STUDIES BY THE INDIAN COUNCIL OF MEDICAL RESEARCH

The Indian Council of Medical Research (ICMR) and affiliated institutes have conducted a number of clinical trials and extensive research on injectable contraceptives in India. A considerable amount of data has been generated.

During the 1970s and 1980s, ICMR carried out multiple exploratory and pharmacodynamics studies of depot-medroxyprogesterone acetate (DMPA) and norethisterone enanthate (NET-EN) alone and in combination with estrogens, in varying dosage schedules. One study addressed the menstrual irregularities women experienced with progesterone-only injectable contraceptives. A randomized clinical trial was carried out with 50-mg NET-EN alone and in various combinations with other hormones. Based on that trial’s results, a multicentric Phase III study compared menstrual patterns and acceptability of monthly injections of a combination of 50-mg NET-EN and 5-mg estradiol valerate (marketed as Mesigyna) with injections every two months of 200-mg NET-EN.\(^1\) The results of the study indicated that Mesigyna is effective and associated with better bleeding patterns. ICMR also initiated a pre-programme introductory study of 200-mg NET-EN at 42 postpartum centers to look at the logistics of adding injectables to existing programmes. A high rate of discontinuation was observed owing to menstrual irregularities.

In 2010 ICMR published the results of a Phase III clinical trial at 16 teaching hospitals of medroxyprogesterone acetate (MPA)/estradiol cypionate, a monthly injectable (marketed as Cyclofem) that combines progestin and estrogen.\(^2\) A total of 1,275 women were enrolled and the continuation rate at one year was 63.2 percent. Although 59 percent of women had acceptable bleeding patterns at 12 months of use, approximately 9 percent discontinued the injectables after a year of use because of menstrual bleeding disruptions. No life-threatening side effects were reported during the study period.

In March 2008, ICMR completed a feasibility study of 200-mg NET-EN. Of 2,352 participants, 1,209 (51.4 percent) accepted injectable contraceptives. The rest sought other available spacing methods. The most common reasons women gave for refusing NET-EN were frequent visits to the clinic for reinjections (27.8 percent), anticipated side effects such as irregular menstrual periods and weight gain (17.4 percent), and objection by family members (11.5 percent). At the end of a year the continuation rate was 65 percent, at the end of 18 months 53.6 percent, and at the end of two years 48.3 percent. The major causes of discontinuation were personal reasons (18.7 percent) and loss to follow-up, because of migration (16.7 percent). Discontinuation because of menstrual disruptions was observed in 15.3 percent of the participants at the end of the two-year study period.\(^3\)

OTHER STUDIES IN INDIA

Aside from ICMR research, a host of studies of injectables has been initiated by international and national organizations in India. Some examples follow.

An early study, conducted in the 1970s by a task force of the World Health Organization, looked at the use and effectiveness of injectables in 10 countries, including India. The study compared NET-EN and DMPA and reported more pregnancies among NET-EN users and more discontinuation because of amenorrhoea (absence of menstruation) among DMPA users.\(^4\)

More recently, in 1996, Parivar Seva Sanstha (PSS) conducted an operations research study in three urban clinics in selected cities in Uttar Pradesh that looked at price and uptake. The results demonstrated that the uptake of DMPA was the highest at Varanasi, where prices
were lowest. Conversely, the uptake of DMPA was the lowest in Lucknow, where prices were highest. Estimates suggest that the product is considered affordable at INR 35 (U.S. $0.70) per injection.5

In 1999, Pharmacia & Upjohn published the results of a post-marketing surveillance study in India that assessed DMPA’s safety and acceptability.6 The majority of the 1,079 participants—84.2 percent—continued with the method through five doses. This research showed that 150-mg DMPA is a safe and effective contraceptive, and that appropriate counseling about side effects will greatly increase the method’s acceptability. Opposition groups had several concerns about the study, including its duration, objectivity, and transparency.7

DKT India and EngenderHealth, in partnership with the Population Council’s Frontiers in Reproductive Health programme, conducted operations research on injectables in Gujarat between July 1999 and August 2001. This study found that service-delivery systems of nongovernmental organizations and the private sector meet the requirements of providing injectable contraceptives, including the capacity to ensure that clients have a choice of methods in addition to injectables and to deliver services of high quality.8

Additionally, in 2002-2003, the United Nations Population Fund and the government of India conducted a multiple-partner study to assess users’ and providers’ perspectives on DMPA. That study’s findings reinforced the importance of contraceptive counseling in helping users to make an informed decision to select and continue with the method. It highlighted the need to build providers’ capacity to use protocols to select clients, offer counseling, and manage side effects to help individual clients and couples achieve their reproductive goals. Finally, the study underscored the need for programmes to address the price of injectables, because both users and providers expressed concern about the method’s expensiveness.9

References