Suid-Afrikaanse Tydskrif vir Geneeskunde : South African Medical Journal

Kaapstad, 2 September 1961 Deel 35 No 35 Volume 35 Cape Town, 2 September 1961

AN OUTBREAK OF UREA POISONING AMONG BANTU FARM LABOURERS IN THE POTGIETERSRUST DISTRICT, TRANSVAAL

DOUW G. STEYN, B.Sc., DR. MED. VET., D.V.Sc.

Professor of Pharmacology, University of Pretoria

On 7 March 1960 Dr. Ernst Kruger, Superintendent of the General Hospital, Potgietersrust, telephoned and requested my assistance in the investigation of an outbreak of suspected poisoning affecting a large number of Bantu farm labourers. Through the kind assistance of Dr. J. D. Verster, Assistant-Director of Transvaal Hospital Services, and Dr. I. J. Louw, Medical Inspector of Hospital Services in the Transvaal, I undertook the investigation immediately.

HISTORY AND SYMPTOMS OF THE DISEASE

Within 3 - 5 hours after the evening meal the first symptoms, suggestive of violent poisoning, set in, and during the ensuing night some 80 patients were taken to the General Hospital at Potgietersrust. The evening meal consisted, as usual, of cooked meat and mealie meal porridge prepared by a cook for all the Bantu workers in the compound where the affected labourers lived.

The first symptoms were nausea and persistent violent vomiting, followed by extreme excitement and severe general convulsions which resembled those seen in cases of strychnine poisoning. Frequent micturition occurred during the convulsions. Some of the patients were almost moribund when they were admitted to hospital. In spite of the extreme gravity of the symptoms, none of the patients died before I arrived at the hospital early the following morning. Most of the patients were calm, had a slow pulse, and some were asleep, probably as a result of the intravenous administration of chlorpromazine hydrochloride by Dr. J. D. Verster. While I visited the ward where the patients were being treated, one of them again developed a type of convulsion which reminded me of similar convulsions I had seen in sheep and rabbits poisoned experimentally with urea.[1] Dr. Kruger at the same time produced a specimen of Kynoch's Urea Fertiliser which had possibly been mistaken for common salt by the affected patients.

All the patients recovered completely in the course of a few days.

CHEMICAL AND BIOLOGICAL TESTS

A. Chemical Tests

The following specimens were collected: (1) Kynoch's Urea Fertiliser from an opened bag and two specimens from unopened bags, (2) prepared mealie meal porridge, (3) water (from the reservoir) used for cooking the porridge, (4) mealie meal from an opened bag and from the remains in a small bucket, (5) 'Kaffir-beer', (6) vomit, (7) urine, and (8) blood.

None of the well-known convulsant poisons, including urea, was detectable in the specimens of porridge, mealie meal, water, 'Kaffir-beer' and vomit. The specimens of blood and urine showed no significant increase in urea.

The results of the chemical analysis of the 3 specimens of Kynoch's Urea Fertiliser agreed with the details supplied on the manufacturer's containers, namely, 98% urea (= 46% N).

B. Biological Tests

The 3 specimens of Kynoch's Urea Fertiliser were compared with urea B.P. The latter had a 'cooler' and more bitter taste than Kynoch's urea and the bitter taste persisted longer in the mouth than that of Kynoch's Urea Fertiliser.

The toxicity of the 3 specimens of Kynoch's Urea Fertiliser was compared with that of urea B.P. The experiments were conducted upon rabbits and the following facts were established:

1. Kynoch's Urea Fertiliser was approximately 3 times more toxic than urea B.P. The approximate $L.D._{50}$ of Kynoch's Urea was 1·5 G./kg., while that of urea B.P. was 5·0 G./kg.
2. Rabbits, starved for 18 hours, were approximately twice as susceptible to Kynoch's urea and urea B.P. poisoning than unstarved animals.
3. Both Kynoch's urea and urea B.P. are more soluble in 'Kaffir-beer' than in water.
4. Large quantities of the 'Kaffir-beer' or tap water appreciably increased the toxicity of both Kynoch's urea and urea B.P.
5. The symptoms and postmortem appearances induced by Kynoch's urea and urea B.P. were very similar.
6. The fatal dose ($L.D._{50}$) of urea lies very close to that of its toxic dose ($T.D._{50}$), and recovery with toxic, but sublethal, doses occurs very quickly, as is seen in cases of hydrocyanic-acid poisoning.

Symptoms of Urea Poisoning

1. *Urea*

In doses of 15 - 60 G. daily, urea is an effective low-threshold diuretic. It is advisable to take it after meals with water in order to prevent nausea.[2]

According to Sollmann,[3] symptoms of urea poisoning (loss of appetite, nausea, and vomiting) in man appear when the urea nitrogen of the blood is about 70 mg. per 100 ml.

After oral administration of 100·0 G. of urea to man, the blood urea increases to 160 - 245 mg. per 100 ml. in a few hours, and the following symptoms are in evidence: Prostration, apathy, and somnolence.[3] These symptoms are also seen in retention uraemia.

According to Glaister[4], in certain cases of uraemia violent delirium may replace convulsions.

Like many poisons, urea causes disruption of enzymes.[5]

2. *Decomposition Products of Urea*

Under ordinary conditions, urea, administered to man as a diuretic, is excreted unchanged in the urine. However, under certain conditions (see below), urea is decomposed into ammonia (NH_3) and carbon dioxide, especially by the action of urease on it.

Dinnings *et al.*[5] found that ataxia sets in when the blood-ammonia-N level rose above 2·0 mg. per 100 ml. and that death occurred when the ammonia-N increased to 5·0 mg. per 100 ml.

