The Influence of Mefenamic Acid on Renal Function in the Normal Male Adult

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MEFENAMIC acid* is a new analgetic, antipyretic and antiinflammatory agent, chemically designated N-(2,3-xylyl)-anthranilic acid.[1] A double blind study has indicated that PONSTEL appears less liable than aspirin to cause gastrointestinal bleeding.[2]

In previous studies of mefenamic acid, slight elevations of blood urea nitrogen (BUN) have been noted. For many individuals the BUN[3] has remained within the acceptance range (9–22 mg %) but has shown an increase over pretreatment values. The purpose of the present study was to determine the influence which mefenamic acid exerts upon renal function, as measured by the phenosulfonphthalein (PSP) and creatinine clearance tests.

Methods and Procedures

Twenty healthy male volunteers were selected from the inmates of the State Prison of Southern Michigan, Jackson. Their ages ranged from 23 to 50.

Ten subjects were given mefenamic acid, 2000 mg/day (in four equal doses) for a period of 28 days. Ten control subjects received placebo. The dose of mefenamic acid was deliberately chosen to be in excess of the recommended dose of 500 mg STAT and 250 mg, q 6 hours (equivalent to 1250 mg the first day and 1000 mg/day thereafter).

PSP tests[4,5] and creatinine clearance tests[6,7] were performed three times prior to medication to establish a baseline for the individual subject. PSP tests were again done two and 16 days after the last day of medication and creatinine clearance measured one and 15 days after medication.

Complete urinalyses, including microscopic examination, were performed three times prior to drug and one and 15 days post-drug.

Results

Of the twenty subjects, nineteen completed the study. Subject number 20, receiving placebo, was hospitalized on day 13 for appendicitis.

All subjects demonstrated normal tubular excretory function, as measured by the PSP test (Tables I and II). Although all subjects were given water prior to the test, one subject in each group was unable to void at the fifteen-minute period. This was evident on one occasion prior to drug and again after medication had ended. Other isolated occurrences of low dye excretion at the fifteen-minute in-

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TABLE I

Results in Normal Male Volunteers Receiving Mefenamic Acid, 2000 mg/day for 28 Days

Parameter	Acceptance Range	Study Day	Treatment Group Receiving CI-473, 500 mg., q.i.d., for 28 days — Subject No. 1	3	5	7	9	11	13	15	17	19
PSP		PreRx	31	19*	16*	28	32	35	37	37	38	38
% in 15 min.	25% or more	PreRx	27	38	42	40	36	40	—	31	34	37
		PreRx	20*	42	43	38	34	39	42	41	32	29
		30	18*	36	36	27	39	38	—	30	38	43
		44	26	44	35	21*	34	48	—	31	39	36
% in 2 hrs.	65% or more	PreRx	70	77	70	70	85	88	89	91	92	90
		PreRx	65	90	86	81	89	101	81	90	89	84
		PreRx	70	101	87	85	90	98	79	96	85	80
		30	75	95	73	71	94	96	75	73	91	93
		44	78	85	74	65	87	95	76	79	89	89
Creatinine clearance	70-150 ml/min/ 1.73 m^2 body surface	PreRx	103	103	129	99	58*	140	128	80	132	112
		PreRx	94	124	122	84	87	116	66*	81	110	121
		PreRx	66*	89	124	66*	77	105	105	75	96	111
		29	69*	119	143	37*	78	128	104	77	70	97
		43	65*	94	132	36*	88	114	100	61*	120	97
BUN	9-22 mg/100 ml	PreRx	9	14	16	14	15	13	12	14	18	11
		PreRx	9	17	19	13	13	14	12	13	18	11
		PreRx	16	17	13	17	15	10	12	14	20	11
		29	21	29*	19	20	18	17	19	16	24*	17
		43	17	19	13	14	15	13	14	15	17	11

* = outside acceptance range.
— = no sample obtained.

TABLE II

Results in Normal Male Volunteers Receiving Placebo for 28 Days

Parameter	Acceptance Range	Study Day	Treatment Group Receiving Placebo, q.i.d. for 28 days — Subject No. 2	4	6	8	10	12	14	16	18
PSP		PreRx	31	36	32	25	21*	42	46	32	36
% in 15 min.	25% or more	PreRx	31	—	32	22*	42	33	28	39	37
		PreRx	30	23*	35	35	38	38	12*	32	32
		30	34	—	33	25	36	42	1**	41	43
		44	32	—	26	23*	34	42	32	35	38
% in 2 hrs.	65% or more	PreRx	75	70	93	73	90	86	78	82	73
		PreRx	84	78	85	87	95	83	75	76	86
		PreRx	71	89	77	78	93	95	77	97	94
		30	75	66	67	74	89	82	76	92	89
		44	74	72	71	69	88	88	82	87	79
Creatinine clearance	70-150 ml/min/ 1.73 m^2 body surface	PreRx	103	90	101	107	128	91	88	108	97
		PreRx	92	107	93	87	129	60*	67*	96	110
		PreRx	89	61*	101	87	89	98	88	79	66*
		29	96	103	86	107	98	78	85	104	98
		43	98	38*	99	67*	78	71	85	101	42*
BUN	9-22 mg/100 ml	PreRx	17	17	14	13	12	17	15	17	12
		PreRx	14	19	15	10	12	15	14	12	12
		PreRx	15	19	11	13	9	14	12	13	10
		29	15	18	12	10	10	14	15	15	14
		43	17	15	13	14	15	13	16	14	12

*=outside acceptance range.
—=no sample obtained.
**=collection error.

terval were associated with diminished urine volume. The total excretion of dye in two hours was within the acceptance range (65% or more) for all subjects.

A reduction in creatinine clearance occurred in three subjects given mefenamic acid and in three subjects given placebo.

An elevation of BUN was noted for all subjects receiving mefenamic acid but in only two instances was this outside the acceptance range. No substantial changes in BUN were noted for subjects receiving placebo.

No abnormal findings were evident by microscopic urinalyses in the group receiving mefenamic acid. One subject receiving placebo was noted to have 45 WBC/hpf one day following the last medication period.

Discussion

There was no substantial change in kidney function noted in subjects given mefenamic acid, 2000 mg/day, for 28 days. Isolated reductions in PSP excretion fifteen minutes after injection of the dye occurred in both drug- and placebo-treated groups. The total excretion of dye in two hours remained within acceptable limits. Reductions in creatinine clearance were noted in both drug and placebo groups. Elevations in BUN were noted for all subjects receiving mefenamic acid. Elevations in BUN (outside the acceptance range) were not accompanied by corresponding reductions in PSP excretion or creatinine clearance. There did not appear to be any correlation between the magnitude of BUN elevation and changes in either kidney function test.

Conclusions

No significant change in kidney function, as measured by the PSP and creatinine clearance tests, was demonstrated in ten subjects given supra-therapeutic doses of mefenamic acid for a period of 28 days. Some elevations in BUN were obtained in all subjects. In only two instances were the observed values outside the acceptance range.

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