated water-bottle and sphygmomanometer. The cuff was tied over the cap after placing it with its serrated edge on the flexor surface of the fore-arm midway between the wrist and the elbow of the subjects. The same site and side were employed in subsequent experiments. Sphygmomanometer was kept in such a way that the subjects were unable to see the mercury column. Pressure was increased in a step wise manner each time by 4 mm of Hg leaving it at each level for 5 sec till the subject experienced pricking pain. The onset of pricking pain was determined three times at an interval of 10 minutes before and after the drug administration and the average of this was taken as an indication of pain threshold and expressed as mm of mercury.

Pain threshold was determined before, one and two hr after administration of 300 mg aspirin or placebo in a coded manner. The whole procedure was repeated 7 days later, the volunteer who received aspirin receiving placebo and vice versa. The results were tabulated and percentage increase in pain threshold was calculated. The maximum effect (at 1 or 2 hr) was taken into consideration instead of pooling all the observations. The observations were statistically analysed using Student's "t" test.

It will be seen (Table I) that aspirin significantly increased the pain threshold ( $36.12\% \pm 1.2\%$  compared to  $4.27 \pm 0.49\%$  increased by placebo).

TABLE I : Mean pain threshold to mechanical stimulus in female volunteers after administration of aspirin placebo.

Age in yrs.	Mean pain threshold in mm of Hg. $\pm$ S.E.					
	Aspirin			Placebo		
	Before	After	% $\uparrow$	Before	After	% $\uparrow$
17-23	85.89	117.95	36.12*	82.19	85.60	4.27
n-25	$\pm 1.61$	$\pm 0.9$	$\pm 1.2$	$\pm 1.2$	$\pm 0.82$	$\pm 0.49$

\*P < 0.01 n=Number of volunteers.

One of the important features of this method is lack of restraint. Restraint can alter the sensitivity to pain (1). The method described a very simple and the subject does not experience fright or stress.

The pain threshold of the individual was found to be fairly stable after repeated determinations. A single individual can serve as its own control in the assessment of an analgesic. The pain threshold was found to vary from one individual to another and during phases of menstrual cycle and the method could detect the same.

A consideration of the method and the results obtained indicate that this method is suitable for producing an objectively quantifiable, reproducible and ethically acceptable mechanical pain model. The method besides being simple, has the advantage that a single person can conduct it without being biased.

S. RAO AND A. Q. SAIFI

*Department of Pharmacology,  
Gandhi Medical College, Bhopal - 462 001*

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