پیشرفت‌های اخیر در درمان مسمومیت با جهش کش‌های فسفردار آبی

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چکیده:

سموم فسفردار آبی به میزان و بسیار در دفع آفات نباتی و هم به عنوان عوامل اعصاب در جنگلهای شیمیایی مورد استعمال قرار گرفته‌اند. حشره‌کش‌های فسفردار بطور فراوان وارد کشور شده و متأسسانه اغلب بدون کنترل در دسترس افراد قرار می‌گیرند. به‌همین دلیل مسمومیت حاد با این سموم بوجود می‌آید تا بیماری شایع زوده به نحوی که ۲۵۰ نفر

(۲/۱۸) از مسمومین بستری بیمارستان امام رضا (ع) مشهد را در سال ۱۳۷۲ شالی مرگ‌یده‌است.

سموم فسفردار آبی با مهار آنزیم کولین استراز موجب وقوع هیپولیزاسیون کولین و در نتیجه احیای این ماده در پاتوژن‌های عصبی می‌گردد که این خود باعث تحریک گیرنده‌های موسکارینی و نیکوتینی می‌شود. آثار تحریک گیرنده‌های موسکارینی با سولفانت آتروپین و تحریک گیرنده‌های نیکوتینی با اکسیما مانند پرالیدوکسیم و اپیدوکسیم درمان می‌شود. با وجود تجزیه و نوع پادزهر یادشده مرم و میر ناشی از سموم فسفردار آبی نسبتاً زیاد (حدود ۱۰/).

گزارش شده‌است در مورد اثر درمانی سولفانت آتروپین در سموم فسفردار آبی قدرت انتقال نظر وجود داشته‌است اما در خصوص میزان و نحوه تجویز این پادزهر از اولین دهه هشتادمیلادی با توجه به تجربیات درمان مسمومین مشهور و تأیید آن از سوی جامعه علمی به‌صورت اینست مقدار زیاد آتروپین تا حد مسمومیت خفیف از میزان مرم و میر سموم فسفردار آبی کاسته‌شده‌است.

اکسیمها با عنوان فعال کننده آنزیم کولین استراز کنترل آثار نیکوتینی مسمومیت با حشره‌کش‌های فسفردار آلی مورد استفاده واقع شده‌اند. تحریکات پلیپنی در درمان مسمومیت با حشره‌کش‌های فسفردار آلی مسمومیت مشهود و گزارش محققین از سرتاها می‌باشد (پیمانه تئوری شماره ۳۲۹ سال ۱۳۹۲) مؤید عدم تاثیر اکسیمها در سیر بهبودی این مسمومیت می‌باشد. پیده‌های پلیپنی ۳۲۱ پیمان مسمومی با حشره‌کش‌های فسفردار آلی که از سالهای ۱۳۷۱-۱۳۷۲ در بخش مسمومیت بستری شده‌اند بهترین مطالعه قرار گرفت. در بیمارانی که اکسیم درد نداشته و بخش میانگین ۳۲۵/<P<۳۲۵/۷۱۸ مشاهده گردید و با تأیید نشانه‌های شایع و عدم تاثیر درمان اکسیم‌ها در درمان مسمومیت حشره‌کش‌های فسفردار آلی مشاهده شده‌است. (مجله دانشگاه علوم پزشکی ایران سال ۱۳۷۵ شماره ۱ و ۳)
RECENT ADVANCES IN TREATMENT OF
OP PESTICIDE POISONING

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ABSTRACT

Organophosphate (OP) compounds have largely been used as pesticides and also as nerve agents in Chemical Wars. OP pesticides have frequently been imported and freely available to the public without usage control. Therefore, OP poisoning, mainly intentional type, is very common; and accounts for 21.8% (250 patients) of the total admission to the hospital between 21 March 1994 and 20 March 1995.

OP compounds induce accumulation of acetyl choline by inhibition of acetyl cholinesterase leading to the stimulation of muscarinic and nicotinic receptors. Muscarinic effects are counteracted successfully by atropine sulfate, but the therapeutic effects of oximes on nicotinic receptors and cholinesterase reactivation have not been observed in clinical practice. Clinical observations of the author and a report from Sri Lanka (Lancet 339, 1992), indicates no therapeutic effects of oximes in OP poisoning. Case notes of 317 Treatment Centres between 21 March 1993 and 20 March 1995 were studied.

There were significant positive correlations between the oxime doses and either hospitalization days (r=0.625, p<0.001) or mortality rate (r=0.718, p<0.01).

It seems that oximes had no therapeutic effects on OP pesticide poisoning. However, a prospective investigation is currently undertaken to confirm this hypothesis.

Key Words: 1) Pesticide Poisoning 3) Acetylcholinesterase
2) Organophosphate (OP) compound 4) Oxime
INTRODUCTION

Organophosphates (OP) have been used mainly as pesticides and also as nerve agents in chemical wars. OP pesticides have been imported, distributed and used in this country without proper control. Therefore, poisoning particularly suicidal attempts with these chemicals are very common and accounted for 250 (21/8%) admissions to the Poisons Treatment Centre and 25 (38%) deaths in the year of 1994.

