GLOBAL MOLYBDENUM-99 SHORTAGE: BASIC FACTS AND POSSIBLE ALTERNATIVES.

Nuclear medicine is the functional imagining modality which employs use of tracer quantity of short lived isotopes (half lives from few minutes to hours) to have enormous information at cellular or molecular levels. About seventy thousands nuclear medicine procedures are performed daily globally and interestingly 50% are done in USA. Technetium-99m (^{99m}Tc) is used in more than 90% of nuclear medicine studies due to its favorable physical characteristics like 6 hr half life, photopeak of 140 KeV and round the clock availability. It is the daughter product of Molybdenum-99 (^{99}Mo) having a half of 66 hr and is supplied in the form of generator (Mo-Tc Generator) on a weekly basis.

In 2008-2010 nuclear medicine has gone through a global crisis due to acute shortage of ^{99}Mo and this has forced the academia and industry to find out possible options in case of recurrence of supply and demand deficit. This brief review will focus on current method of ^{99}Mo production, mechanics of Mo-Tc generator, reasons of global ^{99}Mo shortage and possible alternatives of its production.

Production of ^{99}Mo (Fission Moly): Currently Mo-99 is produced in research reactors by placing a target of high enriched uranium-235 (HEU, containing >90% U^{235}) for interaction with neutrons for 1 week (fission reaction). The resultant fission products are ^{99}Mo (Fission Moly) and other heavy nuclides which are processed and separated from Mo-99 in 48 hours. Currently there are five research reactors (NRU Canada, HFR Netherland, BR2 Belgium, Osiris France and Safari South Africa) which fulfill >95% world demand. However, there are only 4 sites where ^{99}Mo is separated from target and then it is distributed to nine sites where generators (Mo-Tc Generator) are prepared.

The advantage of using HEU in research reactors are high production yield and significantly high specific activity of Mo-99 but the waste is highly radioactive and needs to be disposed off safely due to safety and strategic importance.

^{99}Mo-^{99m}Tc Generators: These generators contains high activity of ^{99}Mo (about 5-25 Giga Becquerel, GBq) adsorbed on alumina column encased in a proper lead shielding which is required to stop 660 and 760 Kev gamma rays of Mo-99. Mo-99 decays by beta emission to ^{99m}Tc (87%) and Tc (13%). Generator is eluted daily (Milking) using normal saline and resultant eluate contains 99mTc as sodium pertechnetate. Maximal yield of generator is about 85% after about 4 half lives of ^{99m}Tc (22-24 hr), and after every elution ^{99m}Tc builds up at a rate of about 10% every hour and elution at 6-8 hour from last elution could give an approximate 80% of usual yield next morning. However, re-elution gives low specific activity in resultant eluate and possibility of failing the ^{99}Mo breakthrough test because of considerably low ^{99m}Tc.

Recent ^{99}Mo Shortage: Since 2008 till mid 2010, nuclear medicine has faced a historical crisis due to ^{99}Mo shortage resulting from simultaneous shut downs of NRU Canada and HFR Netherland reactors for repair which meet about 70% of global demand. Currently the global demand of ^{99}Mo is about 12000 $Ci_{6\text{-day}}$ (6000 Ci6-day for USA) with an estimated rise of about 10% annually. Although these reactors have started functioning since September 2010 but Atomic Canada Limited (AECL) has announced an extended outage of NRU in spring 2011. Furthermore, most of these reactors are old enough and approaching their lives of 50 years. These facts have raised various questions regarding clinical, cost and political aspects of ^{99}Mo shortage. The major stake holders like USA, Canada and Netherland have explored the various options to produce ^{99}Mo.

Alternative Ways for ^{99}Mo Production: First option is the replacement of HEU^{235} target by ^{98}Mo in research reactors but it is limited by significantly low production rate and specific activity too. GE-Hitachi has recently announced to use this method in commercial power reactors to produce large quantities of low specific activity of ^{99}Mo. Second alternative is to use ^{100}Mo as target in accelerator and bombarded with protons (p + ^{100}Mo ------> ^{99m}Tc + 2n). This method provides ^{99m}Tc directly and due to half life of 6 hour, this option is good to meet the regional demand on daily basis and about 500 high power accelerators would be required to meet the global demand. Another option although in its infancy is using liquid uranium target (uranyl nitrate in water) in reactor instead of solid ^{235}U as target. The benefits of this method are low cost and relatively simple method of separation. This needs approval from IAEA for its technicalities. Last option is use of low enriched uranium (LEU, <20% ^{235}U) as target instead of HEU in research reactors. USA is very much in favor of this option as it wants to minimize the use of HEU for ^{99}Mo production due to its strategic importance. However, this option has again limitations of low production rate and low specific activity.

In view of these facts resulting in current ^{99}Mo crisis and limitation of alternative options, we feel that best way to maintain global demand of ^{99}Mo is to replace existing research reactors with new ones till a better and robust option is found.

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