EDITORIAL

HYPERSENSITIVITY TO INTRAVENOUS ANAESTHETIC AGENTS

Until recently there were few reported cases of hypersensitivity to intravenous anaesthetic agents which could be attributed to histamine release. In the 1961 issue of *Appraisal of Current Concepts in Anesthesiology*, Adriani concluded that much of the literature concerning allergic reactions to drugs does not refer specifically to anaesthetic agents, following the use of which such reactions are uncommon. A list of drugs which release histamine, taken from the papers of Paton (1957), Schachter (1952), and Stovner and Endresen (1971), includes such widely used agents as atropine, morphine, amphetamine and suxamethonium, together with pethidine and tubocurarine which has well-known histamine-releasing properties. Although sporadic reports of reactions to thiopentone had appeared for some time it was not until 1971 that Clark and Cockburn highlighted the problem. Their publication was timely as reports of hypersensitivity to propanidid had appeared already in the literature and this might have been regarded as a new syndrome. Unfortunately, today, we are only too aware of this problem, with the numerous reports on sensitivity to Althesin which have appeared in many journals. The latest report from New Zealand, by Fisher (1975), describes two cases of hypersensitivity to Althesin and contains a useful review of histamine-mediated reactions.

Is this an increasing phenomenon? Are our new intravenous anaesthetic agents more likely to cause hypersensitivity reactions than the older established drugs? What is the role of neuromuscular blocking drugs and other adjuvant drugs in these reactions? Are they all histamine-mediated? These are but a few of the questions which must be answered over the next few years. Perhaps we have some of the answers already.

Reviewing what seemed to be authentic reports of anaphylactoid reactions to thiopentone, early in 1974, Dundee and Wyant (1974) found 13 published cases only. Fisher adds another six cases (including one excluded deliberately by Dundee and Wyant, as being ambiguous), while Clarke and others (1975) included a further 11. About 30 reported cases have occurred in response to a drug which has been in use for 40 years. This is not a bad record. However, the time sequence of these events is interesting. Four cases were reported before 1961, three between 1961 and 1965, four between 1966 and 1970 and at least 19 in the past 4 years. To these may be added reports of sensitivity to methohexitone; all this leads one to think that the frequency is increasing.

The position with Althesin is quite different. Although this drug has been available for less than 5 years, there are more than 100 authentic reports of sensitivity to it. This is a true drug phenomenon, estimated to occur once in 11 000–19 000 administrations.

The largest reported series of hypersensitivity was obtained by voluntary reporting. This survey involved 86 cases of definite sensitivity to intravenous induction agents; Althesin was responsible for 70 of these while thiopentone was incriminated in 12. It is worth noting that all the four deaths in this series occurred with thiopentone; although there were some frightening experiences with Althesin, resuscitation was always possible.

With propanidid, it is difficult to differentiate the known dose-related cardiovascular depression from true idiosyncrasy. Clarke (1974) analysed 23 case reports to which Fisher (1975) has added a further seven. Thus, at least 30 authentic sensitivity reactions occurred during the 10 or so years since propanidid was first used.

There has been a persisting impression that hypersensitivity reactions occur more frequently in patients who have had previous exposure to the same intravenous anaesthetic. This had occurred in 13 of the 19 thiopentone cases surveyed by Dundee and Wyant (1974) and Fisher (1975). If one adds known sensitivity to other drugs, the total becomes 17 (90%), which is more than a coincidence.
A further analysis of the 86 patients showing a definite anaphylactoid response to intravenous anaesthetic agents (Clarke et al., 1975) shows that 90% of the thiopentone cases and 83% of the Althesin cases either had received the same anaesthetic on a previous occasion, or had a known sensitivity to other drugs or a history of asthma, hay fever or eczema. These are rather frightening figures and they highlight what may be an increasing problem for the anaesthetist.

If one adds the incidence of sensitivity to other drugs injected by the anaesthetist, then the situation becomes even more serious. Recent case reports have incriminated particularly suxamethonium, pancuronium and other commonly used agents. We must be aware of the fact that drug sensitivity is not limited to the intravenous anaesthetic agents, but may occur in response to any of the parenterally administered drugs. As with any other clinical problem, knowledge can be obtained only by publishing case reports, reporting them to the Committee for Safety of Medicines, and possibly involving workers with a special interest in this field, such as Watkins, Thornton and Clarke (1975).

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REFERENCES