In animals (cattle, sheep, and rabbits) toxic doses of urea induce symptoms typical of ammonia poisoning, namely, irritation of the gastro-intestinal mucosa, restlessness, pronounced excitement, convulsions, and delirium. In fatal cases, death occurs through paralysis of the respiratory centre. If sub-lethal doses of urea have been ingested, or in the case of successful treatment, especially with barbiturates, recovery takes place very quickly. It is the above symptoms in the Bantu labourers which reminded me so much of urea poisoning.

According to the dose of urea administered to the animals, the above symptoms appeared half an hour to 5 hours after administration. Within an hour after administration the urine and faeces of the animals smelt very strongly of ammonia.

Factors which Play a Rôle in the Determination of the Toxicity of Urea

One or more of the following factors may play a rôle in inducing symptoms of ammonia poisoning when excessive quantities of urea are ingested:

(*a*) The presence of some catalyst or other in urea mixtures which assists in the rapid elimination of free ammonia. The 3 specimens of Kynoch's Urea Fertiliser were approximately 3 times as toxic as urea B.P.

(*b*) Starvation renders animals much more susceptible to urea poisoning. It appears that the speed of liberation of ammonia from urea is much quickened by starvation.

(*c*) Large quantities of liquid taken with, or shortly after, urea markedly increase its toxicity. As in the case of starved animals, it appears that the liberation of ammonia from urea is speeded up when it is taken with excessive quantities of liquid. In the above biological experiments, urea dissolved in 'Kaffir-beer' did not appear to be more toxic than when it was dissolved in the same concentration in tap-water.

Urea is most toxic when taken on an empty stomach with large quantities of liquid.

(*d*) Fitzgerald and Murphy[6] studied the distribution of urease in the tissues of different species and found that it is widely distributed in all animal species. The concentration of urease is far higher in the stomach than in the duodenum. The amount of urease in the gastric mucosa is variable and can be increased by (1) a high protein diet, (2) a soybean diet, (3) injection of urogastrone, and (4) a high urea intake. It is interesting to note that enterogastrone had no effect on the concentration of urease in the gastric mucosa.

(*e*) Bernheim and Bernheim[7] found that 'caffeine injected into rabbits causes a slight diuresis, no change of the pH of the urine, an increase in the NH_3-N excretion, and some decrease in the urea-N excretion'. The longer urea is retained in the gastro-intestinal tract, the greater the likelihood of its being split into ammonia and carbon dioxide.

(*f*) Experimenting on male West Africans and comparing them with European men, Kenney[8] found that, when urea is administered to these males, the West Africans excrete less of it than the European men. This may possibly result in more urea being broken up into ammonia and carbon dioxide in the African than in the European.

TREATMENT

Treatment is symptomatic. It appears that tranquillizers (e.g. chlorpromazine) serve a very useful purpose in quietening the delirium and convulsions. The intravenous administration of suitable barbiturates would also have a beneficial effect. In moribund patients, where the violent delirium and convulsions are followed by coma and beneficial effect. In moribund patients, where the violent should be wisely used. The less active analeptics ('megimide', methedrine, amiphenazole) should be tried first since the more active ones (picrotoxin), in large doses, are more inclined to cause dangerous secondary depression of the vital centres in the cortex.

DISCUSSION

There seems little doubt that the serious outbreak of disease among the Bantu farm labourers was caused by the fact that they had mistaken a bag of Kynoch's Urea Fertiliser for common salt. Unfortunately, the common salt was stored in the same room as the urea fertiliser. According to Sollmann,[2] 100·0 G. of urea induce symptoms of poisoning in man. It would therefore seem very unlikely that an adult could consume this quantity of urea (mistaken for common salt) in the course of one meal. However, the following factors played a very important rôle in the outbreak of urea poisoning under consideration: (*a*) The Bantu labourers had not had common salt for quite a period and were thus inclined to consume larger amounts with their food than they would ordinarily have done; (*b*) the labourers did manual work in a hot and dry climate, consequently, their salt intake would be appreciably higher than in people not exposed to such hard physical exercise; (*c*) it is customary among many Bantu peoples not to eat on Sundays until the late afternoon or evening, as happened in the above case; consequently they consumed a large quantity of porridge which, in turn, resulted in the consumption of large quantities of salt, and the starvation made them more susceptible to urea poisoning; (*d*) further, it is a general custom among these people not to mix common salt into their food, but to place it in the hollow of their one hand, or in the lid of a tin, and dip every bit of meat or porridge in the salt. In this way, I have seen them ingesting an ounce, or more, of common salt in the course of one meal; (*e*) during week-ends, and especially on Sundays, Bantu people consume large quantities of 'Kaffir-beer', and there was ample evidence that the labourers concerned in this case had consumed large quantities of beer with the evening meal which preceded the outbreak of the disease.

SUMMARY

An outbreak of urea poisoning in Bantu farm labourers as a result of mistaking Kynoch's Urea Fertiliser for common salt is described.

I wish to thank Dr. Ernst Kruger, Superintendent of the Potgietersrust Hospital, and Dr. J. D. Verster, for details concerning the history, symptoms, and treatment of the disease; Dr. L. S. de Villiers, Senior Lecturer, Department of Pathological Anatomy, University of Pretoria, and members of his staff for the chemical analysis of the food, blood, and urine specimens collected; Dr. Tom Adelaar and Mr. J. A. Minnie of the Section of Toxicology, Onderstepoort Laboratories; and Dr. F. W. K. Grotepas, Senior Lecturer, Department of Physiology, University of Pretoria, for the chemical analysis of the specimens of Kynoch's Urea Fertiliser.

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