Op inhibits cholinesterase enzyme and thus acetylcholine accumulates at nerve ending and stimulates muscarinic and nicotinic receptors. Muscarinic stimulation is reduced by atropine sulphate. Oximes have been used for relief of nicotinic stimulation and cholinesterase reactivation\(^{(2)}\), but the mortality rate is still around 10%\(^{(3)}\). The effects of atropine sulphate have long been established, although the dosing regimens were different. Based on clinical experience, the proposed high doses of atropine by Mashhad Poisons Treatment Centre are now universally approved. The following mechanisms for oximes have been reported\(^{(4)}\):

1) Dissociation of phosphorylated binding of the enzyme and OP.
2) Direct attack of oxime at free molecule of OP.
3) Antimuscarinic effects

Based on clinical experience at Mashhad Poisons Treatment Centre and a report from Sri Lanka\(^{(5)}\), oximes revealed no significant therapeutic effects on OP poisoning. Over the past few years, there has been shortage of oximes and thus most of the OP cases were treated by atropine alone. It was aimed to compare the cases treated by atropine with those who have received oxime as well. Therefore, the case notes of the OP patients who were treated at the centre between 21 March 1992 and 21 March 1995 were investigated.

PATIENTS & METODS

Case notes of all patients with OP pesticide poisoning who were hospitalised for more than three days were reviewed. Relevant parameters such as age, sex, clinical features, serum cholinesterase activity (estimated spectrophotometrically using Behring kit), atropine and oxime doses, hospitalisation days and outcome of treatment were recorded. The data were processed by FoxPro program and analysed by Statistical Package for Social Sciences (SPSS). Comparisons were made by Student-t. Pearson and Chi-Square tests.

RESULTS

A total of 317 case notes of OP poisoning including 114 males (36%) and 203 females (64%) with a mean±SD age of 25±14(1-80) years were reviewed. Apart from accidental cases in seven children (2.2%), the remainder were self-poisoning. the most
frequent age group was 16-20 years (107 cases) as shown in figure 1. Seasonal
distribution revealed 32% in spring, 22% in summer, 25% in autumn and 21% in winter
with no significant differences between them. Based on oxime therapy, 185(58%)
patients were treated by atropine and oximes and 132 (24%) were treated by
atropine alone. There were no age and sex differences between the two groups. Main
clinical conditions on admission were pulmonary edema, coma and convulsions
that were observed in 28, 28, and 16 patients of the oxime group compared with
16,15 and 13 patients of the atropine alone group, respectively. There were no
statistically significant differences between them.

Oximes were given as obidoxime (158 patients), pralidoxime (24 patients) and
mixture of both (three patients) with a dose of 0.25 to 38g (3.5±4.2g) based on severity
of poisoning (Fiurre 2). Atropine was given based on the severity of intoxication in the
doses ranging from 16 to 4650 (314±567)
mg in the oxime group compared with 13 to
1685(205±214) mg in the group receiving
atropine alone. The atropine dose difference
between the two groups was significant
(P<0.05).

Serum cholinesterase (SChE) activities of
the patients were all lower than normal on
admission and were less than 200U/L in
46% of the patients (Normal value>2000U/L). There was a good
relationship between the clinical severity and

reduction of SChE. Reactivations of the
enzyme during treatment were different in
each group as shown in figures 3 and 4.
SChE reactivation was even quicker in the
group receiving atropine alone compared to
the oxime group, although the difference
was not statistically significant (figure.5)

Hospitalization days in the oxime group
were 4 to 19 (6.7±2.9) days. There was a
significant positive correlation between the
hospitalisation days and oxime doses
(r=0.5149, P<0.001) as shown in figure 6.

Mortality rate in the group of atropine
alone was 6(4.5%), whereas in the oxime
group was 15 (98.1%) patients. The
mortality rate in the obidoxime subgroup
was 12(7.6%) and in the pralidoxime
subgroup was 3(13%) as shown in figure 7.
However, there were no statistically
significant differences between the groups.
There was a small number of patients in the
pralidoxime subgroup, thus, statistical
analysis between the subgroups was not
carried out.

DISCUSSION & CONCLUSION

Since the clinical finding on admission of
the oxime group was not significantly
different from the group of atropine alone,
thus the two groups were comparable
clinically. However, atropine doses used in
the oxime group were significantly higher
than the group of atropine alone. It seems
that first of all the oxime group patients were
more severely intoxicated than the group of
atropine alone, secondly the use of oximes
did not reduce the atropine doses as previously reported\(^4\). Similar hospitalisation days of the two groups suggest similar severity of intoxication. The significant positive correlation between the hospitalisation days and oximes particularly the obidoxime group may also have two different explanations: First, those patients who had received more obidoxime were more intoxicated. Second, the adverse effects of obidoxime have more morbidity and thus more hospitalisation days.

SChE reactivations were similar in both groups. It appears that oximes did not increase the reactivations previously reported\(^6,7,8\).

The dose and duration of oxime therapy in Sri Lanka\(^5\) Study were evaluated in sufficient by the European colleagues\(^9\). In the present study, we did not find any significant difference between the low and high doses of oximes.

Mortality rate was slightly higher in the oxime group than in the atropine alone. It can be concluded that oximes particularly obidoxime had no therapeutic effects on acute OP poisoning. However, a prospective double blind clinical trial is currently undertaken to investigate more carefully about the therapeutic effects of oxime in OP poisoning.

REFERENCES


